INAHTA Briefs

INAHTA

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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

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Introduction

The International Network of Agencies for Health Technology Assessment (INAHTA) is a global network linking 40 non-profit, governmental institutions from 20 countries (2003).

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

INAHTA Briefs

Issue 2002/40

Title Transmyocardial Laser Revascularisation (TMR), October 1999

Agency MSAC, Medicare Services Advisory Committee
Commonwealth Department of Health and Ageing,
GPO Box 9848 Canberra ACT 2601 Australia;
tel: +61 2 6289 6811, fax: +61 2 6289 8799, http://www.msac.gov.au

Reference MSAC application 1004. Assessment report ISSN 1443-7120

Aim

To assess the safety and effectiveness of the procedure and under what circumstances public funding should be supported for the procedure.

Conclusions and results

Safety: TMR carries risks: 3% to 5% perioperative mortality and adverse events common to thoractomy.

Effectiveness: Studies do not demonstrate that TMR is clinically effective in avoiding myocardial infarction, increasing exercise tolerance, and prolonging survival. The evidence shows that it significantly reduces the severity of angina (studies show a reduction of 39% in patients with disabling angina) and the incidence of unstable angina (studies show a reduction of 69% in patients with unstable angina). However, it is not certain whether these benefits will be sustained beyond 12 months.

Cost effectiveness: TMR is estimated to cost $18 000 to $21 000 per patient freed from unstable or disabling angina. Savings of $4300 per year are estimated to result from reduced cost of angina treatment if symptom relief is sustained.

Recommendations

Public funding should not be supported due to insufficient evidence that clinical benefits outweigh potential risks.

Methods

MSAC conducted a systematic review of medical literature on TMR from 1986 to 1998 through the MEDLINE, Cochrane Library, and DARE databases. Cost effectiveness was measured as the increment of TMR over medical management costs divided by the proportion of patients freed from the angina condition.

Further research

Overseas and Australian studies currently in progress may provide valuable data on the long-term effectiveness of TMR. It would be useful to compare holmium with CO2 laser treatments.

INAHTA Briefs

Issue 2002/61

Title Intraoperative Transoesophageal Echocardiography – May 2002

Agency MSAC, Medical Services Advisory Committee
Commonwealth Department of Health and Ageing
GPO Box 9848 Canberra ACT 2601 Australia;
tel: +61 2 6289 6811, fax: +61 2 6289 8799, http://www.msac.gov.au

Reference MSAC Reference 08. Assessment Report ISBN 0 642 82100 0

Aim

To assess the safety, effectiveness, and cost effectiveness of intraoperative TOE for the monitoring of cardiac function during closed heart surgery, open heart surgery, and other surgery, and under what circumstances public funding should be supported for the procedure.

Conclusions and results

Safety: The semi-invasive procedure has a small but definite risk. There are reports of probe-related complications, such as thermal or pressure injuries, compression of the aorta or trachea, and procedure-related adverse events involving injury to the cardiovascular, pulmonary, and gastrointestinal systems, but the incidence of such events are uncertain. The incidence of gastro-esophageal injury in unanesthetized patients is estimated at 1 in 20 000. The incidence is uncertain in anesthetized patients, but is thought to be higher.

Effectiveness: The diagnostic accuracy of TOE in the outpatient setting was not reviewed in this evaluation. Intraoperative TOE may be useful for detecting endocarditis, abscesses associated with endocarditis, coronary artery stenosis, and left atrial thrombi, and changes in cardiac function. The effectiveness of TOE as a monitoring intervention during surgery on clinical management and patient outcomes was also assessed. Evidence identified from less than ideal study designs suggested that the use of intraoperative TOE may result in changes to the preoperative surgical plans of patients during cardiac surgery. There was no evidence to date ideally designed to assess whether the use of intraoperative TOE benefits the patient in terms of reduced mortality or morbidity.

Cost effectiveness: Studies from the USA indicate that the use of intraoperative TOE during cardiac valve surgery is cost effective due to revisions in surgical management which prevent the need for reoperation later. However, the data were insufficient to assess whether the use of intraoperative TOE is cost effective in the Australian setting.

Recommendations

There is limited evidence of the safety, effectiveness, and cost effectiveness of intraoperative transoesophageal echocardiography. MSAC recommends that public funding for this procedure should be supported on an interim basis and restricted to intraoperative assessment of cardiac valve competence following valve replacement or repair. The provision of funding should be reconsidered no later than June 2005 to ascertain whether further additional evidence has become available which supports continued funding.

Methods

MSAC conducted a systematic review of the biomedical literature (Cochrane Library, EBM-Reviews-ACP Journal Club, MEDLINE, PreMedline, Current Contents, Biological Abstracts, and PsychINFO) from commencement to November 2001. These sources were searched to identify studies examining the accuracy of intraoperative TOE in detecting changes in cardiac function and the effect of intraoperative TOE on patient management and patient outcomes.

Prepared by Renea Johnston, Monash Institute of Health Services Research, Australia

INAHTA Briefs

Issue 2002/67

Title **Prevention, Diagnosis, and Treatment of Venous Thromboembolism – A Systematic Review**

Agency **SBU, The Swedish Council on Technology Assessment in Health Care**
PO Box 5650, Tyrgatan 7, SE-114 86 Stockholm, Sweden;
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Reference SBU Report 158, 2002. ISBN 91-87890-76-3, Available at http://www.sbu.se

Aim

This report systematically reviews the literature on prevention, diagnosis, and treatment of venous thromboembolism (VTE), focusing mainly on patient benefits and risks, but also on the costs to the healthcare system and society.

Conclusions and results

The scientific evidence strongly suggests that low molecular weight heparin can replace unfractionated heparin in preventing and treating venous thrombosis and pulmonary embolism. The treatment effects of a single injection per day of low molecular weight heparin are equally favorable as the effects achieved from two injections per day. The risk for hemorrhage is lower with low molecular weight heparin, and management is simpler, which facilitates outpatient treatment. Longer-term secondary prophylaxis with warfarin reduces the risk for relapse, but treatment lasting several years also increases the risk for severe hemorrhage.

In outpatients, the presence of treatment-demanding VTE can be ruled out by using a combination of D-dimer measurement and clinical probability assessment (based on clinical decision rules). Thorough ultrasonic examination of the leg and a CT scan of the pulmonary vessels usually achieve sufficient diagnostic reliability, strongly supporting the use of these methods in clinical practice.

It is not meaningful to conduct extensive investigations of patients with venous thrombosis to detect possible underlying cancer. It is essential to develop more cost-effective methods to investigate genetic predisposition for thrombosis.

Methods

A literature search was conducted using MEDLINE and the Cochrane Library (up to July 2001), reference lists, and personal communications. Only randomized controlled studies were included. To assess diagnostic methods, we included only studies that used an independent comparison with a known reference method. Approximately 1300 scientific studies met the requirements for high scientific quality. Current clinical practice was surveyed, and national data on in-hospital care and costs were also analyzed.

Written by Dr Mats Eliasson, SBU, Sweden

INAHTA Briefs

Issue 2002/70

Title Implantable Defibrillator (ICD)

Agency SMM, The Norwegian Centre for Health Technology Assessment
SINTEF Unimed, P.O. Box 124 Blindern, 0314 Oslo, Norway;
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Reference SMM Report No. 1/2002. ISBN 82-14-02624-5

Aim

To evaluate the clinical effect and health economics of treatment using an implantable defibrillator (ICD) compared to drug treatment. Clinical effect includes effect on survival, complications, and quality of life.

Conclusions and results

ICD as secondary prophylaxis:

Three randomized studies show that ICD has a significant, beneficial effect on survival of patients who have survived cardiac arrest, ventricular tachycardia or syncope, ventricular tachycardia with seriously affected circulation and concomitant reduced heart function. Annual mortality was reduced from 12.3% to 8.8%. Implantation of ICD in 29 patients would prevent one death per year of followup.

Observational studies indicate benefit among patients with syncope with concurrent structural heart disease and inducible ventricular tachycardia, with tachycardia seriously affecting the circulation without syncope or cardiac arrest and with good heart function. There is limited knowledge of the effect of such treatment on patients with ventricular tachycardia and few symptoms, but there is probably a beneficial effect on those with reduced heart function.

ICD as primary prophylaxis:

Two randomized studies show a significant, beneficial effect on patients with coronary heart disease, reduced cardiac function, non-sustained ventricular tachycardia, and inducible ventricular tachycardia. In these studies, ICD had to be implanted in 10 and 20 patients, respectively, to prevent one death per year of followup. One randomized study showed no effect on total survival among patients with coronary heart disease and planned coronary surgery, ejection fraction less than 36%, and positive late potential ECG.

Cost effectiveness

Treatment with ICD is expensive. The units cost about NOK 250 000, and total annual expenses of ICD treatment in Norway can be estimated at approximately NOK 30 million. In high-risk patients the cost effectiveness of this treatment is acceptable. If ICD is used in low-risk patients the cost effectiveness becomes less favorable.

Methods

The report is based upon a systematic review from New Zealand published in 1997. In addition, a literature search was performed in MEDLINE and EMBASE to identify more recent studies. In total, 521 journal articles were retrieved and read by at least two of the investigators. The studies were rated according to study design.

Written by Dr Kurt I Myhre, SMM, Norway

INAHTA Briefs

Issue 2002/89

Title Radiofrequency Catheter Ablation for Cardiac Arrhythmias: A Clinical and Economic Review

Agency CCOHTA, Canadian Coordinating Office for Health Technology Assessment
865 Carling Avenue, Suite 600, Ottawa, ON, K1S 5S8 Canada;
tel: +1 613 226 2553, fax: +1 613 226 5392, http://www.ccohta.ca

Reference CCOHTA Technology Report, Number 25, March 2002. ISBN 1-894620-39-9 (print); ISBN 1-894620-40-2 (online): http://www.ccohta.ca/ccohta_production/entry_e.html

Aim

- To evaluate the evidence for the clinical efficacy of catheter ablation delivered by radiofrequency energy (RFA)
- To evaluate the cost effectiveness of RFA.

Conclusions and results

Clinical Review: The 111 primary research studies that met the inclusion criteria included only 10 randomized controlled trials. Reviewers found that catheter ablation for most cardiac arrhythmias is associated with good procedural success rates. Due to insufficient evidence, however, conclusions cannot be drawn regarding its long-term clinical efficacy. RFA is considered primarily as an adjunct procedure to pacemaker implantation for atrial fibrillation and to antiarrhythmic drugs and implantable cardioverter defibrillator therapy for ventricular fibrillation. Few high-quality outcome studies compare ablation with alternative therapies.

Economic Review: Twenty-one studies were considered, including three cost effectiveness studies from the United States whose findings are likely generalizable to the Canadian context. Although several studies evaluated the costs and quality of life associated with ablation techniques independently, the data are insufficient to determine whether such interventions are cost effective, relative to other treatment options.

Conclusion: More conclusive evidence of the benefits of ablation, especially in patients with atrial fibrillation and atrial flutter, could lead to a significant increase in utilization as this technology continues to evolve.

Methods

Clinical Review: Published literature (Jan. 1985 to Nov. 2001) was identified by searching electronic bibliographic databases. Relevant studies and reports were classified based on tachycardia type: pre-excitation syndromes (most commonly the Wolff-Parkinson-White syndrome), atrioventricular node re-entrant tachycardia, atrial flutter, other atrial tachycardias, atrial fibrillation, and ventricular tachycardia.

Economic Review: For the literature search, appropriate economic terms were substituted for the clinical terms used for the clinical review. Reviewers classified the studies as model-based or trial-based. Cost effectiveness studies were included in the primary analysis. Studies that considered only costs or quality of life, or did not provide sufficient data to calculate an incremental cost effectiveness ratio, were summarized qualitatively.

Further research/reviews required

High-quality outcome studies comparing RFA with alternative therapeutic approaches are needed for all of the different types of ablation procedures.

Written by Noorani, HZ, Yee R, Marshall D, Connolly S, Nichol G, O'Brien B, CCOHTA, Canada

INAHTA Briefs

Issue 2002/93

Title A Systematic Review of the Effectiveness, Cost Effectiveness, and Barriers to Implementation of Thrombolytic and Neuroprotective Therapy for Acute Ischaemic Stroke in the NHS

Agency NCCHTA, National Coordinating Centre for Health Technology Assessment
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Reference Health Technol Assess 2002; 6(26). Nov 2002. www.ncchta.org/execsumm/summ626.htm

Aim

1. To assess the effectiveness of thrombolytic drugs.
2. To assess the effectiveness of neuroprotective drugs.
3. To map current pathways of acute stroke care, identify barriers to implementation of emergency drug treatments for acute stroke in the NHS, and to suggest ways to overcome the barriers.
4. To model the economic impact of thrombolytic therapy.

Conclusions and results

For the efficacy of thrombolysis, 17 trials (5216 patients) of urokinase, streptokinase, recombinant tissue plasminogen activator (rt-PA), or recombinant pro-urokinase were included. About 50% of the data came from trials testing intravenous rt-PA, mostly given within 6 hours of stroke onset. Thrombolytic therapy significantly increased the odds of fatal intracranial hemorrhage (OR = 4.15) and increased the odds of death at the end of followup (OR = 1.31). Despite the increase in deaths, thrombolytic therapy within 6 hours significantly reduced the proportion of patients who were dead or dependent at the end of followup (OR = 0.83). Heterogeneity between trials may be due to: the thrombolytic drug used, variation in concomitant use of aspirin and heparin, stroke severity, and time to treatment. The most widely tested agent, rt-PA, shows slightly less hazard and more benefit than other agents.

Key barriers to acute stroke treatment: patient/family inability to recognize stroke symptoms or failure to seek urgent help; patient/family calls general practitioner instead of ambulance; inefficient process of emergency stroke care in hospital; delay in neuroimaging.

The model suggested that if eligible patients were treated with rt-PA there was a 78% probability of a gain in quality-adjusted survival during the first year at a cost of £13,581 per QALY gained. Over a lifetime, rt-PA was associated with a cost saving of £96,565 per QALY. However, the estimates were imprecise and susceptible to assumptions used in the model.

Recommendations

The evidence on thrombolysis does not support widespread unselective use of thrombolytic therapy for acute ischemic stroke in routine clinical practice in the NHS. Data on thrombolytic drugs are limited and estimates of effectiveness and cost effectiveness are imprecise. The data were insufficient to estimate the cost of modifying NHS services to enable safe and effective delivery of rt-PA. A neuroprotective drug with even modest benefit is likely to be cost effective, but none is available. The cost of overcoming known barriers to acute stroke treatment is likely to vary by center and depend on the baseline level of stroke services.

Methods

Many sources were searched to identify: all unconfounded randomized trials comparing either a thrombolytic or a neuroprotective agent with placebo (or open control) in acute stroke patients; all published reports of studies identifying barriers to effective acute stroke care. A panel developed an economic model of acute stroke care. The data on thrombolysis were checked, where possible, with the original trialists. Completed systematic reviews on

Title A Systematic Review of the Effectiveness, Cost Effectiveness, and Barriers to Implementation of Thrombolytic and Neuroprotective Therapy for Acute Ischaemic Stroke in the NHS

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Reference Health Technol Assess 2002; 6(26). Nov.2002 www.ncchta.org/execsumm/summ626.htm

neuroprotection were sought. To review barriers to acute care and interventions to overcome them, two reviewers independently selected studies meeting the inclusion criteria and extracted data. Differences were resolved by discussion. Standard Cochrane quantitative systematic review methods were used; a fixed-effect model was used and results were expressed as odds ratios (ORs). A Markov model was created to estimate the number of life-years and quality-adjusted life-years (QALYs) gained with thrombolytic therapy.

Further research/reviews required

1. Determine the effects of rt-PA on short- and long-term survival and identify patients most likely to benefit (large-scale randomized trials comparing thrombolytic therapy with control).
2. Determine the nature and costs of changes in NHS services needed to deliver rt-PA therapy safely and effectively to acute stroke patients (including admitting suspected acute ischemic stroke patients to hospital much more quickly).

Written by Professor Peter Sandercock, Dept of Clinical Neurosciences, University of Edinburgh, UK

INAHTA Briefs

Issue 2003/03

Title A Systematic Review Update of the Clinical Effectiveness and Cost-Effectiveness of Glycoprotein IIb/IIIa Antagonists

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Reference Health Technol Assess 2002; 6(25). Dec 2002. www.ncchta.org/execsumm/summ625.htm

Aim

This systematic review focuses on the use of glycoprotein IIb/IIIa antagonists (GPAs) in three indications: as part of medical management of non-ST-elevation acute coronary syndrome (ACS) in conjunction with aspirin and heparin; as an adjunct to percutaneous coronary intervention (PCI) in various groups of patients; and as a supplement to thrombolytic therapy in patients with acute myocardial infarction (AMI).

Conclusions and results

1. The effectiveness of GPAs as adjuncts to PCI is further confirmed by additional large studies showing similar effect sizes and bleeding rates.
2. There is no evidence for the clinical superiority of tirofiban or eptifibatide over abciximab; however, drug costs of the newer agents are slightly lower.
3. Evidence that GPAs are effective in non-ST-elevation ACS when PCI is not undertaken is weakened by the GUSTO IV-ACS study. A meta-analysis of individual patient data from all major trials including GUSTO IV-ACS showed a small overall effect in such patients.
4. Based on current evidence, it may be considered that the extra benefits of GPAs adjunctive to thrombolysis in AMI are not justified by the risks of extra bleeding.

Most trials were conducted in the USA. Extrapolation of results from trials to routine practice creates some uncertainty since these trials were conducted outside the UK, eg, early invasive strategies are less common in the UK than elsewhere. The effectiveness of GPAs may be related to the frequency of PCI, as shown by the results from an international trial (PURSUIT) and by the results from GUSTO IV-ACS. Also, the mean age of the trial subjects (59–67 years) is lower than that generally seen in clinical practice.

Recommendations

See conclusions and results.

Methods

The search strategy, trial validity assessment, and data abstraction and analysis were generally unchanged from previous reviews. Papers reporting results in high-risk subgroups were considered together with equivalent results from the main reports.

Further research/reviews required

1. Potential benefits of GPAs in non-ST-elevation ACS, in particular in subgroups such as women and those not scheduled for PCI.
2. Potential benefits of GPAs in similar troponin-negative patient subgroups.
3. The benefits of GPAs as an adjunct to PCI in urgent and elective patients already receiving clopidogrel or starting clopidogrel at the time of randomization, and the optimal timing in conjunction with urgent PCI.
4. The cost effectiveness of GPAs used with thrombolytics in selected patients with AMI, preferably in a revised formulation that reduces unwanted bleeding.

Written by Dr Mike Robinson, Nuffield Inst for Health, University of Leeds, UK

INAHTA Briefs

Issue 2003/17

Title The Role of Clopidogrel in the Secondary Prevention of Recurrent Ischemic Vascular Events after Acute Myocardial Ischemia: A Critical Appraisal of the CURE Trial

Agency CCOHTA, Canadian Coordinating Office for Health Technology Assessment
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Reference CCOHTA Technology Report, Issue 32, November 2002. ISBN 1-894620-18-6 (print); ISBN 1-894620-17-8 (online): http://www.ccohta.ca

Aim

- To determine the population most likely to benefit from using a combination of clopidogrel and acetylsalicylic acid (ASA) to prevent recurrent ischemic vascular events after an episode of acute coronary syndrome (ACS)
- To assess the efficacy and safety of the clopidogrel/ASA combination.

Conclusions and results

Target Population: The randomized, double-blind, placebo-controlled CURE trial examined two co-primary outcomes: a) the composite of cardiovascular death, non-fatal MI, or stroke, and b) the composite of (a) or refractory ischemia. Secondary outcomes included severe ischemia, recurrent angina, a need for coronary revascularization procedures, and heart failure. The population studied in the CURE trial included mainly ACS patients with non-ST-segment elevation who were at high risk of cardiac ischemia or necrosis.

Efficacy and Safety: Results suggest that the early addition of clopidogrel to ASA reduces subsequent cardiovascular morbidity, compared to ASA alone, in this specific group of patients. In the CURE trial, this clinical benefit was mainly due to a reduced number of non-fatal heart attacks. The advantages of using the clopidogrel/ASA combination must, however, be interpreted in light of the increased risk of bleeding complications experienced by patients.

Recommendations

Not applicable.

Methods

A literature search confirmed that only two clinical trials addressing the objectives of this report have been conducted: CURE (Clopidogrel in Unstable angina to prevent Recurrent Events) and CAPRIE (Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events). A Canadian representative of the manufacturer of clopidogrel was invited to submit information. The CURE trial was critically appraised, including an overall assessment of the quality of the trial using the Jadad scale.

Further research/reviews required

Not applicable.

Written by Boucher M, Armstrong P, Pharand C, Skidmore B, CCOHTA, Canada

INAHTA Briefs

Issue 2003/18

Title **Endovascular Repair Compared With Open Surgical Repair of Abdominal Aortic Aneurysm: Canadian Practice and a Systematic Review**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
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Reference CCOHTA Technology Report, Issue 33, December 2002. ISBN 1-894620-60-7 (print); ISBN 1-894620-59-3 (online): http://www.ccohta.ca

Aim

- To examine the current status of endovascular grafts (EVG) for the elective repair of abdominal aortic aneurysms (AAA) in Canada
- To critically review the literature comparing EVG with open repair or with a "wait and see" approach, in terms of morbidity and mortality.

Conclusions and results

Current Canadian Practice: The response rate to a postal survey of Canadian vascular surgeons was 81%, or 104 of 129 eligible respondents. Responding surgeons had performed 3876 elective AAA repairs over a 12-month period. Of the responders, 40% had used EVG for this application; an additional 4% had plans to start using EVG technology. Of those using EVG, 52% considered it an investigational procedure. It appears that, in Canada, EVG is used predominantly for patients who meet specific anatomical criteria and are considered to be at moderate to high surgical risk. Reasons cited for not using EVG included lack of resources (34%), lack of training (13%), and lack of confidence that EVG offers an advantage over open repair (25%).

Review of Evidence: At present, EVG for AAA repair is still a new technology. Advances and modifications in device design have not been fully evaluated. The reduced invasiveness and quicker recovery enabled by EVG may offer a slight advantage over open repair in terms of perioperative mortality. However, possible drawbacks (such as lower rate of successful primary placement of the device, need for more extensive long-term followup, risk of continued aneurysm growth and possible rupture) must be weighed against potential gains. Potential biases in the available evidence may contribute to the lack of conclusive results in this review.

Recommendations

Not applicable.

Methods

Vascular surgeons in Canada were surveyed by mail to assess the current use of EVG for elective repair of AAA. To critically appraise comparative studies, two researchers independently selected, reviewed, and collected data from relevant studies obtained through a comprehensive literature search. Study information was summarized qualitatively, and outcomes were pooled where possible. Four main biases-selection, performance, detection, and attrition – that can impact internal validity were considered.

Further research/reviews required

The role of EVG in the elective repair of AAA is being examined further through the UK endovascular aortic aneurysm repair (EVAR) trials; results are expected in 2005. Further research also awaits longer-term outcomes from the various data registries.

Written by McAuley LM, Fisher A, Hill AB, Joyce J, CCOHTA, Canada

INAHTA Briefs

Issue 2002/54

Title **Monitoring Blood Glucose Control in Diabetes Mellitus: A Systematic Review.**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
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Reference Health Technol Assess 2000;4(12). May 2000. www.ncchta.org/execsumm/summ412.htm

Aim

To evaluate evidence for the clinical and cost effectiveness of different methods for monitoring blood glucose control in diabetes mellitus (DM).

Conclusions and results

- Blood or urine glucose self-monitoring is widely used by patients with type 2 diabetes, but there is a lack of evidence to show that the technique is effective at improving blood glucose control or other clinical and patient outcomes. No evidence shows that blood glucose control is better in patients who use blood rather than urine glucose monitoring.
- Blood glucose monitoring is well-established in the management of type 1 diabetes, but more evidence for the optimal use of the technique is needed.
- There is a lack of evidence concerning the use of self-monitoring in diabetes in pregnancy.
- Results from the Diabetes Control and Complications Trial in type 1 DM and the UK Prospective Diabetes Study in type 2 DM have demonstrated the clinical effectiveness of measuring glycated hemoglobin (HbA1c) to monitor blood glucose control. Greater emphasis should be given to extending use of HbA1c in assessing blood glucose control and to assay standardization.

Recommendations

Standard protocols for evaluation of blood glucose monitoring devices should be developed.

Methods

The literature was systematically reviewed. The authors' personal collections, Diabetes Care and Diabetic Medicine (1990–99), MEDLINE, EMBASE, and the Index and Bibliography of Social Sciences were searched.

Citations from papers retrieved were screened. Letters were sent to the British Diabetic Association and leading manufacturers. Retrieved papers were evaluated for quality by two independent reviewers. Data were abstracted and synthesized using meta-analysis where possible.

Further research/reviews required

- Randomized studies should be carried out to provide decisive evidence on the clinical and cost effectiveness of blood glucose self-monitoring in type 2 DM and gestational DM (GDM).
- Observational studies should be carried out in samples of subjects with type 1 DM to identify groups of patients in whom blood glucose self-monitoring is of benefit and groups in whom it is not.
- Studies should include not just assessment of glycated hemoglobin (GHb), but also the occurrence of hypoglycemia, patients' satisfaction with care, and health-related quality of life.

Written by Dr Martin Gulliford, GKT School of Medicine, London

INAHTA Briefs

Issue 2002/97

Title **Clinical Effectiveness and Cost-effectiveness of Growth Hormone in Children: A Systematic Review and Economic Evaluation**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
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Reference Health Technol Assess 2002; 6(18). Nov 2002. www.ncchta.org/execsumm/summ618.htm

Aim

This review considers the clinical effectiveness and cost effectiveness of growth hormone (GH) therapy in children with growth hormone deficiency, Turner syndrome, chronic renal failure, Prader-Willi syndrome, or idiopathic short stature.

Conclusions and results

The assessment of clinical effectiveness included 34 publications reporting 32 studies. Short-term growth and final height outcomes, and also body composition and psychological outcomes were evaluated. Jadad quality scores ranged from 1/5 to 4/5. Economic evaluations were not found, nor were studies reporting appropriate quality-of-life measures.

Although the quality of evidence varied, the studies suggest that GH treatment can increase short-term growth and improve final height. The reported effects of GH on short-term growth should be considered more reliable due to higher quality evidence. Effects of GH on final height should be considered with caution since the quality of studies is poorer. Results suggest that the effects of GH on short-term growth velocity (at 1 year) can range from no improvement to approximately 1 standard deviation above the normal growth velocity for children of the same age. Final height gains for treated children over untreated children range from about 2cm to 11cm.

GH treatment is expensive. The lifetime incremental cost of treating one child with GH ranges from £43,100–53,400 (for GHD) to £55,500–83,000 (for PWS). These costs, applied to children aged 8–15 years with the analyzed indications in England and Wales, yield total discounted costs of £904 million for complete treatment. The cost to treat children only in the four licensed conditions would be about £180 million. The data suggest that, under base case conditions, the incremental cost per centimeter gained in final height is approximately £6000 for GHD, £16,000–17,400 for TS, £7400–24,100 for CRF, £13,500–27,200 for ISS, and possibly around £7030 for PWS. Impacts of parameter values were evaluated by sensitivity analyses. The economic evaluation is limited by the quality of the trials.

Recommendations

The evidence suggests that prescribing GH to children improves their short-term growth and/or their final height (although the quality of evidence varies). GH treatment is expensive. Since a minority of children with licensed conditions currently receive GH, the budgetary impact of large increases in prescribing would be substantial.

Methods

Main electronic databases were searched (English language) up to April 2001. Bibliographies of related papers were assessed for relevant studies, and experts were contacted for advice, peer review, and to identify other references. Manufacturer submissions to the National Institute for Clinical Excellence were reviewed. Studies that met specified criteria were included, data were extracted, and quality was assessed. RCT quality was assessed using Jadad criteria, and non-RCTs were assessed using modified Spitzer criteria. Internal validity of economic evaluations was assessed using the BMJ checklist , and external validity was assessed using a series of relevant questions. Clinical effectiveness of GH in children was synthesized via a narrative review, with full tabulation of study results. A cost-effectiveness model was constructed using the best available evidence and applied to a UK setting.

Further research/reviews required

Large, multicenter RCTs are needed. These RCTs should focus on final height, which is the best outcome for assessing the effectiveness of GH, and should address quality-of-life factors for use in economic modeling.

Written by Mrs Jackie Bryant, SHTAC, University of Southampton, UK

INAHTA Briefs

Issue 2003/14

Title **Efficacy of Rosiglitazone and Pioglitazone Compared to Other Anti-diabetic Agents: Systematic Review and Budget Impact Analysis**

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

Reference CCOHTA Technology Report, Issue 29, October 2002. ISBN 1-894620-57-7 (print); ISBN 1-894620-58-5 (online): http://www.ccohta.ca

Aim

- To evaluate the evidence that compares rosiglitazone or pioglitazone with other oral anti-diabetic agents, either as monotherapy or when added to a non-thiazolidinedione agent in the treatment of type 2 diabetes
- To perform a budget impact analysis projecting costs associated with the listing of thiazolidinediones on formularies of publicly funded drug plans in Canada.

Conclusions and results

Clinical Efficacy: Eleven rosiglitazone trials and eight pioglitazone trials met the selection criteria. Most studies involved an observation period of one year or less. When used as monotherapy in adults with type 2 diabetes, both rosiglitazone and pioglitazone have an effect on HbA1c (glycosylated hemoglobin) and FPG (fasting plasma glucose) similar to the effect observed with non-thiazolidinedione comparator drugs. These findings are, however, based on a small number of comparative trials.

When added to another anti-diabetic agent, both thiazolidinediones produce a significantly greater effect on HbA1c and FPG than continuing monotherapy with the other agent, in patients with type 2 diabetes not well controlled on a single agent. Both drugs were generally well tolerated, with no serious liver adverse events reported.

Budget Impact Analysis: If rosiglitazone and pioglitazone were to receive formulary listing throughout Canada, it is estimated that by 2004 the net expenditure for publicly funded drug programs would increase nationally between $11.8 and $88.5 million per year. This estimate depends on utilization and number of patients treated.

Recommendations

Not applicable.

Methods

The published literature from 1990 to 2001 was searched, and information received from the manufacturers of the two drugs was reviewed. Two independent reviewers selected relevant studies and extracted data. FPG and HbA1c were considered as primary outcomes, along with secondary outcomes such as cholesterol and triglyceride levels. The budget impact analysis was undertaken from the perspective of a Canadian provincial drug plan. This analysis focused on the potential impact on macro-level costs that the introduction of pioglitazone and rosiglitazone could cause for the year 2004.

Further research/reviews required

Longer-term studies are required to evaluate the effect of rosiglitazone and pioglitazone on the development of diabetic complications and to assess the long-term safety of these drugs.

Written by Boucher M, McAuley L, Brown A, Keely E, Skidmore B, CCOHTA, Canada

INAHTA Briefs

Issue 2002/44

Title A Systematic Review of Stapled Hemorrhoidectomy

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,
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Reference ASERNIP-S Report No. 24, ISBN 0 909844 45 3
Full text available: http://www.surgeons.org/open/asernip-s/publications.htm

Aim

To systematically review the literature regarding the safety and efficacy of stapled hemorrhoidectomy in comparison to conventional methods of hemorrhoidectomy.

Conclusions and results

The evidence base for circular stapled hemorrhoidectomy shows that it is as safe as conventional hemorrhoidectomy. The evidence base was inadequate to determine efficacy of circular stapled hemorrhoidectomy in comparison to conventional hemorrhoidal procedures.

Small sample size and short followup times limited the level II evidence. Few studies assessed similar endpoints, and the reporting of important outcomes was incomplete.

Safety: At 2 weeks, stapled hemorrhoidectomy conferred a 45% (95% CI, 18%–63%) reduction in the risk of bleeding compared to the conventional technique. Comparison of the other reported complications tended to favor the stapled technique.

Efficacy: Prolapse occurred at higher rates in the stapled group, and as this is one of the indications for surgery, its persistence may be viewed as treatment failure. Patient satisfaction with overall postoperative symptom control was similar in both treatment groups.

Recommendations

It was recommended that surgeons practicing stapled hemorrhoidectomy should conduct a careful audit of their results. It was also suggested that, as a minimum requirement, surgeons wishing to use the stapled technique of hemorrhoidectomy should undergo appropriate training and supervised instruction in accordance with training guidelines developed by The Colorectal Surgical Society of Australasia.

Methods

All original, published human studies on stapled hemorrhoidectomy were identified by searching Current Contents, EMBASE, MEDLINE, HealthSTAR, and the Cochrane Collection Library from when the databases began entering data (1966 or later) until June 2001. Randomized controlled trials of patients with all levels of hemorrhoids comparing conventional hemorrhoidectomy (excision-ligation, closed hemorrhoidectomy, or diathermy which may or may not be ligated) with circular stapled hemorrhoidectomy were included for review. Only English language articles were included for review as, based on the abstracts of foreign language articles, they did not offer any significantly different or more extensive results.

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

INAHTA Briefs

Issue 2002/75

Title The Clinical Effectiveness and Cost effectiveness of Surgery for People with Morbid Obesity: 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, www.ncchta.org/execsumm/summ612.htm

Reference Health Technol Assess 2002;6(12). July 2002

Aim

To systematically review the clinical effectiveness and cost effectiveness of surgery for managing morbid obesity and to develop a cost effectiveness model using the best available evidence to determine cost effectiveness in a UK setting.

Conclusions and results

- 17 RCTs and 1 nonrandomized clinical trial were included in the systematic review of clinical effectiveness. Methodological quality in the studies varied. Surgery was more effective than conventional treatment in achieving long-term weight loss (23–37kg more weight, maintained to 8 years) and improving quality of life (QoL) and comorbidities. Gastric bypass surgery was more beneficial than gastroplasty or jejunoileal bypass, with laparoscopic placement producing fewer complications than open procedures. Four economic evaluations, all of poor quality, were included in the systematic review of cost effectiveness. Surgery was shown to be cost-effective or cost-saving compared with nonsurgical treatment or no treatment.
- Comparing surgery to nonsurgical management over a 20-year period showed that surgery offered additional quality-adjusted life-years (QALYs) at an additional cost. When compared to nonsurgical management, gastric bypass had a net cost per QALY of £6289 while vertical banded gastroplasty and silicone adjustable gastric banding had net costs per QALY of £10,237 and £8527, respectively. Gastric bypass appears to have a modest net cost per QALY gained compared to vertical banded gastroplasty (£742/QALY). In contrast, silicone adjustable gastric banding has a large net cost per QALY gained compared to gastric bypass (£256,856/QALY). Caution should be taken when comparing surgical procedures as the economic evaluation is based on several unsophisticated assumptions, and evidence of clinical effectiveness varies among procedures.
- Surgery was found to be more effective than conventional treatment in achieving long-term weight loss. Expert opinion suggests that any service would need to be provided within specialist facilities with adequately trained multidisciplinary teams to operate and provide long-term support to patients.
- If implemented, the additional total cost to the NHS in England and Wales may be £136.5 million over the 20-year life-expectancies of the 50 000 patients estimated to be morbidly obese and who may meet the criteria for surgery. An estimated 800 morbidly obese people may meet the criteria for surgery each year, at an additional cost of £2.2 million over their 20-year-life expectancies.

Recommendations

Further research is required addressing long-term consequences of surgery, incorporating economic evaluations on the different surgical interventions.

Methods

A systematic review of the literature and an economic evaluation were undertaken. Sixteen electronic databases were searched. Relevant bibliographies were assessed, and experts were contacted for advice, peer review, and to identify other published/unpublished references. Manufacturer submissions to the National Institute for Clinical Excellence were reviewed.

Title **The Clinical Effectiveness and Cost effectiveness of Surgery for People with Morbid Obesity: A Systematic Review and Economic Evaluation**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**

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Reference Health Technol Assess 2002;6(12). July 2002

Systematic reviews of RCTs and/or prospective controlled clinical trials and RCTs and/or prospective controlled clinical trials were included, as were economic evaluations of surgery for people with morbid obesity that included a comparator and both the costs and consequences of treatment.Studies in non-English languages, abstracts, and conference poster presentations were excluded. A model using the best available evidence was constructed to determine cost effectiveness in a UK setting. Sensitivity analyses were performed.

Further research/reviews required

Although surgery appears effective in treating weight change, evidence on long-term consequences and influence on QoL in patients is limited. Few economic evaluations have compared the different surgical options, and the availability of costing and resource use data is limited. Good quality research of these issues would be beneficial.

Written by Dr Andy Clegg, Southampton HTA Centre, University of Southampton, UK

INAHTA Briefs

Issue 2002/86

Title The Efficacy of Proton Pump Inhibitors in Adults with Functional Dyspepsia

Agency CCOHTA, Canadian Coordinating Office for Health Technology Assessment
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Reference CCOHTA Technology Report, Issue 22, January 2002. ISBN 1-894620-29-1 (print);
ISBN 1-894620-30-5 (online): http://www.ccohta.ca/ccohta_production/entry_e.html

Aim

- To determine the efficacy of proton pump inhibitors (PPI) in reducing symptoms in adults with functional dyspepsia compared with placebo, prokinetic agents, and H2-antagonists
- To determine the safety of PPIs
- To determine if the effect of PPIs differs between symptom subgroups and in H. pylori positive patients with functional dyspepsia.

Conclusions and results

Three published randomized controlled trials and three abstracts satisfied the inclusion criteria: one study was of high quality, two of moderate quality, and the three abstracts were of low quality. All six studies compared PPI treatment with placebo, for a total of 2368 patients. One study also compared PPIs with an H2- antagonist. No studies comparing a PPI with a prokinetic agent were identified.

Meta-analysis demonstrated that PPIs, when compared with placebo, reduce symptoms in functional dyspepsia and do not have significant side effects. No significant heterogeneity was observed across studies in either "excellent" outcome or combined "good-to-excellent" response. Sensitivity and subgroup analyses were limited by lack of data. The relationship between H. pylori status and PPIs in functional dyspepsia remains unclear. No significant difference was observed for "excellent" or combined "good-to-excellent" outcomes between PPIs and H2-antagonists. PPIs produced no significant side effects.

Recommendations

- Exercise caution in comparing the efficacy of PPIs with the efficacy of prokinetic agents and H2-antagonists, given the lack of valid trials directly comparing these three agents.

Methods

A comprehensive literature search of online databases was supplemented by manually searching reference lists from retrieved articles and hand searching for recent articles from two journals, *Gastroenterology* and *Gut*. Pharmaceutical manufacturers were contacted to identify further unpublished materials. The outcomes of randomized, controlled trials comparing PPIs with placebo, motility agents or H2-antagonists in adults diagnosed with functional dyspepsia were simplified within the meta-analysis to either "experiencing no symptoms" (excellent relief of dyspepsia) or "experiencing a significant improvement in symptoms" (combined good-and-excellent relief of dyspepsia).

Further research/reviews required

While prokinetic agents and H2-antagonists may appear more efficacious based on other meta-analyses, direct comparison trials are needed to provide conclusive evidence. Further randomized controlled trials are needed to compare PPIs, other prokinetic agents (such as domperidone), and H2-antagonists in both H. pylori positive and negative patients with functional dyspepsia.

Written by Shiau J, Shukla V, Dubé C, CCOHTA, Canada

INAHTA Briefs

Issue 2002/88

Title **Infliximab for the Treatment of Crohn's Disease: A Systematic Review and Cost-Utility Analysis**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
865 Carling Avenue, Suite 600, Ottawa, ON, K1S 5S8 Canada;
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Reference CCOHTA Technology Report, Issue 24, March 2002. ISBN 1-894620-33-X (print); ISBN 1-894620-34-8 (online): http://www.ccohta.ca/ccohta_production/entry_e.html

Aim

- To review available data on the efficacy, effectiveness, and adverse effects of infliximab in treating patients with Crohn's disease (CD)
- To review available data evaluating the economic impact of infliximab
- To conduct a primary cost-utility analysis of infliximab treatment for patients with active CD that is resistant to conventional therapy.

Conclusions and results

Infliximab appears to be clinically effective for treating fistulizing CD and active CD resistant to conventional therapy. Its short-term safety profile is acceptable, however, increased rates of acute respiratory infection were observed. The long-term risk, including malignancy and autoimmune disease, are not known. Cost-utility analysis of infliximab in treatment-resistant active CD suggests that the incremental costs per additional quality-adjusted life-year exceed traditional benchmarks. Results were sensitive to extreme reductions in the cost of infliximab and increases in the rate of medical admission for drug-refractory disease. Limitations to the economic analysis include assumptions about natural history, resource utilization, drug dosing, a limited time horizon, and that only direct medical costs were assessed.

Infliximab's economic impact may continue to evolve with changes in delivery, dose, and cost.

Decision makers must recognize that few, if any, treatment alternatives are available to patients with severe, refractory CD.

Methods

Clinical Effectiveness: Because only four eligible randomized controlled trials that evaluated the efficacy of infliximab for treatment of CD were identified, a qualititative summary of the available clinical data was undertaken.

Economic Analysis: Six previous economic analyses of infliximab and two observational studies of infliximab-associated resource utilization were identified, along with four unpublished economic evaluations prepared by industry. Reviewers undertook a cost-utility analysis of infliximab for active CD that is resistant to conventional therapy. The use of infliximab for fistulizing CD was not evaluated. A Markov model was used to compare three infliximab treatment strategies to usual care. Advanced probabilistic sensitivity analysis was used to explore the impact of parameter uncertainty.

Further research/reviews required

Further information on the long-term adverse effects of infliximab therapy is needed, particularly with respect to maintenance therapy.

Written by Marshall J, Blackhouse G, Goeree R, Brazier N, Irvine E, Faulkner L, Dipchand C, O'Brien B, CCOHTA, Canada

INAHTA Briefs

Issue 2002/84

Title New Fluoroquinolones in Community-Acquired Pneumonia: A Clinical and Economic Evaluation

Agency CCOHTA, Canadian Coordinating Office for Health Technology Assessment
865 Carling Avenue, Suite 600, Ottawa, ON, K1S 5S8 Canada;
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Reference CCOHTA Technology Report, Issue 20, November 2001. ISBN 1-894620-14-3 (print); ISBN 1-894620-13-5 (online): http://www.ccohta.ca/ccohta_production/entry_e.html

Aim

- To critically review the efficacy and safety of new fluoroquinolones (FQs) for the empiric treatment of community-acquired pneumonia (CAP)
- To compare these drugs, both clinically and economically, with comparator antibiotics.

Conclusions and results

Of the 16 randomized controlled trials that met the selection criteria, 1 was of high quality, 9 of moderate quality, and 6 of low quality. Twelve of these trials compared orally administered FQs with other orally administered antibiotics used in the treatment of CAP. Eight of these reported intention-to-treat analyses (ITT). Three studies compared intravenous (IV) therapy, or IV with step-down to oral (IV to PO) FQ therapy, with another IV or IV oral antibiotic; in these studies, ITT analyses were not reported. One study compared two IV/oral FQs to each other; gatifloxacin and levofloxacin.

Analysis of the trials on an ITT basis indicates that the orally administered FQs offer no statistically significant additional clinical successes when compared to other antibiotics. The "evaluable subjects" analysis found FQs to be slightly more effective. Considering the limitations of the evidence, this study concludes that the new FQs are at least as effective as, and maybe slightly more effective than, comparative antibiotics for the empiric treatment of CAP. No overall differences in serious adverse effects were observed.

Due to significant limitations of the cost-effectiveness analysis (CEA), resulting from the limited evidence of any real difference between FQs and comparative antibiotics, the cost-minimization analysis (CMA) was considered the primary economic analysis. CMA indicates that the new FQs approved for use in Canada have a cost advantage over some alternative antibiotics, but this advantage is lost compared to the lower cost alternative antibiotics.

Recommendations

In light of relative similarities in costs and effects among treatment strategies, treatment decisions should consider additional factors such as regional pattern of bacterial resistance, adverse drug reaction profile, patient convenience, and potential for cross-resistance among FQs.

Methods

A systematic review and meta-analyses of randomized controlled trials was undertaken. Across all trials considered, the main outcome measures were both clinical success at the end of treatment and the number of subjects designated "clinically cured or improved" based on causative pathogen. Using meta-analyses, estimates of the differences in clinical success rates between FQs and comparative antibiotics were expressed as risk differences. A CMA and CEA were used to compare the cost-effectiveness of oral and IV/oral treatments from a provincial government payer perspective.

Further research/reviews required

To confirm a class effect for the new FQs, higher quality clinical trials comparing the FQs among themselves would be required.

Written by Metge C, Vercaigne L, Carrie A, Zhanel G, CCOHTA, Canada

INAHTA Briefs

Issue 2002/85

Title: Oseltamivir for the Treatment of Suspected Influenza: A Clinical and Economic Assessment

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865 Carling Avenue, Suite 600, Ottawa, ON, K1S 5S8 Canada;
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Reference CCOHTA Technology Report, Issue 21, November 2001. ISBN 1-894620-26-7 (print); ISBN 1-894620-25-9 (online): http://www.ccohta.ca/ccohta_production/entry_e.html

Aim

- To assess and quantify the effectiveness of treating suspected influenza with oseltamivir
- To assess the cost effectiveness of treating suspected influenza with oseltamivir in a primary care setting.

Conclusions and results

Clinical Effectiveness: Six trials, all sponsored by the industry and all of generally high quality, met the inclusion criteria. Of the 1735 participants, 469 were at risk of developing complications. Oseltamivir treatment resulted in an absolute reduction for a combined outcome of death, hospitalization, and complications of 1% (95%CI: -2% to 3%) and 2% (95%CI: -5% to 8%) in otherwise healthy individuals and at-risk individuals, respectively, who were suspected of having influenza. Analysis of these three outcomes separately indicated similarly small and statistically insignificant results. Overall, the data suggest that the benefits of oseltamivir are limited to treating otherwise healthy individuals suspected of having influenza, and that its effects are, at best, palliative.

Economic Analysis: Results in terms of cost per quality-adjusted life-year showed that treatment with oseltamivir is unlikely to be cost effective for the healthy population, based on reasonable assumptions about diagnostic accuracy in primary care when influenza is circulating in the community. For oseltamivir to be even marginally cost effective from a government payer perspective, very favorable assumptions are needed: high diagnostic accuracy, few late presenters treated inappropriately, and optimistic assumptions about clinical effectiveness. Although clinical evidence is inconclusive, the analysis suggests that oseltamivir is also unlikely to be cost effective for treating adults at risk of developing influenza-related complications.

Methods

Reviewers selected relevant studies from a systematic review of randomized controlled trials obtained by searching electronic databases, contacting experts in the field and the drug manufacturer, and conducting bibliographic searches and hand searches of reviews and conference abstracts. The quality of these studies was assessed, and the data were independently extracted and combined, if appropriate, by meta-analysis. For the economic evaluation, a decision analytic model was used to compare the health outcomes, resource use, and costs associated with treating suspected influenza with oseltamivir to using symptomatic relief medication only. Two populations were assessed from the perspective of a government payer in Canada: healthy persons aged 18 to 65 years, and those at risk of developing influenza-related complications. Both cost-effectiveness and cost-utility analyses were performed.

Further research/reviews required

Further trials comparing oseltamivir with placebo, as well as the other antiviral medications, are needed to adequately assess outcomes, especially in the at-risk population.

Written by Husereau D, Brady B, McGeer A, CCOHTA, Canada

INAHTA Briefs

Issue 2002/31

Title Hospitalization for Internal Radiotherapy

Agency CEDIT, Committee for Evaluation and Diffusion of Innovative Technologies
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Reference CEDIT Report (in French) No. 01.05/Ra1/01/Recommendation 01.05/Re1/01

Aim

CEDIT was consulted by Professor Serge Askienazy, Head of Nuclear and Biophysical Medicine of Saint-Antoine Hospital (Paris) and President of the Association of Nuclear Medicine in Paris Area Hospitals, for an evaluation of requirements relating to internal radiotherapy (formerly called metabolic radiotherapy) in light of the expected development of this technique within the AP-HP. Internal radiotherapy involves the use of radiopharmaceuticals, or a combination of a radioisotope and a specific vector on a target to be irradiated. Effective treatment requires selective concentration of the radiopharmaceutical in the targeted organ and its retention by the tumor, without causing major damage to surrounding healthy tissues. Treatment outcome depends on the total dose absorbed and the lesion's sensitivity to radiation.

Results

Iodine 131 has now been used over several decades for differentiated thyroid carcinoma or hyperthyroidism. All professionals in the field do not agree upon the benefit of regular administration of Iodine 131 following treatment for a thyroid carcinoma by thyroidectomy. Many radiopharmaceuticals made their appearance in various clinical studies in the late 1980s, reinforcing the benefit of internal radiotherapy in the palliation of painful bone metastases that did not respond to conventional treatment. Among these new agents, two received approval for sale in France: Quadramet® and Metastron®. According to the literature, an analgesic effect is obtained in over 50% of patients. The use of Lipiocis® also offers new prospects for treating hepatocellular carcinoma. Encouraging results have been obtained in treating neuroendocrine tumors with somatostatine analogues, of which the most studied is the octreotide radiolabeled with different isotopes. In hematology, radioimmunotherapy seems promising for treating certain advanced lymphomas. The cost of doses ranges between 91€ for hyperthyroidism treated with Iodine 131 and up to 12 000 € for a series of 3 injections in treating neuroendocrine tumors by indium 111-pentreotide. Regulatory changes could require mandatory hospitalization for patients currently treated in outpatient departments. This would incur additional costs due to the need for new rooms. Given staffing constraints, it would thus prove more cost effective to assemble internal radiotherapy activities in specialized centers.

Recommendations

The conditions required for the practice of nuclear medicine in the AP-HP, the very probable increase of indications for internal radiotherapy, and the implementation of regulations governing radioactive safety, all lead CEDIT to recommend an increase in the capacity of hospitals to house patients requiring internal radiotherapy. However, for acute cancerology indications, where internal radiotherapy seems to offer new opportunities, it is very difficult to forecast how much development needs to be planned. It appears beneficial, therefore, that all technical facilities be concentrated in specialized and highly specialized cancer centers. CEDIT emphasizes that all plans to increase the number of beds for internal radiotherapy in the AP-HP be part of current availability within and outside of the AP-HP.

Methods

A literature search was conducted, five databases were scanned: MEDLINE, EMBASE, Pascal, BIOSIS and Current Contents. Five experts were interviewed on the innovative character and on the medical benefit of this technology.

Written by Edlinger C, Perrin JP, Baffert S, Elie C, Charpentier E, Fery-Lemonnier E, CEDIT, France

INAHTA Briefs

Issue 2002/38

Title **Samarium153-lexidronam (SML) for Bone Pain due to Skeletal Metastases, August 1999**

Agency **MSAC, Medicare Services Advisory Committee**
Commonwealth Department of Health and Ageing,
GPO Box 9848 Canberra ACT 2601 Australia;
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Reference MSAC application 1016. Assessment report ISSN 1443-7120

Aim

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

Conclusions and results

Safety: SML appears to be as safe as the alternative Strontium89, in terms of hematological toxicity and other adverse events. The prognosis for the majority of patients is poor and most will only receive a single dose. Still, the toxicity risk of repeated dosages should be investigated.

Effectiveness: SML is effective in relieving bone pain due to skeletal metastases from carcinoma of the breast and at least as effective as Strontium89 for carcinoma of the prostate. In one trial, SML led to decreased use of analgesics.

Cost effectiveness: Cost minimization analysis would be useful, but was not undertaken due to insufficient costing data and because the proposed fee for SML is significantly less than for Strontium89.

Recommendations

SML should receive public funding for relief of bone pain in patients with skeletal metastases from:

- Carcinoma of the prostate where hormonal therapy has failed, or
- Carcinoma of the breast where hormonal and chemotherapy have failed, and
- The disease is poorly controlled by conventional radiotherapy, or where this is inappropriate due to wide distribution of the sites of bone pain.

Methods

MSAC conducted a systematic review of medical literature on SML from 1966 until September 1998 via MEDLINE, HEALTHSTAR, TOXLINE, EMBASE, SciSearch, Current Contents, the Cochrane Library, BIOSIS, CANCERLIT, Pascal, and Elsevier Biobase and Derwent databases. Due to a lack of clinical trial data directly comparing SML with Strontium89 a placebo was chosen as the common comparator.

INAHTA Briefs

Issue 2002/59

Title The Clinical Effectiveness of Trastuzumab for Breast Cancer

Agency NCCHTA, National Coordinating Centre for Health Technology Assessment
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tel: +44 2380 595586, fax: +44 2380 595639

Reference Health Technol Assess 2002;6(13). June 2002. www.ncchta.org/execsumm/summ613.htm

Aim

To evaluate the effectiveness of trastuzumab in managing breast cancer.

Conclusions and results

One RCT of trastuzumab plus chemotherapy (cyclophosphamide plus anthracycline or paclitaxel) versus chemotherapy alone. Study population included women with HER2-overexpressing metastatic breast cancer (MBC) at level 2+ or 3+ who had not received prior treatment for MBC. Overall quality of the trial considered to be good. Trastuzumab administered for the duration of the trial in weekly infusions as long as the treatment was considered to be beneficial. Addition of trastuzumab to chemotherapy resulted in significantly less disease progression and treatment failure, longer progression-free survival, and greater complete and overall tumor response when compared to chemotherapy alone. A significantly greater incidence of congestive heart failure was reported among those receiving trastuzumab plus chemotherapy compared to those on chemotherapy alone. The incidence seemed to be highest with trastuzumab plus anthracycline, rather than with trastuzumab plus paclitaxel.

No RCTs found that met the initial inclusion criteria for trastuzumab used as monotherapy. Hence, this section is based on noncomparative Phase II studies. The overall quality of these studies according to the checklist for case series was found to be moderate. Trastuzumab monotherapy was shown to have some antitumor effects in terms of overall tumor response (partial and complete), which ranged from 12% to 24% in the three studies. An independent response committee assessed tumor response outcomes in two studies, whereas tumor response was assessed by the investigators in the third study. Similar durations of tumor response were reported by two studies of 9 and 9.1 months.

One study reported the number of complete (five (3%)) or partial (26 (15%)) tumor responses for participants with tumors overexpressing HER2 at level 3+. In another study, the overall tumor response rate for this group of participants was reported for both treatment groups combined as 31% (26/85). These results demonstrated that most tumor responses occurred in participants with tumors overexpressing HER2 at level 3+.

Trastuzumab when used in combination with chemotherapy seemed to be more effective than chemotherapy alone for treatment of MBC overexpressing HER2 at level 3+ in individuals who had not received prior treatment for MBC. However, it seemed to be associated with congestive heart failure, particularly in patients that received anthracycline-based chemotherapy.

- Trastuzumab monotherapy when used as second-line or subsequent therapy for the treatment of MBC over expressing HER2 at level 3+ appeared to have some antitumor effects in terms of overall tumor response based on noncomparative studies (which provide relatively weak evidence) of moderate quality.

Recommendations

Further large, well-conducted RCTs are required to provide more evidence of the effectiveness of trastuzumab when used within its licensed indications, in addition to other indications.

Title The Clinical Effectiveness of Trastuzumab for Breast Cancer

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Reference Health Technol Assess 2002;6(13). June 2002. www.ncchta.org/execsumm/summ613.htm

Methods

Only randomized controlled trials (RCTs) were initially considered for inclusion. Included trials had to evaluate trastuzumab alone or in combination with other agents vs systemic therapy without trastuzumab, and had to include individuals with breast cancer. No RCTs of trastuzumab used as monotherapy for treating breast cancer were found. The National Institute for Clinical Excellence (NICE), therefore, requested that noncomparative Phase II studies of trastuzumab used as monotherapy for the treatment of HER2-overexpressing (at level 3+) breast cancer be evaluated for inclusion in the review, and these data have subsequently been added. Several databases were searched using strategies designed specifically for each database. Additional references were identified through reviewing manufacturer and sponsor submissions made to NICE, the bibliographies of retrieved articles, conference proceedings, and by searching the Internet.

Further research/reviews required

Further large, well-conducted RCTs are required to provide more evidence of the effectiveness of trastuzumab when used within its licensed indications, in addition to other indications.

Written by Ms Ruth Lewis, CRD, University of York, UK

INAHTA Briefs

Issue 2002/69

Title Brachytherapy for Prostate Cancer

Agency SMM, The Norwegian Centre for Health Technology Assessment
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Reference SMM Report No. 2/2002. ISBN 82-14-02762-4

Aim

Brachytherapy is increasingly being used to treat localized prostate cancer. This report undertakes a critical and systematic review of the clinical and cost effectiveness of brachytherapy compared with radical prostatectomy, external beam radiation, or watchful waiting in patients with localized prostate cancer.

Conclusions and results

No randomized controlled trials or large prospective studies compared prostate brachytherapy with other treatment modalities. In general, studies were of poor quality (cohort, case-control, and case-series), and many had poor validity. Only 5 of the 16 studies considered to be relevant were included in the final summary of evidence. Reasons for exclusion were that the groups were incomparable with respect to age and clinical stage or followup was incomplete.

- None of the included studies had sufficient followup for overall or disease-free survival.
- No difference in "no biochemical evidence of disease" (PSA) for followup of 5 to 10 years.
- No major difference in complications (urinary tract irritation, impotence, and proctitis), and long-term complications are not known.
- No studies allowed for valid comparison regarding quality of life.

Cost effectiveness

The estimated 1-year costs for the Norwegian healthcare system suggested no major cost differences between the three treatment modalities.

– Radical prostatectomy: 10 700 Euros
– Brachytherapy: 12 000 Euros
– External beam radiotherapy: 14 700 Euros

In conclusion, brachytherapy is neither better nor worse than other treatment options for prostate cancer. A search for ongoing studies showed that information from randomized controlled trials remains at least 10 years into the future. Prostate cancer patients face a choice of three treatment options, each with poor documentation of clinical effectiveness.

Methods

Studies were identified by searches in the HTA Database, Cochrane, MEDLINE, and EMBASE (August 2001). Only comparative studies were included (RCT, CT, cohort or case-control studies). Outcomes assessed: total or disease-free survival, surrogate-free survival (PSA), complications, and quality of life. The validity judgment considered whether groups were comparable with respect to age, disease severity, comorbidity, and followup.

Written by Inger Norderhaug, SMM, Norway

INAHTA Briefs

Issue 2002/95

Title **Treatment of Inoperable Advanced Non-small-cell Lung Cancer: Regimens with or without Taxane**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
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Reference CCOHTA Technology Report, Issue 28, September 2002. ISBN 1-894620-55-0 (print); ISBN 1-894620-56-9 (online): http://www.ccohta.ca

Aim

To compare the clinical efficacy of taxane-containing regimens (TRs) with regimens not containing taxanes (NTRs) in the treatment of inoperable advanced non-small-cell lung cancer (NSCLC) with respect to four outcomes: response, survival, toxicity, and quality of life.

Conclusions and results

Nineteen trials with 7433 patients were selected for review. Meta-analysis showed pooled odds ratios and 95% confidence intervals for response rate and 1-year mortality of 1.34 (1.09, 1.66) and 0.94 (0.83, 1.05) respectively. For inoperable, advanced NSCLC, TRs produced a statistically significant effect on response rate when compared to NTRs. However, TRs did not statistically significantly alter 1-year survival when compared to NTRs. The pooled results of this review should be viewed cautiously because the drug combinations used in treatment regimens varied across trials. Toxicity profiles varied considerably across the different studies, hindering valid comparison. Only 6 trials reported on quality of life (QoL); based on these limited data, TRs and NTRs appeared to be similar in terms of overall impact on QoL.

Methods

Published and unpublished reports were identified by three methods: a) searching electronic databases and websites; b) hand searching the bibliographies of selected papers and conference proceedings; and c) contacting drug manufacturers and content experts. Reviewers considered only randomized controlled trials whose participants had advanced NSCLC with inoperable tumors. Eligible trials reported data on 1-year survival rate, response rate, toxicity, or QoL. Selected trials included at least one intervention with a taxane and one without a taxane. Two reviewers extracted study information independently.

Further research/reviews required

More randomized trials using uniform drug combinations are needed to allow valid comparisons between TRs and NTRs. Also, to enable meaningful QoL comparisons, researchers should make an effort to collect sufficient data on QoL.

Written by Banerjee S, Moher D, Stewart DJ, CCOHTA, Canada

INAHTA Briefs

Issue 2003/02

Title The Clinical Effectiveness and Cost-Effectiveness of Vinorelbine for Breast Cancer: A Systematic Review and Economic Evaluation

Agency NCCHTA, National Coordinating Centre for Health Technology Assessment
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Reference Health Technol Assess 2002; 6(14). Dec 2002. www.ncchta.org/execsumm/summ614.htm

Aim

To evaluate the clinical effectiveness and cost effectiveness of vinorelbine in managing breast cancer.

Conclusions and results

Based on evidence from randomized controlled trials (RCTs), vinorelbine monotherapy as first-line, second-line, or subsequent therapy for advanced breast cancer, may be more effective in terms of progression-free survival and survival than melphalan. Vinorelbine monotherapy was not found to be more effective than other chemotherapy regimens in terms of response rates. The poor quality of the data on which these findings were based should be considered. Vinorelbine combined with doxorubicin, 5-fluorouracil, or mitoxantrone did not appear to be more effective than alternative combinations of chemotherapy in treating metastatic breast cancer. Vinorelbine plus mitoxantrone may be associated with less nausea/vomiting and alopecia than 5-fluorouracil plus doxorubicin or epirubicin plus cyclophosphamide, but may result in more febrile neutropenia.

Evidence from uncontrolled Phase II studies suggests that vinorelbine has antitumor activity and an acceptable toxicity profile, but may be associated with leukopenia, granulocytopenia, nausea/vomiting, and constipation when used as monotherapy and neutropenia, alopecia, and nausea/vomiting when used in combination. Data from the uncontrolled studies alone are inadequate. Economic studies compared vinorelbine with taxane therapy. When comparing the cost effectiveness of vinorelbine, paclitaxel, and docetaxel one economic evaluation found vinorelbine to be the most cost-effective, one found vinorelbine to be the least expensive but the least effective, and another found docetaxel to be the most cost effective.

Recommendations

No data support the use of vinorelbine as a single agent or in combination over standard first-line chemotherapy with anthracyclines or other non-taxane containing regimens. Vinorelbine may be a possible option when an alternative agent is required.

Methods

Only RCTs and full economic evaluations were initially considered. The trials had to evaluate vinorelbine alone or combined with other agents versus systemic therapy without vinorelbine. Only trials with breast cancer patients were included. The National Institute for Clinical Excellence (NICE) requested that noncomparative Phase II studies of vinorelbine (alone or combined with other agents) as first-line therapy for advanced breast cancer be evaluated for inclusion. These data were added to update the review.

Further research/reviews required

1. Further large, well-conducted RCTs are required to investigate the use of vinorelbine alone or in combination with other chemotherapy agents.
2. Further cost effectiveness analyses of vinorelbine used in the same combinations as examined in the included trials are required.

Written by Ms Ruth Lewis, CRD, University of York, UK

INAHTA Briefs

Issue 2003/07

Title A Systematic Review and Economic Evaluation of Pegylated Liposomal Doxorubicin Hydrochloride for Ovarian Cancer

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Reference Health Technol Assess 2002; 6(23). Oct 2002. www.ncchta.org/execsumm/summ623.htm

Aim

To examine the clinical effectiveness and cost effectiveness of intravenous pegylated liposomal doxorubicin hydrochloride as second-line treatment for advanced ovarian cancer after failure of first-line platinum-based therapy.

Conclusions and results

Of 143 titles/abstracts screened for relevance, 53 articles were assessed for inclusion. Schering-Plough Ltd supplied further details of 1 RCT, 3 Phase II studies, and the economic evaluations. One international multicenter RCT comparing pegylated liposomal doxorubicin hydrochloride with topotecan was used to assess clinical effectiveness (trial 30–49, reasonably good quality). Two cost-minimization analyses based on the trial were used to assess cost effectiveness. The economic analyses used a cost-minimization design, justified by the RCT being designed to show equivalence in overall survival. However, no equivalence in Health-related QoL (HRQoL) was established. The economic evaluations were generally of high quality. Clinical effectiveness was assessed on the best available evidence, ie, data from trial 30–49 on 474 participants. Apart from minor exceptions, no significant differences were found between pegylated liposomal doxorubicin hydrochloride and topotecan. The company data showed a mean cost saving from the use of pegylated liposomal doxorubicin hydrochloride of £2657. The mean cost with pegylated liposomal doxorubicin hydrochloride was £9970 compared to £12,627 with topotecan. In the other study, the mean saving was US$2909.

Recommendations

When effectiveness was based on survival duration, pegylated liposomal doxorubicin hydrochloride had a high probability of being cost effective. However, differences between the two therapies are likely in overall HRQoL, which when expressed in quality-adjusted life-years, could alter the cost effectiveness results markedly. The choice between pegylated liposomal doxorubicin hydrochloride and other drugs for second-line ovarian cancer is difficult.

Methods

The search included 23 electronic databases, databases of ongoing research, and Internet resources up to June 2001. Bibliographies of retrieved articles and pharmaceutical company submissions were examined. Only RCTs and full economic evaluations comparing pegylated liposomal doxorubicin hydrochloride to non-pegylated liposomal doxorubicin hydrochloride regimens or standard care were included. Only second-line therapy of advanced disease after failure of first-line platinum-based therapy was considered. Clinical effectiveness data were discussed according to outcome. RCTs were discussed separately from Phase II studies. For time to event data, hazard ratios with 95% confidence intervals were presented where available. For other outcomes, relative risks were reported or calculated where appropriate and where sufficient data were available, and also presented as forest plots without pooled estimates. Economic data were presented as a summary and critique of the evidence. Additional analysis explored cost effectiveness more fully.

Further research/reviews required

Further good quality RCTs comparing pegylated liposomal doxorubicin hydrochloride with other licensed and potentially useful second-line chemotherapy agents for ovarian cancer are needed. Such studies should also generate data for cost effectiveness analysis.

Written by Dr Carol Forbes, CRD, University of York UK

INAHTA Briefs

Issue 2003/19

Proton Therapy

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Reference CEDIT Report (in French) No. 01.10/Ra1/01/Recommendation 01.10/Re-1/02

Aim

AP-HP, Institut Curie, Institut Gustave Roussy, and Centre René Huguenin, are members of an interhospital body that manages the Orsay Center for Proton Therapy (CPO: Centre de Protonthérapie d'Orsay). The General Director of the AP-HP requested advice from CEDIT. The ballistic advantages of protons enable irradiation of small areas in high doses while sparing surrounding structures. Proton therapy is part of hadron therapy, as are neutron therapy and all treatments using heavy ions with good ballistic and biological properties.

CPO was created in 1989 following the sale of a synchrocyclotron from CNRS (French research institute). Today CPO has two treatment rooms with fixed beam lines. Numerous projects could help modernize this aging installation and increase patient levels. The first stage would be quicker beam alternation between the two rooms. Setting up a third room, either with a new fixed line and a robot for patient positioning, or, preferably, an isocentric gantry, would enable better adaptation of the facilities to current needs and future development.

Worldwide, about 20 centers offer proton therapy and hadron therapy with heavy ions (most offer only proton therapy). Two of these are in France (Orsay and Nice). About 20 new centers are planned, most for proton therapy. A European network has been created to oversee 6 heavy-ion hadrontherapy projects (one to be created in Lyon).

Conclusions and results

The effectiveness of proton therapy is documented, but the rarity of indications makes it difficult to undertake systematic patient series reporting and prospective comparative randomized trials. Treatment of uveal melanomas by protons is a well-established indication (ANDEM report, 1995), particularly for posterior tumors or those astride the equator. For skull-base chordomas and chondrosarcomas, the combined use of photons and protons (protons accounting for 1/3 of the dose) provides very positive results with acceptable toxicity. Many applications attempt to benefit from the ballistic properties of protons. This benefit is particularly sought in treating tumors in children where irradiation of healthy tissue in full-growth phases can cause heavy sequellae. The modernization of CPO would cost from 0.46 € (quick alternation between rooms) to 7.17 € (a third room with an isocentric gantry). Building a new proton therapy center could cost between 25 € and 85 €, depending on the type of accelerator and number of rooms involved. Treatment costs using protons are estimated to be 2 to 3 times the cost of conventional radiotherapy.

Recommendations

CEDIT acknowledges the effectiveness of proton therapy in melanomas of the eye and skull-base chordomas and chondrosarcomas. However, the role of this new form of treatment in comparison with radio surgery remains uncertain. The proposed extension of indications needs to be validated. The excellence of the CPO is acknowledged. Its patient treatment load from France and abroad makes it the most active in Europe. To maintain performance and patient growth levels, we propose a fundamental reorganization, perhaps creating a new center for proton therapy, with it administration being more national in character.

Methods

A literature search of 3 databases, ie, MEDLINE, EMBASE, Pascal). Nine experts were interviewed on the medical benefits of this technology.

Written by Edlinger C, Fay A-F, Baffert S, Charpentier E, Fery-Lemonnier E, CEDIT, France

INAHTA Briefs

Issue 2003/21

Title **Systematic Review of Intraoperative Radiotherapy for the Treatment of Early Stage Breast Cancer**

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 27. ISBN 0 909844 48 8 Full text available: http://www.surgeons.org/asernip-s/publications.htm

Aim

To compare the safety and efficacy of breast conserving surgery and intraoperative radiotherapy (IORT) for the treatment of early stage breast cancer and standard breast conserving surgery with postoperative radiotherapy (BCT).

Conclusions and results

Studies that examined the use of IORT in early breast cancer were limited in number. Only 8 unique studies of IORT in early breast cancer could be identified. One was a randomized controlled trial of 70 patients, one was a concurrently controlled study, and the remainder were case series providing Level IV evidence. In terms of safety, the IORT studies reported only minor postoperative complications that typically resolved within a few months after surgery. In terms of efficacy, short-term followup results from the 8 IORT studies were similar to breast conserving therapy in terms of local recurrence, disease-free survival, and overall survival, but the immaturity of the current evidence base made any definitive assessment of its efficacy tenuous at best.

The ASERNIP-S review group concluded that the current evidence base on IORT and its use in early breast cancer is poor. Therefore, both the relative safety and efficacy of IORT compared to BCT cannot be determined at this time.

Methods

Relevant literature on IORT and BCT was identified by searching Ovid preMEDLINE and MEDLINE, Current Contents, Cochrane Library, EMBASE, UK National Research Register, NIH Clinical Trials.Gov database, PubMed, and the HTA Database until March 2002. Only studies of patients treated with IORT were included for review.

Written by Astrid Cuncins-Hearn et al, ASERNIP-S, Australia

A Systematic Review of Radiofrequency Ablation for the Treatment of Liver Tumors

Agency ASERNIP-S, Australian Safety and Efficacy Register of New Interventional Procedures – Surgical
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Reference ASERNIP-S Report Number 28. ISBN 0 909844 49 6. Full text available: http://www.surgeons.org/asernip-s/publications.htm

Aim

To compare the safety and efficacy of radiofrequency ablation for primary hepatocellular carcinoma or metastatic colorectal liver carcinoma, in comparison to other surgical (resection or hepatic artery infusion chemotherapy) and nonsurgical (percutaneous ethanol injection, cryotherapy, microwave coagulation therapy or laser-induced thermotherapy) therapeutic techniques, on the basis of a systematic assessment of the literature.

Conclusions and results

The evidence was limited by small sample size, short followup times, and a lack of comparability between the outcome measures. Despite the limitations of the data, RFA generally resulted in larger and more complete areas of ablation and may also be associated with higher survival rates compared to the other ablative techniques assessed in this review. Surgical resection was associated with a lower rate of recurrence and an increased time interval to recurrence compared to RFA. However, these two procedures are usually performed on different patient groups, with RFA being performed on patients who are unable to undergo surgical resection.

Evidence Rating – Average.

Safety – At least as safe compared to comparator procedure(s).

Efficacy – Efficacy cannot be determined.

Recommendations

It was recommended that surgeons practicing radiofrequency ablation for primary hepatocellular carcinoma or metastatic colorectal liver carcinoma should participate in an audit of their outcomes of RFA, preferably at a national level.

Methods

Studies were identified by searching MEDLINE, PREMEDLINE, PREMEDLINE and MEDLINE, EMBASE, Current Contents, Cochrane Library, Science Citation Index, from inception to week 18 in 2002. Clinical Trials Database (US), NHS Centre for Research and Dissemination (UK), NHS Health Technology Assessment (UK), National Research Register (UK), EORTC Protocols Database, National of Institute Health (US), and CancerLit (US) were searched on 18/4/2002. This was supplemented by hand-searching recent conference proceedings from specialist societies and conducting Internet searches. Additional articles were identified through the reference sections of the studies retrieved. Randomized controlled trials, quasi-randomized controlled trials and non-randomized comparative studies assessing patients treated with RFA and either one or more other comparative invention/s were included for review.

Written by Sutherland et al, ASERNIP-S, Australia

INAHTA Briefs

Issue 2003/24

Radiotherapy for Cancer

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Reference SBU Report 162/1-2 2003, ISBN91-87890-82-8 and ISBN91-87890-84-4
Available in Swedish (Volume 1) and in English (Volume 2) at www.sbu.se

Aim

In 1996, SBU published a scientific review of radiotherapy for cancer. This review of the recent scientific literature updates the 1996 report.

Conclusions and results

- Treatment of cancer patients includes surgery, chemotherapy, and radiotherapy, all of which are part of the concept of oncology treatment.
- In Sweden, radiotherapy for solid tumors is practiced in general agreement with the evidence presented in the scientific literature.
- The role which radiotherapy plays in the curative and palliative treatment of patients with certain types of cancer has been documented. However, the evidence must be substantially strengthened by randomized controlled trials addressing the following issues:
  1. The relative advantages and disadvantages of different types of palliative treatment.
  2. Comparative studies of radiotherapy in relation to other treatment options for certain types of cancer.
  3. Comparative studies of side effects and patients´ quality of life from different methods of radiotherapy and other types of treatment.
- More patients must be included in clinical trials to develop and improve the care and treatment of cancer.
- Curative radiotherapy is an important complement to treatment, mainly surgery, for most types of cancer addressed in this report.
- Palliative radiotherapy has increased, which is in line with the projection presented in the previous SBU report.
- The volume and capacity of radiotherapy in Sweden is now largely the same as in other Western nations.
- The direct cost for radiotherapy averages approximately 55 000 SEK for a curative treatment and approximately 17 000 SEK for a corresponding palliative series.
- It is essential to review the structure, organization, and resource utilization of oncology services. The advantages and disadvantages of centralizing treatment resources for patients with unusual types of cancer should be investigated. Such review is essential to assure access to adequately trained staff and the medical outcome of treatment. Staff requirements for cancer radiotherapy are uncertain, and it is essential to study this issue.
- Routines for quality assurance in radiotherapy should be developed and should cover the quality of care and services.
- Future studies on the effects of various treatment options for cancer patients should investigate the impact on the patient's quality of life and wellbeing. Detailed studies of immediate and long-term side effects are needed.

Method

Systematic literature review of scientific studies published during the past 5 to 10 years.

Further research/reviews required

See above.

Written by Gunilla Lamnevik, SBU, Sweden

INAHTA Briefs

Issue 2002/48

Title Efficacy of Suicide Prevention Programs for Children and Youth

Agency AHFMR, Alberta Heritage Foundation for Medical Research
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Reference ISBN-1-896956-48-3 HTA 26: Series A (English), January 2002

Aim

To assess and update the published evidence on the efficacy/effectiveness of suicide prevention programs for children and youth, and analyze the elements related to the different suicide prevention programs.

The intent was to provide guidance for decision-makers with program planning and implementation strategies, to inform program evaluations, and to direct future research.

Conclusions and results

Ten primary studies and two systematic reviews were identified that evaluated school-based suicide prevention programs. Most of the studies focused on the general student population, while a few studies initially categorized students as 'at-risk' or 'in need' before the intervention. Six out of 10 studies were rated as 'moderate' to 'strong' in relation to their methodological quality. Two out of these six studies using similar approaches for risk stratification and delivering intervention programs with similar objectives, showed consistent and encouraging evidence on the program effects such as decrease in depression, hopelessness, stress, anxiety, and anger. The findings from other studies were inconsistent. All of the primary studies published since 1991, except for one, either failed to evaluate the program for harmful effects or showed that no harmful effects were found. The potential for harmful effects indicated in this one study were not verified in a followup study.

This assessment revealed that the findings from published research are inconsistent. There is insufficient evidence to either support, or not to support, curriculum-based suicide prevention programs in schools.

Recommendations

There is a good opportunity for the Alberta Mental Health Board to sponsor and design a good quality Canadian study. As this review highlights, research on effectiveness of suicide prevention strategies is complex because of the multidimensional nature of children and adolescents. There are various school-based programs currently being offered throughout Alberta. As a first step, it is necessary to evaluate the effectiveness of these programs and then proceed with research to address the questions of highest priority.

Methods

A systematic review of the literature published from 1991 and onwards and a critical appraisal of primary quantitative studies was conducted.

The following databases were searched: PubMed, EMBASE, HealthSTAR, CINAHL, PsycINFO, ERIC database, Sociological Abstracts, EBM Reviews – Best Evidence, Web of Science, Cochrane Library.

Ten methodological or field experts externally reviewed this report.

Written by Bing Guo and Christa Harstall, AHFMR, Canada

INAHTA Briefs

Issue 2002/51

Title **Clinical and Cost Effectiveness of Donepezil, Rivastigmine, and Galantamine for Alzheimer's Disease: A Rapid and Systematic Review**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
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Reference Health Technol Assess 2001;5(1) March 2001

Aim

To provide a rapid and systematic review of the clinical effectiveness and cost effectiveness of donepezil, rivastigmine, and galantamine in the symptomatic treatment of people suffering from Alzheimer's disease.

Conclusions and results

It is difficult to quantify benefits from the evidence available in the literature. Statistically significant improvements in tests such as ADAS-cog (Alzheimer's Disease Assessment Scale cognitive subscale) may not be reflected in changes in daily life.

Donepezil – three systematic reviews and five RCTs (plus four studies from industry*) were found. Results suggest that donepezil is beneficial when assessed using global and cognitive outcome measures.

Rivastigmine – three systematic reviews and five RCTs (plus two studies from industry*) were found. Results suggest that rivastigmine is beneficial in terms of global outcome measures.

Galantamine – one systematic review and three RCTs (plus three studies from industry*) were found. Results suggest that galantamine is beneficial in terms of global, cognitive, and functional scales.

Economic implications of prescribing these drugs are uncertain. The main issue is not drug costs per se, but the impact across different sectors. Any cost savings would depend mainly on release of funds from residential care.

Recommendations

On the basis of the current evidence, the implications of using donepezil, rivastigmine, or galantamine to treat patients with Alzheimer's disease remain unclear. The main issue is whether the modest benefits seen in the outcome measures used in the trials would translate into benefits significant to patients. Ongoing research should provide valuable evidence.

Methods

A systematic review of the literature was undertaken. The main electronic databases were searched up to March/July 2000. Bibliographies of related papers were assessed for relevant studies, and experts were contacted for advice, peer review, and to identify additional published and unpublished references. Manufacturer submissions to the National Institute for Clinical Excellence were reviewed.

Studies included were systematic reviews of randomized controlled trials (RCTs) and RCTs comparing donepezil, rivastigmine, or galantamine with placebo, each other, or non-drug comparators. Economic studies that included a comparator (or placebo) and both the costs and consequences of treatment were included in the review of cost effectiveness. Non-English language studies, abstracts, and conference poster presentations were excluded. Two reviewers identified studies by independently screening study titles and abstracts, and then by examining the full text of selected studies to decide inclusion. Data extraction and quality assessment were undertaken by one reviewer and checked by a second reviewer.

Title **Clinical and Cost Effectiveness of Donepezil, Rivastigmine, and Galantamine for Alzheimer's Disease: A Rapid and Systematic Review**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
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Reference Health Technol Assess 2001;5(1) March 2001

Further research/reviews required

Future research should include: development of quality-of-life instruments for patients and their caregivers; comparisons of benefits from drugs with those from other interventions; identification of those patients likely to benefit from drug treatment; development of protocols of treatment withdrawal if not beneficial; good quality economic evaluations.

* Unpublished data, submitted as commercial in confidence

Written by Dr Andrew Clegg, Southampton HTA Centre, University of Southampton, UK

INAHTA Briefs

Issue 2002/52

Title **Systematic Reviews of the Effectiveness of Day Care for People with Severe Mental Disorders**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
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Reference Health Technol Assess 2001;5(21) July 2001

Aim

- To assess the effectiveness and feasibility of day hospital versus inpatient care for people with acute psychiatric disorders. (Review (1))
- To assess the effectiveness of Prevocational Training (PVT) and Supported Employment (SEm) relative to each other and to standard care (in hospital or the community) for people with severe mental disorders. In addition, the review examined the effectiveness of: (a) special types of PVT ("clubhouse" model) and SEm (individual placement and support model); and (b) modifications for enhancing PVT (eg, payment or psychological interventions). (Review (2))
- To assess the effectiveness of day treatment programs versus outpatient care for people with non-psychotic disorders; and to assess the effectiveness of day care centers versus outpatient care for people with severe long-term disorders. (Review (3))

Conclusions and results

- Acute day hospitals are an attractive option in situations where demand for inpatient care is high and facilities exist that are suitable for conversion. They are a less attractive option when demand for inpatient care is low and where effective alternatives already exist.
- Supported employment is more effective than prevocational training for patients suffering from a severe mental disorder who want to work. There is no evidence that prevocational training is more effective than standard community care or hospital care. The implication of these findings is that people suffering from mental disorders who want to work should be offered the option of supported employment.
- There is some limited evidence to support the use of day treatment programs for patients with anxiety or depression who have not responded to standard outpatient treatment. There is no evidence to support the use of day hospitals as day care centers.

Recommendations

The interpretation of day hospital research would be enhanced if future trials made use of the common set of outcome measures used in this review. It is important to examine how acute day hospital care can be most effectively integrated into a modern community-based psychiatric service.

Methods

Eligible studies were randomized controlled trials (RCTs). Data sources included the Cochrane Controlled Trials Register, MEDLINE, EMBASE, CINAHL, PsycLIT, and the reference lists of articles. Researchers were approached to identify unpublished studies. Trialists were asked to provide individual patient data. Data were extracted independently by two reviewers and cross-checked.

Further research/reviews required

The cost effectiveness of SEm should be examined in larger multicenter trials, both within and outside of the USA. There is a case for countries outside the USA to survey their existing VR services to determine the extent to which the most effective interventions are being offered. Also, future research should address the feasibility of day treatment programs and how far they are cost effective against other alternatives, such as outpatient cognitive behavioral therapy.

Written by Dr Max Marshall, Reader/Consultant Psychiatrist, University of Manchester, UK

INAHTA Briefs

Issue 2002/53

Title **Home Treatment for Mental Health Problems: A Systematic Review**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
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Reference Health Technol Assess 2001;5(15). July 2001. www.ncchta.org/execsumm/summ515.htm

Aim

To investigate the effectiveness of 'home treatment' for mental health problems in terms of hospitalization and cost effectiveness.

Conclusions and results

- The evidence for home treatment over inpatient treatment in terms of days in hospital was clear, but over other community-based alternatives it was inconclusive.
- There is evidence that visiting patients at home regularly and taking responsibility for both health and social care each reduce days in hospital.

Recommendations

The need for further studies is a clear, particularly in the UK. The evidence base for home treatment compared with other community-based services is not strong, although it does show that home treatment reduces days spent in hospital compared with inpatient treatment. Therefore, it is no longer recommended that home treatment be tested against inpatient care, or that small, localized studies replicate existing, more highly powered studies.

Methods

'Home treatment' was defined as a service that enables mental health patients to be treated outside hospital as far as possible and remain in their usual place of residence. The review was based on Cochrane methodology, but nonrandomized studies were included if they compared two services; these were only analyzed if they provided evidence of the groups' baseline clinical comparability. In total, 91 studies were found, conducted over a 30-year period. Most (87) focused on people with psychotic disorders. Authors of all the studies were followed up for data on service components, sustainability of programs, and service utilization. Economic evaluations among the studies found were reviewed against established criteria. However, the 22 studies that included economic evaluations provided little conclusive evidence about cost effectiveness. A three-round Delphi exercise ascertained the degree of consensus among expert psychiatrists about the components of community-based services that enable them to treat people outside the hospital. This was used to identify components for inclusion in the followup questionnaire.

A comparative analysis compared experimental to control services in terms of reducing hospital days. It analyzed all studies with available data, divided into 'inpatient-control' and 'community-control' studies, and tested for associations between service components and difference in hospital days. An analysis of experimental services analyzed only experimental service data and tested for associations between service components and hospital days.

Further research/reviews required

A centrally coordinated research strategy, with attention to study design, is recommended. Studies should include economic evaluations that report health and social service utilization. Service components should be collected and reported for experimental and control services. Studies should be designed with adequate power and longer followup and use comparable outcome measures to facilitate meta-analysis. Research protocols should be adhered to throughout the studies. It may be advisable that independent researchers conduct studies in future.

Written by Professor Tom Burns, Community Psychiatry, St George's Hospital Medical School, London, UK

INAHTA Briefs

Issue 2002/55

Title **Randomized Controlled Trial of Non-directive Counseling, Cognitive-behavior Therapy and Usual General Practitioner Care in the Management of Depression as well as Mixed Anxiety and Depression in Primary Care**

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

Reference Health Technol Assess 2000;4(19). End of 2000. www.ncchta.org/execsumm/summ501.htm

Aim

The determine the clinical and cost effectiveness of usual general practitioner (GP) care compared with two types of brief psychological therapy (non-directive counseling and cognitive-behavior therapy) in managing depression and mixed anxiety and depression in the primary care setting.

Conclusions and results

- Non-directive counseling and cognitive-behavior therapy were both more effective clinically than usual GP care after 4 months (short term) treatment, but at 12 months the patients in all three groups had improved to the same extent.
- Psychological therapy provided in primary care was found to be cost effective in reducing depressive symptoms in the short term, but the benefits did not endure over the long term.
- No differences in direct or indirect costs among the three treatments were observed at either 4 or 12 months. The additional costs associated with providing practice-based psychological therapy were recouped due to savings in visits to primary care, psychotropic medication, and other specialist mental health treatments.

Recommendations

Based on this study's observed equivalence in the clinical and economic outcomes of usual GP care compared with on-site psychological therapies in primary care, the commissioners of psychological services would be justified in considering additional factors when determining service configuration. These factors could include patient satisfaction, preferences of practitioners, and staff availability.

Methods

The design was principally a pragmatic randomized controlled trial, but was accompanied by two additional allocation options allowing patient preference: a specific choice of treatment (preference allocation) and randomization between the psychological therapies only. Of the 464 patients allocated to the three treatments, 197 were randomized among the three treatments, 137 chose a specific treatment, and 130 were randomized between the psychological therapies only. The patients underwent followup assessments at 4 and 12 months.

Further research/reviews required

(1) Long-term outcome for patients treated with psychological therapies; (2) Relationship between the quality of psychological therapies and patient outcomes; (3) Effectiveness of other therapies, different modes of treatment administration, and the comparative effectiveness of psychological and pharmacological treatments; (4) Statistical techniques and methods for dealing with issues such as missing data and clustering of patients around therapists, GPs, and practices; (5) Psychological and social processes involved in patient preferences and how these relate to other psychological processes of relevance to controlled trial research, eg, placebo and Hawthorne effects; (6) Content and interpretation of 'usual GP care'; (7) Patients who refuse to consider participation in trials, even when treatment preference arms are available.

Written by Professor Michael King, Royal Free & University College Medical School, London, UK

INAHTA Briefs

Issue 2002/80

Title **Novel Antipsychotics for Patients with Bipolar Disorder: A Systematic Review**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
865 Carling Avenue, Suite 600, Ottawa, ON, K1S 5S8 Canada;
tel: +1 613 226 2553, fax: +1 613 226 5392, http://www.ccohta.ca

Reference CCOHTA Technology Report, Issue 16, July 2001. ISBN 1-894620-05-4 (print); ISBN 1-894620-06-2 (online): http://www.ccohta.ca/ccohta_production/entry_e.html

Aim

To assess the efficacy of four novel antipsychotic drugs (olanzapine, risperidone, quetiapine, and clozapine) both as monotherapy and as add-on therapy for acute and maintenance treatment of bipolar disorder, as compared to each other, and to classic antipsychotics.

Conclusions and results

Of 58 potentially relevant studies identified, eight randomized controlled trials met the inclusion criteria. Four of these studies were found to be of moderate quality, and four of low quality. Novel antipsychotic drugs were used as monotherapy for the acute treatment of mania in four studies; the other four studies considered novel antipsychotics as add-on therapy to regular treatment. In two studies, olanzapine was shown to be more effective than placebo for treating acute attacks of mania in patients with bipolar disorder. Along with a battery of other continuous clinical assessment measures, the Young Mania Rating Scale was used to measure improvement in primary clinical outcome. No clear advantage was observed in trials that compared olanzapine compared to lithium. Information on the efficacy of novel antipsychotics other than olanzapine as either monotherapy or add-on therapy of acute mania is limited and is not transparent. Studies show no significant difference between novel antipsychotics and traditional agents in the incidence of extrapyramidal side effects. At this stage, any conclusion regarding the costs and benefits of using novel antipsychotics over traditional therapies is premature.

Recommendations

Because of the limited information available about the use of novel antipsychotics to treat bipolar disorders, clinicians and patients should carefully weigh evidence concerning benefits and side effects when considering this therapy.

Methods

Clinical trials in which a novel antipsychotic drug was compared prospectively with placebo or with another agent for treating bipolar disorder were systematically reviewed. The Jadad scale was used to assess the quality of the included studies. Extracted data were analyzed using Cochrane Review Manager.

Further research/reviews required

Further analysis awaits new information from other trials that will soon be completed in this rapidly changing field.

Written by Shukla VK and McAuley L, CCOHTA, Canada

INAHTA Briefs

Issue 2002/81

Title **Novel Antipsychotics for Patients With Attention-Deficit Hyperactivity Disorder: A Systematic Review**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
865 Carling Avenue, Suite 600, Ottawa, ON, K1S 5S8 Canada;
tel: +1 613 226 2553, fax: +1 613 226 5392, http://www.ccohta.ca

Reference CCOHTA Technology Report, Issue 17, July 2001. ISBN 1-894620-07-0 (print); ISBN 1-894620-08-9 (online): http://www.ccohta.ca/ccohta_production/entry_e.html

Aim

- To assess evidence regarding the efficacy and safety of using the novel antipsychotic drugs (olanzapine, risperidone, and quetiapine) to treat children and adolescents with attention-deficit/hyperactivity disorder (ADHD)
- To assess the financial implications, in terms of the Canadian healthcare system, of adopting these drugs for treating ADHD.

Conclusions and results

A formal quantitative meta-analysis could not be performed due to lack of data. The literature review identified no randomized controlled trials or comparative trials assessing efficacy and/or safety. Five noncomparative studies described 54 ADHD patients. Nine secondary evidence studies were found involving 59 patients: these included studies that either reported data from patients who had ADHD as a secondary indication, or did not clearly present separate results for patients having only ADHD.

- *Efficacy:* As the studies considering the use of risperidone and olanzapine (either alone or as an add-on therapy with methylphenidate) are not controlled or comparative, no conclusions can be drawn concerning their efficacy for treating children and adolescents with ADHD. No published data regarding the use of quetiapine for this indication were identified.
- *Safety:* In the studies reviewed, the most common adverse drug reaction reported was sedation, which usually dissipated either on its own or after a dose reduction. Extrapyramidal effects were report in 4% of the patients studied. Also, many children gained weight.
- *Cost:* According to this analysis, adopting these newer drugs would require a substantial increase in drug expenditures by the Canadian healthcare system without good evidence of clear benefits.

Methods

Clinical efficacy, safety, and cost issues were evaluated using a structured approach. First, pharmacological treatment of ADHD was summarized using a qualitative review of the literature based on the principles of critical appraisal and evidence-based medicine. Second, acceptable standard therapies and regimens were identified, and the efficacy and safety of novel antipsychotics was compared with those of standard therapies. Third, a model was developed for estimating the cost impact in Canada of using novel antipsychotics in place of standard therapies to treat ADHD. Rather than a full economic evaluation, however, the only resource examined was the cost of medication.

Further research/reviews required

When further clinical data become available, formal pharmacoeconomic analyses may be warranted to clarify the overall balance between costs and outcomes, especially for risperidone.

Written by Einarson TR and Iskedjian M, CCOHTA, Canada

INAHTA Briefs

Issue 2002/82

Behavioral Interventions for Preschool Children With Autism

Agency CCOHTA, Canadian Coordinating Office for Health Technology Assessment
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tel: +1 613 226 2553, fax: +1 613 226 5392, http://www.ccohta.ca

Reference CCOHTA Technology Report, Issue 18, August 2001. ISBN 1-894620-11-9 (print);
ISBN 1-894620-12-7 (online): http://www.ccohta.ca/ccohta_production/entry_e.html

Aim

- To summarize the evidence and expert opinions regarding behavioral therapy for preschool children with autism or pervasive developmental disorders (PDD)
- To describe current practice regarding behavioral therapy for preschool children with autism or PDD
- To analyze legal case findings
- To summarize key factors that influence the provision of services in Canada.

Conclusions and results

Based on the secondary reviews evaluated, only a few controlled primary studies regarding the efficacy of behavioral interventions have been published. Most of these studies have methodological flaws that make interpretation of results difficult. Although limited, evidence suggests that preschool children with autism show cognitive and functional improvement when they receive behavioral intervention with applied behavioral analysis for about 20 hours per week or more. However, it is unclear which subset of children with autism derive the most benefit, which components of therapy are integral to positive outcomes, whether similar results would be observed in older children, whether there are definable long-term functional benefits, or whether reported gains in IQ translate into happier people with greater functioning in the community. Legal decisions to date offer little guidance on how Canadian courts are likely to resolve claims for provincial funding of services. Key factors that influence the delivery of services in Canada include universal health care, the shift to community-based programming and integration, and the evolution of the diagnostic classification system. It is important for policy makers, program developers and clinical researcher to consider identifying pre-treatment characteristics of those receiving therapy, measuring treatment fidelity, evaluating progress in therapy to determine whether therapy is or continues to be of benefit, and comparing the value of early intensive behavioral therapy to other early interventions for autism.

Methods

Published literature reporting on autism and behavioral interventions was obtained by searching several databases and the Internet, and hand searching selected journals and documents and the bibliographies of selected papers. Retrieval was primarily limited to secondary reviews. Information about Canadian initiatives regarding behavioral interventions and current service provision was retrieved through contacts identified in a survey previously commissioned by the British Columbia Ministry for Children and Families. Contacts with the Canadian Autism Intervention Research Network provided further information.

Further research/reviews required

Future research would benefit from:

- Using standard measures for assessing progress
- Including long-term evaluation of progress
- Comparing therapies using sound study design, including an adequate control group
- Focusing on determining which therapy, at what level of intensity, works best for which subset of children with autism.

Written by McGahan L, CCOHTA, Canada

INAHTA Briefs

Issue 2002/98

Title A Systematic Review and Economic Evaluation of Computerised Cognitive Behaviour Therapy for Depression and Anxiety

Agency NCCHTA, National Coordinating Centre for Health Technology Assessment
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom
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Reference Health Technol Assess 2002; 6(22). Oct 2002. www.ncchta.org/execsumm/summ622.htm

Aim

To assess the clinical effectiveness of computerized cognitive behavior therapy (CCBT) in treating anxiety, depression, and phobias and to compare the cost effectiveness of CCBT with cognitive behavior therapy (CBT) by conventional methods and with treatment as usual (TAU).

Conclusions and results

Sixteen studies met the inclusion criteria, whereof 11 were randomized controlled trials (RCTs) and 5 were pilot studies or cohort studies. Quality of the studies ranged from poor to moderate. An additional 3 studies addressed CCBT as a treatment adjunct for therapist-led CBT (TCBT). Thirteen papers were identified for the cost effectiveness review, but none dealt specifically with CCBT. Some evidence of poor-to-moderate quality shows that CCBT is as effective as TCBT in clinically depressed, anxious, or phobic outpatient and primary care populations. Limited evidence of poor-to-moderate quality shows that CCBT is more effective than TAU in clinically depressed, anxious, or phobic outpatient and primary care populations. CCBT may be as effective or less effective than bibliotherapy, but no evidence shows it to be more effective. CCBT may form a useful component of a stepped-care program. Some evidence supports the effectiveness of Beating the Blues and FearFighter.

No studies gave an economic analysis. The only economic evidence appeared in the 4 sponsor submissions. The data were critically reviewed and used in modeling. CCBT using Stresspac was found to cost more, but patient outcomes were not superior to TAU. The cost per patient of Cope was less than the corresponding costs for CBT and drug therapy. CCBT using FearFighter was stated to be less costly than CBT and drug therapy. Data in the Calipso submission were insufficient to judge the efficiency of Calipso relative to alternative treatments. Economic analysis of CCBT using Beating the Blues indicated that, compared to TAU, Beating the Blues is a cost-effective way to treat patients with anxiety/depression. The report presents estimated annual costs and costs per QALY.

Recommendations

Limited evidence of poor-to-moderate quality shows that CCBT may be effective in treating depression, anxiety, and phobias. The evidence for CCBT is uncertain as the studies varied widely in setting, patient populations, comparators, and outcome measures.

Methods

A systematic literature review identified all studies describing trials of CCBT either alone or as part of a package and either via a computer interface or over the telephone with a computer-led response. Databases were searched from 1966 to September 2001. The cost-effectiveness review included a review of economic evidence and a modeling exercise. The effect of CCBT was estimated in terms of quality-adjusted life-years (QALYs).

Further research/reviews required

1) Determine the level of therapist involvement needed to produce optimal outcomes for patients. 2) Studies within the general practice setting. 3) Efforts to include patients with comorbidities routinely treated within GP care. 4) Identify the position of CCBT in a stepped-care program and its relationship to other efforts to increase access to CBT and psychological therapies. 5) Include appropriate comparison groups in studies, eg, bibliotherapy and other self-help approaches that reduce therapist time. Further suggestions in the full report.

Written by Dr Eva Kaltenthaler, ScHARR, University of Sheffield, UK

INAHTA Briefs

Issue 2003/01

Title Pharmacotherapeutic Interventions in Drug Addiction

Agency GR, Health Council of The Netherlands (Gezondheidsraad)
PO Box 16052, 2500BB The Hague, The Netherlands;
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Reference Publication no.2002/10. ISBN: 90-5549-439-9. Full text available at www.gr.nl (in Dutch, with Executive Summary in English).

Aim

To inform the Minister of Health, Welfare and Sport on the state of the art in the pharmacotherapeutic treatment of drug addiction.

Conclusions and results

Drug addiction is a relapsing brain disease with a tendency towards chronicity. Therefore, treatment of drug addiction should be considered as a part of the medical domain. However, it should be noted that biological, psychological, and sociocultural factors all play a role in the onset and course of the disease.

For the treatment of heroin addiction, more effective pharmacological interventions are becoming available – although not all are currently available in the Netherlands (eg, buprenorphine, lofexidine). For the treatment of cocaine addiction, no effective pharmacotherapies are currently known. In polydrug addicts, pharmacotherapeutic interventions should be directed at the various addictions separately.

Pharmacotherapy can, in many cases, be no more than part of an integrated treatment approach in which psychosocial interventions are also important. Long-term continuation of treatment is usually indicated.

Recommendations

- Medical schools should pay attention to practical aspects in the treatment and management of addicts. The organization and workforce of addiction treatment services should comply with the demands that are placed on healthcare services.
- Public information campaigns about addiction and the treatment options for addicts can contribute to the destigmatization of this patient category.
- Research should be directed at the physiological and cognitive processes (conditioning, memory) that constitute the basis for addiction.

Methods

Systematic review of published scientific literature by an expert committee, combined with clinical knowledge based on experiences in the Netherlands. Peer review of draft report.

Written by Marie Anne Goppel, GR, The Netherlands

INAHTA Briefs

Issue 2003/04

Title **Clinical Effectiveness and Cost Consequences of Selective Serotonin Reuptake Inhibitors in the Treatment of Sex Offenders**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
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Reference Health Technol Assess 2002; 6(28). Nov 2002. www.ncchta.org/execsumm/summ628.htm

Aim

Systematically review the evidence on the clinical effectiveness and cost consequences of using selective serotonin reuptake inhibitors (SSRIs) in treating sex offenders.

Conclusions and results

The effectiveness review included 9 case series, but methodological quality was generally poor: only 2 enrolled consecutive patients, only 1 was prospective, and only 2 stated that participants were sex offenders. Followup was too short to assess long-term consequences on re-offence. Two-thirds of the studies reported some significant changes from baseline in the frequency of masturbation and the intensity of deviant fantasies. However, the scales used to assess the outcomes were subjective, and the validities not stated. This, along with openness to bias in the study designs, suggest that the results should be approached with caution. The search identified no cost effectiveness studies on SSRI treatment of sex offenders. Three cost-benefit analyses assessed the efficiency of treatment of sex offenders in general. The main costs associated with SSRI treatment were drug costs, estimated at £750/annum (max.). Optimal treatment duration was a source of uncertainty concerning the total cost of SSRI treatment. Considering the main identifiable costs and consequences indicated that assessing the efficiency of SSRIs is overly speculative, particularly in the absence of valid information on their effectiveness and the magnitude of any effect on recidivism.

Recommendations

Although SSRIs are clearly of potential importance in treating sex offenders, there is great uncertainty about their effectiveness. Hence, further research should be the main priority.

Methods

Bibliographic databases, including MEDLINE, EMBASE, and PsycINFO were searched up to Oct. 2001, supplemented by searching the Internet, recent conference abstracts, and the National Criminal Justice Reference System. Enquiries were made to pharmaceutical companies and experts. Inclusion criteria were predefined and allowed many research designs, including case series. Quality was assessed on criteria from the Cochrane Collaboration. Analysis was qualitative. Economic analysis involved systematic review of past economic evaluations, collation of cost information, and a cost-consequences analysis.

Further research/reviews required

A double-blind, randomized controlled trial is needed, preferably involving several centers, to compare best treatment plus SSRIs with best treatment plus placebo. Psychometric methods and/or measures of sexual arousal to assess the progress of sex offenders over at least 2 years may need to be used. The need to assess the cost effectiveness of SSRIs should be anticipated in future research. Decision analytic modeling may contribute directly and help further define information to which estimates of cost effectiveness are sensitive. Since sex offences are not a uniform entity, future research should distinguish among different types. The relationship between benefit and cost of SSRI treatment may vary considerably.

Written by Dr Yaser Adi, WMHTAC, University of Birmingham, UK

INAHTA Briefs

Issue 2002/41

Title **Vertebral Axial Decompression (VAX-D) Therapy for Chronic Low Back Pain, April 2001**

Agency **MSAC, Medicare Services Advisory Committee**
Commonwealth Department of Health and Ageing,
GPO Box 9848 Canberra ACT 2601 Australia;
tel: +61 2 6289 6811, fax: +61 2 6289 8799, http://www.msac.gov.au

Reference MSAC Application number 1012. Assessment report ISSN 1443-7120

Aim

To assess the safety and effectiveness of vertebral axial decompression (VAX-D) therapy and under what circumstances public funding should be supported for this service.

Conclusions and results

Safety: Detailed evidence on the safety and complication rates of the VAX-D table is lacking.

Effectiveness: For patients with radiculopathy or radicular pain associated with a herniated intervertebral disc, there is some evidence to suggest that surgical discectomy is more effective than VAX-D therapy at relieving pain in the short to medium term. No comparisons can be made between these two therapies in this patient group over the long term (ie, 10 years). For other patient groups (ie, patients with radiculopathy or radicular pain associated with degenerated intervertebral discs, and patients with non-specific low back pain) the evidence is insufficient to make any conclusions regarding the relative effectiveness of VAX-D therapy.

Cost effectiveness: No evidence based conclusions can be drawn regarding the cost effectiveness of VAX-D therapy in any patient group. However, it is likely that discectomy is more cost effective than VAX-D therapy for treating patients with radiculopathy or radicular pain associated with herniated intervertebral discs.

Recommendations

As there is currently insufficient evidence pertaining to the effectiveness of VAX-D therapy, MSAC recommended that public funding should not be supported at this time for this procedure.

Methods

The applicant requested that VAX-D therapy be subsidized for the treatment of chronic low back pain resistant to conservative treatment. Accordingly, a review of the medical literature was limited to evidence of second-line treatment administered to patients with low back pain of at least 3 months duration. Three distinct patient groups were identified (see table below), and each of these groups was associated with a particular treatment. In this review, the most common conservative treatment for non-specific low back pain was defined as oral analgesics or non-steroidal anti-inflammatory drugs (NSAIDs), with or without physiotherapy. In addition to evaluating the evidence pertaining to VAX-D therapy in each of the three patient groups, the evaluation included a review of evidence related to each of the three comparator treatments.

INAHTA Briefs

Issue 2002/41

Title: Vertebral Axial Decompression (VAX-D) Therapy for Chronic Low Back Pain, April 2001

Agency MSAC, Medicare Services Advisory Committee
Commonwealth Department of Health and Ageing,
GPO Box 9848 Canberra ACT 2601 Australia;
tel: +61 2 6289 6811, fax: +61 2 6289 8799, http://www.msac.gov.au

Reference MSAC Application number 1012. Assessment report ISSN 1443-7120

Patient group	Patient description	Most common treatment (Comparator)
1	Radiculopathy or radicular pain caused by–herniatedintervertebral disc, unresponsive to conservative therapy	Discectomy or microdiscectomy
2	Radiculopathy or radicular pain caused caused by degenerated intervertebral disc, unresponsive to conservative therapy	Laminectomy, with or without fusion, or laminotomy
3	Chronic non-specific low back pain, unresponsive to conservative therapy	Ongoing conservative treatment

One prospective, controlled clinical trial of VAX D therapy was identified, which was conducted in patients corresponding to Patient Group 1. This study suffers from several significant design problems and was conducted in a relatively small number of patients. The remaining evidence is from quasi-experimental nonrandomized studies and case series conducted predominantly in mixed patient populations.

Produced by Dr Sarah Norris, M-Tag Pty Ltd, Australia

INAHTA Briefs

Issue 2002/58

Title A Systematic Review of the Effectiveness and Cost Effectiveness of Metal-on-metal Hip Resurfacing Arthroplasty for Treatment of Hip Disease

Agency NCCHTA, National Coordinating Centre for Health Technology Assessment
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom
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Reference Health Technol Assess 2002;6(15). June 2002. www.ncchta.org/execsumm/summ615.htm

Aim

To assess the effectiveness and cost effectiveness of metal-on-metal hip resurfacing arthroplasty compared with watchful waiting, total hip replacement (THR), osteotomy, arthrodesis, and arthroscopy of the hip joint.

Conclusions and results

- Evidence with which to assess the benefits of metal-on-metal hip resurfacing arthroplasty compared with the other interventions was limited. Over a 3-year followup period, 0% to 14% of patients who received metal-on-metal hip resurfacing arthroplasty required a revision. In comparison, those managed by watchful waiting avoided an immediate operation, but had a 30% chance of an operation over 3 years. THR was associated with revision rates of 10% or less over a 10-year followup period, while revision rates for osteotomy were, between 2.9% and 29% over a period of 10 to 17 years. The estimated revision rates for patients receiving arthroscopy were slightly higher than those for metal-on-metal hip resurfacing arthroplasty. No data were identified reporting revision rates following arthrodesis.
- Patients who underwent metal-on-metal hip resurfacing arthroplasty experienced less pain than those who were managed by watchful waiting, with data from one study suggesting that 91% of patients were pain free at 4 years. This compares with an estimate of 84% at 11 years for THR, 22% for arthrodesis at 8 years, and fewer patients pain free following arthroscopy. Similar data for osteotomy were not available.
- The cost of metal-on-metal hip resurfacing arthroplasty for a patient aged under 65 years was estimated to be £5515 (2000/2001). Other estimated intervention costs were: £4195 for THR, £6027 for revision THR, £951 for arthroscopy, and £2731 for osteotomy. The annual cost per patient for watchful waiting was estimated at £642.
- Results for patients under age 65 years at treatment showed that metal-on-metal hip resurfacing arthroplasty was dominated (ie, more costly with the same or less benefits) by THR, owing to the assumptions about metal-on-metal revision rates and the lower cost of THR. Metal-on-metal hip resurfacing arthroplasty dominated (ie, generated cost savings and the same or more benefits) the watchful waiting alternative within a 20-year followup period.

Recommendations

The low quality of life experienced by young people with hip disease who have been advised to delay undertaking THR means that if metal-on-metal hip resurfacing arthroplasty can be proven (1) to have lower revision rates than THR over an extended period and (2) to result in better outcomes from subsequent THR, then such a procedure could possibly be considered cost effective or even dominant. If metal-on-metal revision rates are sufficiently below those for primary THR, then metal-on-metal hip resurfacing arthroplasty could possibly be judged cost effective for older people who are more active and may outlive a primary THR.

INAHTA Briefs

Issue 2002/58

Title **A Systematic Review of the Effectiveness and Cost Effectiveness of Metal-on-metal Hip Resurfacing Arthroplasty for Treatment of Hip 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 2002;6(15). June 2002. www.ncchta.org/execsumm/summ615.htm

Methods

A structured search of electronic databases, websites and relevant audit databases between 1990 and 2001 used free text terms to identify potentially relevant papers evaluating metal-on-metal hip arthroplasty, osteotomy, arthrodesis, and arthroscopy.

A search was also carried out for randomized controlled trials (RCTs) of THR and systematic reviews of RCTs for THR. A Markov model comparing the comparators was developed, using the results of the review of effectiveness data together with data on costs from previous studies.

Further research/reviews required

All the limited data available and results obtained by modeling these data indicate that metal-on-metal hip resurfacing arthroplasty merits further investigation. The lack of any controlled studies comparing it with any of the comparators (but principally watchful waiting and THR) should be addressed in trials with long-term followup. Any comparison with watchful waiting is hampered by the absence of long-term data on metal-on-metal hip resurfacing arthroplasty, health outcome data following revision, and virtually any data on watchful waiting. Research is required to define more clearly what watchful waiting entails and how its outcomes compare with the other comparators, especially metal-on-metal hip resurfacing arthroplasty.

Written by Mr Luke Vale, Health Economics Research Unit & Health Services Research Unit, University of Aberdeen, UK

INAHTA Briefs

Issue 2002/77

Title A Systematic Review of Effectiveness and Economic Evaluation of New Drug Treatments for Juvenile Idiopathic Arthritis: Etanercept

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tel: +44 2380 595586, fax: +44 2380 595639, http://www.ncchta.org/execsumm/summ617.htm

Reference Health Technol Assess 2002;6(17). Aug 2002

Aim

To review the background on juvenile idiopathic arthritis (JIA), including epidemiology, current and emerging therapy options, and impact of disease on individuals and health services.

To systematically review the clinical benefits and hazards of the anti-TNF agent etanercept in JIA compared with currently available treatments and to review economic evidence on the cost effectiveness of this agent compared with other treatment options.

Conclusions and results

One high quality RCT of etanercept in patients with methotrexate-resistant JIA was identified. Compared to placebo, etanercept reduces relapse rates in children and young people. In an open phase, 51 of 69 children (74%) improved on etanercept (30% response based on 6 outcome variables). In the randomized phase, 28% of the etanercept arm experienced disease flare compared to 81% of the placebo arm. At the end of the study, 20 (80%) of the etanercept double-blind phase group compared to 9 (35%) of the placebo group still met the definition of improvement ($p < 0.01$). 18 (72%) compared to 6 (23%) met the definition of improvement set at 50% improvement, and 11 (44%) compared to 5 (19%) met the definition of improvement set at 70%. The trial continued with an open-label extension phase. At 20 months, 83% of all patients had achieved a 30% response, 78% a 50% response, and 63% a 70% response. Adverse events occurred infrequently and were comparable to placebo. The manufacturer's submission included a cost-utility analysis. No other economic analyses were found. Sensitivity analyses ranged between £3900 (cost offsets assumption changed to exclude nursing home and home help costs, but to include indirect costs) and £34,000, though changes in most variables did not make a great difference. The validity and accuracy of this estimate must be questioned due to insufficient knowledge about the outcomes of JIA, particularly the quality of life and long-term outcomes; the model was constructed for rheumatoid arthritis in adults; the strong assumptions used were not based on evidence; and technical problems were identified with the model.

Recommendations

Given the novel biological action of etanercept, long-term followup is desirable and required by regulatory agencies to detect unexpected adverse events. No evidence compares etanercept with other treatments in this patient group. Safety concerns and relative lack of efficacy would place ethical constraints on trials of relative effectiveness. The effectiveness of etanercept in treating other forms of JIA, including psoriatic and enthesitis arthritis, is unknown.

Methods

A systematic review of effectiveness was undertaken. Databases (MEDLINE, EMBASE, Science Citation Index, Cochrane Library) were searched from 1966 through 2000. RCTs comparing etanercept with any agent in JIA and other rheumatic childhood diseases were considered. Manufacturer and sponsor submissions to the National Institute for Clinical Excellence (NICE) were reviewed. For the health economic and cost studies, the databases MEDLINE, DARE, and UK health economic websites were searched from 1997 through February 2001, and manufacturer and sponsor submissions to NICE were reviewed.

Further research/reviews required

The effectiveness of etanercept in the treatment of other forms of JIA including psoriatic and enthesitis arthritis is unknown. International trials would be required due to the rarity of these conditions. Using etanercept earlier in the disease process and in less severe disease might yield greater health gains. Trials are required to test these hypotheses.

Written by Dr Carole Cummins, WMHTAC, University of Birmingham, UK

INAHTA Briefs

Issue 2002/87

Title The Cost Effectiveness of Celecoxib and Rofecoxib in Patients with Osteoarthritis or Rheumatoid Arthritis

Agency CCOHTA, Canadian Coordinating Office for Health Technology Assessment
865 Carling Avenue, Suite 600, Ottawa, ON, K1S 5S8 Canada;
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Reference CCOHTA Technology Report, Issue 23, February 2002. ISBN 1-894620-35-6 (print); ISBN 1-894620-36-4 (online): http://www.ccohta.ca/ccohta_production/entry_e.html

Aim

This study evaluates the cost effectiveness of using two COX2 nonsteroidal antiinflammatory drugs (NSAIDS) versus the "traditional" NSAIDS to treat patients with osteoarthritis (OA) or rheumatoid arthritis (RA) who are not on low-dose aspirin for the prevention of cardiovascular (CV) disease:

– Celecoxib, in comparison to diclofenac and ibuprofen

– Rofecoxib, in comparison to naproxen (rofecoxib is currently not approved in Canada for treating RA).

Conclusions and results

While rofecoxib and celecoxib were found to be cost effective in high-risk patients (ie, those with proven histories of upper gastrointestinal (UGI) events), these drugs do not provide cost-effective therapy in patients who are at average risk (ie, those who have not experienced UGI events). Also, the drugs are not cost effective in a population with a typical mix of average-risk and high-risk patients. However, both drugs were shown to provide cost effective therapy for older patients without additional risk factors: rofecoxib for patients over the age of 76, and celecoxib for patients over 81. If a low-priced proton pump inhibitor becomes available, however, these drugs may no longer be cost effective in comparison to therapy that combines a "traditional" NSAID with a proton pump inhibitor.

Methods

A decision analysis model was constructed where UGI and CV events were modeled as a consequence of NSAID intake. The model used the Markov technique and extrapolated clinical trial results over 5 years. Major events included:

– Clinical UGI events (symptomatic ulcer)

– Complicated UGI events (perforation, obstruction, or major bleeding)

– Non-fatal myocardial infarctions.

Key estimates of event rates and the relative effectiveness of COX2 NSAIDS in reducing these rates were based on data from two key clinical trials: the Vioxx® Gastrointestinal Outcomes Research (VIGOR) study and the Celecoxib Long-Term Arthritis Safety Study (CLASS). Remaining probability estimates were obtained though a comprehensive literature search. Utility estimates for arthritis health states that are complicated by UGI events were gathered through a separate study of 60 randomly selected members of the general public. Cost estimates were obtained from provincial databases. Incremental cost effectiveness was calculated from the perspective of the Ontario Ministry of Health in 1999 dollars. The sensitivity of the cost effectiveness results to changes in individual variables was tested, as was the effect of an additional risk factor.

Written by Maetzel A, Krahn M, Naglie G, CCOHTA, Canada

INAHTA Briefs

Issue 2002/99

Title A Systematic Review of the Effectiveness of Interventions Based on a Stages-of-change Approach to Promote Individual Behaviour Change

Agency NCCHTA, National Coordinating Centre for Health Technology Assessment
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Reference Health Technol Assess 2002; 6(24). Nov.2002 www.ncchta.org/execsumm/summ624.htm

Aim

To systematically assess the effectiveness of interventions using a stage-based approach to bring about positive changes in health-related behavior.

Conclusions and results

The review included 37 RCTs. Three studies evaluated interventions aimed at prevention (2 for alcohol consumption and 1 for cigarette smoking). Interventions in 13 trials targeted smoking cessation, 7 studies evaluated interventions aimed at promoting physical activity, and 5 studies evaluated interventions aimed at dietary change. Six trials evaluated interventions aimed at multiple lifestyle changes. Two studies evaluated interventions aimed at promoting mammography screening. One study evaluated an intervention aimed at promoting treatment adherence. Methodological quality was mixed. The main problems were lack of detail on the methods used to produce true randomization; lack of blinding of participants, outcome assessors, and care-providers; and failure to use intention-to-treat analysis. The main issue with the quality of implementation was lack of information on the validity of the instrument used to assess an individual's stage of change. The full report gives more detailed information on the results.

Recommendations

Little evidence suggests that stage-based interventions are more effective than non-stage-based interventions, no intervention, or usual care. There is no apparent relationship between the methodological quality of the study, the targeted behavior, or quality of the implementation and effectiveness of the stage-based intervention. Given the limited evidence on the effectiveness of interventions tailored to the stages-of-change approach, practitioners and policy makers need to recognize that this approach has a status which appears to be unwarranted when it is evaluated in a systematic way.

Methods

Numerous electronic databases were searched from inception to May 2000. Other Internet searches were done using various search engines. The bibliographies of retrieved references were scanned for further relevant publications. Authors of abstracts appearing in conference proceedings identified by the literature search were contacted for further information. Two independent reviewers assessed full papers against the review selection criteria. Disagreements were resolved through discussion. Information on the implementation of each intervention and training of relevant professionals was also recorded. Each trial was assessed against a comprehensive checklist for methodological quality and quality in implementing the intervention. Quality was assessed by one reviewer and checked by a second, with disagreements resolved by discussion.

Further research/reviews required

There is a need for well-designed and appropriately implemented RCTs that tailor interventions derived from accurate stage measurement, and which involve frequent reassessment of readiness to change to permit evolving, stage-specific, interventions.

Written by Dr Rob Riemsma, CRD, University of York, UK

INAHTA Briefs

Issue 2003/09

Title The Effectiveness of Infliximab and Etanercept for the Treatment of Rheumatoid Arthritis: A Systematic Review and Economic Evaluation

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Reference Health Technol Assess 2002; 6(21). Oct 2002. www.ncchta.org/execsumm/summ621.htm

Aim

To review the evidence for the clinical effectiveness and cost effectiveness of etanercept and infliximab, agents that inhibit tumor necrosis factor alpha (TNFa) when used in treating rheumatoid arthritis (RA) in adults and referred to as anti-TNFs.

Conclusions and results

Six randomized controlled trials (RCTs) of etanercept in patients with RA were identified (1710 patients, of whom 1230 received etanercept). Five of these compared etanercept to placebo; one compared etanercept to methotrexate. Four RCTs of infliximab in patients with RA were identified (630 patients, of whom 497 received infliximab). All compared infliximab to placebo. Compared to placebo, both etanercept and infliximab improve outcomes in adults with RA. Only one trial directly compared a disease-modifying, anti-rheumatic drug (DMARD) with an anti-TNFa agent. This study failed to show a convincing treatment difference between etanercept and methotrexate.

Anti-TNFs are very effective, as shown by the number-needed-to-treat (NNT). Both anti-TNF agents consistently and rapidly improved all relevant clinical outcomes and reduced joint damage assessed radiographically. An incremental economic analysis estimated the additional costs and quality-adjusted life-year (QALY) gains associated with the use of either etanercept or infliximab, either as the third DMARD in a sequence of DMARDs or separately as last-resort therapy (ie, used last in a DMARD sequence). The results are presented in the report.

Recommendations

Etanercept and infliximab improve the outcomes in adults with RA when compared to placebo. Both agents improved all relevant clinical outcomes and also reduced joint damage. Serious adverse events occurred infrequently and were comparable to placebo.

Methods

Systematic literature review, with meta-analysis of clinical effectiveness data. The literature review was based on searching databases and contacting leading researchers and industry. Industry submissions to the National Institute for Clinical Excellence, including economic models, were reviewed in detail. The preliminary incremental cost analysis involved a simulation model developed specifically for this purpose.

Further research/reviews required

Comparative studies of anti-TNF agents and other DMARDs (new and old) are needed, as only one study compared anti-TNF directly with another DMARD. This showed equivalent efficacy. Such direct comparisons have a potential for informing practice, especially where therapeutic choices that take cost into account are to be made. Studies of the quality of life of RA patients in the long term and the impact of DMARDs and other interventions on quality of life are needed. Also needed are studies of the impact of DMARDs on joint replacement, and other disease and drug-related morbidity, and on mortality. Future economic models need to include other aspects of RA, such as disease complications, to improve current models.

Written by Dr Amanda Burls, WMHTAC, University of Birmingham, UK

INAHTA Briefs

Issue 2002/36

Title Sacral Nerve Stimulation for Refractory Urinary Urge Incontinence or Urinary Retention, June 2000

Agency MSAC, Medicare Services Advisory Committee
Commonwealth Department of Health and Ageing,
GPO Box 9848 Canberra ACT 2601 Australia;
tel: +61 2 6289 6811, fax: +61 2 6289 8799, http://www.msac.gov.au

Reference MSAC application 1009. Assessment report ISSN 1443-7120

Aim

To assess the safety and effectiveness of the procedure and under what circumstances public funding should be supported for the procedure.

Conclusions and results

Safety: Incidence of adverse events is relatively high (50%), with one third requiring further surgery and devices removed in 9% of cases. The major problems were pain at the pulse generator or lead implant site and lead migration.

Effectiveness: One randomized controlled trial indicated benefit for females with urge incontinence (durability of benefit is 18 months to 5 years), and urinary retention (18 month durability). Impact on quality of life is uncertain.

Cost effectiveness: The procedure is expensive: the cost per patient freed of urge incontinence is estimated at $35 000 at 6-month followup.

Recommendations

Public funding should not be supported at this time because of relatively high rates of adverse events, uncertain long-term effectiveness, and unfavorable cost effectiveness ratios.

Methods

MSAC conducted a systematic review of the biomedical literature from 1988 to October 1999 by accessing biomedical electronic databases, the Internet, and international health technology agency websites.

Further research/reviews required

Further research is required on recent refinements to the device and procedure especially as these effect safety, long-term effectiveness, and quality-of-life changes.

Produced by the Centre for Clinical Effectiveness, Australia

INAHTA Briefs

Issue 2002/57

Title **Implantable Contraceptives (subdermal implants and hormonally impregnated intrauterine systems) Vs Other Forms of Reversible Contraceptives: Two Systematic Reviews to Assess Relative Effectiveness, Acceptability, Tolerability and Cost Effectiveness**

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

Reference Health Technol Assess 2000;4(07). June 2000. www.ncchta.org/execsumm/summ407.htm

Aim

To assess the contraceptive efficacy, tolerability, and acceptability of subdermal implants and hormonally impregnated intrauterine systems (IUSs) in comparison with other reversible contraceptive methods and to use these data to determine the relative cost effectiveness.

Conclusions and results

- *Subdermal implants:* Thirty-four comparative studies met the inclusion criteria. Most studies were comparisons of different types of implant, but with a broader range of comparisons in the nonrandomized controlled trials (non-RCTs). In many of the non-RCT studies the intervention groups were often dissimilar at baseline. It was possible to combine data from only a few studies as it was deemed inappropriate to use data from investigations of prototypes. For Norplant, the most common comparison was with other types of subdermal implant, followed by comparisons with intrauterine devices (IUDs). There was no significant difference in pregnancy rates among users of Norplant compared to users of other contraceptive methods. There was no evidence of differences between Norplant users and users of other contraceptive methods in relation to planned pregnancy following removal, hormonal side effects, or adverse clinical events. Norplant users were 90% less likely to discontinue for menstrual reasons compared to women having DMPA injections. The only other significant difference observed was that Norplant users were less likely than pill users to discontinue the method for personal reasons.
- *Hormonally impregnated IUSs:* Twenty-nine intervention studies with IUSs met the inclusion criteria. With one exception, all were comparisons between different types of IUS or between IUSs and IUDs. It was possible to pool data from only a few studies. In terms of unplanned pregnancy, there was no evidence that levonorgestrel (LNG)-20 IUS users differed from users of copper IUDs (surface area >250 mm^3). Rate ratios calculated in the comparison of the LNG-20 IUS with copper IUDs <250 mm^3 showed that LNG-20 IUS users were significantly less likely to have either intrauterine or extrauterine pregnancies. There was insufficient evidence from the comparative studies in these systematic reviews to suggest that one type of subdermal implant was any more or less effective in preventing pregnancy than another, that implants were any more or less effective than the other methods with which they were compared, or that the LNG-20 IUS was any more or less effective than IUDs >250 mm^3. LNG-20 IUS users were significantly less likely to experience intrauterine or extrauterine pregnancies than IUD <250 mm^3 users. Women using the LNG-20 IUS were more likely to experience amenorrhea, and this event was a notable reason for discontinuing IUSs.
- *Cost effectiveness analysis:* Generally, the cost-effectiveness ratios for subdermal implants and IUSs, calculated from the results of the meta-analysis, were quite high, indicating that they were on balance more costly per pregnancy averted than the contraceptive methods with which they were compared.

Recommendations

Poor study design, lack of clarity in measuring contraceptive effectiveness, and heterogeneity between studies hindered synthesis of data. It is recommended that standardization of methods and measurements used in contraceptive research should be encouraged, with consumer involvement in the development of contraceptive research to identify

Title	**Implantable Contraceptives (subdermal implants and hormonally impregnated intrauterine systems) Vs Other Forms of Reversible Contraceptives: Two Systematic Reviews to Assess Relative Effectiveness, Acceptability, Tolerability and Cost Effectiveness**
Agency	**NCCHTA, National Coordinating Centre for Health Technology Assessment** Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom
Reference	Health Technol Assess 2000;4(07). June 2000. www.ncchta.org/execsumm/summ407.htm

user-related questions. Evaluation should be carried out to determine the most effective training for healthcare workers in the insertion and removal of implantable contraceptives.Economic endpoints should be included in primary research on methods of contraception.

Methods

Literature was identified through electronic database searches, reference lists, and by contacting individuals/ organizations working in the field. All prospective intervention studies that compared subdermal implants or IUSs with other forms of reversible contraceptives and reported predetermined outcomes in women of reproductive years were included.

Further research/reviews required

An RCT is required to assess the impact of counseling on discontinuation rates of subdermal implants and IUSs, particularly in relation to the effect of amenorrhea.

Written by Ms Rebecca French, Dept of Sexually Transmitted Diseases, Royal Free and University College Medical School, UK

INAHTA Briefs

Issue 2002/62

Title **Transurethral Needle Ablation (TUNA) – February 2002**

Agency **MSAC, Medical Services Advisory Committee**
Commonwealth Department of Health and Ageing
GPO Box 9848 Canberra ACT 2601 Australia;
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Reference MSAC Application 1014, Assessment Report ISBN 0 642 82100 0

Aim

To assess the safety, effectiveness, and cost effectiveness of Transurethral Needle Ablation (TUNA) for the treatment of benign prostatic hyperplasia (BPH) and under what circumstances such services should be supported with public funding.

Conclusions and results

Safety: TUNA appears to be a relatively safe procedure. Randomized trial evidence suggests that TUNA has fewer postoperative complications, such as bleeding, than does TURP. Nonrandomized data suggest that apart from urinary retention, which appears more common with the TUNA procedure, the early adverse event rate for TUNA and TURP is similar. It is also likely that TUNA results in fewer complications relating to sexual function than does TURP. However, as TUNA has also evolved over time, it is possible that the newer TUNA procedures may result in fewer complications than older procedures, although at this stage this remains unclear. TUNA may also be of value in patients with a high anesthetic risk as it can be performed as an outpatient or in-clinic procedure. Again, further evidence is needed.

Effectiveness: This review is based on a relatively small body of evidence. Overall, TUNA appears to be relatively effective for the short-term management of symptoms associated with BPH. However, data suggest that the duration of maximum benefit for TUNA is between approximately 3 and 12 months, depending on the parameter measured. This duration of benefit is shorter than that seen for patients treated with TURP (longer than 3 years), with more TUNA patients than TURP patients experiencing a return of BPH symptoms and more requiring retreatment in the longer term.

Cost effectiveness: A decision analysis model was designed, based on a set of plausible assumptions, to assess the comparative cost effectiveness of TURP and TUNA as initial treatment for symptomatic BPH. The base case analysis indicated that treating patients initially with TURP was both more effective and less costly than treating initially with TUNA. Over a range of sensitivity analyses, this conclusion varied from TURP being a cost effective initial treatment to TUNA being a cost effective initial treatment for patients with BPH. The analysis was particularly sensitive to the annual failure rate of both procedures and, subsequently, to the duration of followup. The conclusion regarding optimal initial treatment changed over the plausible ranges evaluated. Additional clinical data are required to strengthen our certainty concerning particular variables before definitive conclusions can be drawn regarding the relative cost effectiveness of TUNA and TURP in this setting.

Recommendations

MSAC recommended that interim funding for 3 years be supported, and that this funding be restricted to treating particular patient groups and acquiring data on the type of patients treated and safety data to monitor the use of TUNA under these interim arrangements.

Methods

The NHMRC Clinical Trials Centre at the University of Sydney conducted a systematic review of the literature on the role of TUNA. The following sources were searched from commencement to June 2001: MEDLINE, PreMedline, NLM Health Services Research Databases, Biological Abstracts, Best Evidence, Australian Medical Index, Current Contents, EMBASE, Cochrane Library, ISTAHC, and the NHS Databases; DARE, EED, and HTA. Internet and health technology assessment agency sources were searched; studies were also identified from MSAC applications and members of the Supporting Committee.

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

INAHTA Briefs

Issue 2002/71

Title Intracytoplasmic Sperm Injection

Agency SMM, The Norwegian Centre for Health Technology Assessment
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Reference SMM Report No. 3/2002. ISBN 82-14-02763-2

Aim

To evaluate the risk of developmental defects in children conceived by intracytoplasmic sperm injection (ICSI), an in vitro fertilization (IVF) method that enables fertilization in spite of severely compromised semen characteristics.

Conclusions and results

No meta-analyses or randomized controlled studies were identified, and all studies were classified either as cohort studies or case series. Of these, 13 studies were rated as acceptable quality, having adequate and well-defined control groups, whereas 17 studies were rated as fair quality due to weak or undefined control groups.

Birth defects were the most frequently reported outcome. Two reports and seven cohort studies of acceptable quality were included in the meta-analysis of birth defects. Overall, the risk for birth defects was 1.13 (95% confidence interval: 1.00–1.29, p=0.06). Studies that met our criteria were fairly homogenous (test for heterogeneity p=0.35). Separate meta-analysis on specific categories of malformations did not show any increased risk after ICSI.

Parents with chromosomal abnormalities or other genetic defects may transfer their defects to their offspring via ICSI. Sons of infertile males with Y chromosome microdeletions will inherit the same abnormality and therefore probably be infertile. With regard to the other outcomes, the number of accepted studies are few and heterogeneous, which makes the findings uncertain.

In conclusion, there is a small increased risk for major birth defects in offspring resulting from ICSI used to treat severe male infertility. However, this increase is not significant. Currently, there is little evidence of an increased risk for other health problems.

Methods

A systematic review was undertaken of literature reporting the outcome of ICSI pregnancies. Publications were identified by searches in MEDLINE, EMBASE, and Cochrane. International birth defects monitoring networks were contacted in an attempt to identify relevant data published as reports. Studies were critically assessed and systematized according to the presence of a relevant control group (children conceived by conventional IVF and/or naturally conceived children), and five clinical outcomes: 1) birth defects, 2) growth disturbances, 3) neurological developmental disturbances, 4) chromosomal abnormalities, and 5) transmission of subfertility to male offspring. In total, 30 studies with acceptable and fair quality were found to fulfill the inclusion criteria. Two reports providing new data were also included. Data on major birth defects from studies and reports comparing children conceived by ICSI versus conventional IVF were pooled and subjected to a meta-analysis.

Written by Anita Lyngstadaas, SMM, Norway

INAHTA Briefs

Issue 2002/74

Title Hormone Replacement Therapy (HRT)

Agency SBU, The Swedish Council on Technology Assessment in Health Care
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Reference SBU Report 159, 2002, ISBN 91-87890-77-1. Available in Swedish at http://www.sbu.se

Aim

In 1996, SBU published a scientific review of estrogen treatment following menopause. After 6 years there was reason to review the recent scientific literature and update the report.

Results and conclusions

- HRT has many advantages, but some risks. Women themselves – after being thoroughly informed should decide on the option of treatment.
- Treatment using estrogen agents of moderate potency have good effects on climacteric symptoms of hot flushes and sweating.
- Treating climacteric symptoms for a limited number of years has a confirmed benefit. None of the scientific evidence shows that such treatment measurably increases the risk for breast cancer and endometrial cancer, assuming that treatment adheres to accepted recommendations.
- Treatment using low-potency estrogen agents has good effects on vaginal and urinary tract symptoms.
- The scientific evidence is insufficient to make general recommendations on hormone therapy aimed at prevention in asymptomatic women following menopause, although HRT can preserve bone mass around the time of menopause.
- Long-term estrogen replacement therapy increases the risk for endometrial cancer, but this increase can be counteracted by also administering gestagens.
- Longer treatment periods are associated with a risk for breast cancer. The risk depends on the duration of treatment, but it is moderate even in long-term treatment. The potential benefits of HRT must be balanced against the risks. Hence, it is important to thoroughly inform women who are deciding about treatment.

It may be difficult to explain why the risk for breast cancer increases from HRT. The magnitude of this risk during and following treatment should be studied in terms of the difference in absolute risk between no treatment and treatment. The estimated risk for developing breast cancer from age 50 to 75 years in women not treated with hormones is 7 cases per 100. This risk can increase to 9 cases per 100 with hormone replacement therapy.

Methods

A literature search was conducted in databases from 1995 to 2001 in MEDLINE, PubMed, and the Cochrane Library.

Further research/reviews required

Generally, there is a need for clinical studies on the effects of different treatment strategies. The report presents detailed requirements for further research.

Written by Gunilla Lamnevik, SBU, Sweden

INAHTA Briefs

Issue 2002/56

Title Evidence Based ICU Bed Planning

Agency ITA, Institute of Technology Assessment, HTA-Unit
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Reference ITA/ HTA Report 2/02: available in German only, 90 pages http://www.oeaw.ac.at/ita/hta/

Aim

The demand for ICU services is increasing in all western countries, and complaints concerning a lack of ICU beds arise – independent of the actual density of ICU services available. The demand for more ICU beds triggered a debate on whether it is possible to define an "objective" need. This assessment aims to analyze conventional and innovative planning approaches and to define the determinants of demand.

Conclusions and results

In countries with a high density of ICU services – such as Austria – a better use of existing resources is recommended rather than an expansion of capacity. For a fair comparison, participation in national databases, registers, benchmarking, and quality assurance programs should be enforced.

Applying an "appropriateness" approach, the ICU data of an Austrian region (Tyrol) are being analyzed, and we are devising a plan for the region.

- Recent planning documents: A review of trends in recent planning shows that all planners calculate on the basis of existing styles of practice within their countries; the figures change only marginally. But while planners in countries with a relatively low ICU bed density (GB, Australia, Canada) report some need for an increase, planners in countries with a high density (USA, Germany, Austria) report a "satisfied need" and possibly an over-provision of ICU services.
- Innovative planners apply an "appropriateness of ICU use" approach in analyzing the scores (esp. TISS) and propose a more flexible organization of ICUs and a higher proportion of IMCU beds.
- Clinical and ICU management tools, such as admission and discharge guidelines, strategies to reduce treatment variability, certain organizational changes (leadership, horizontal hierarchy), and costing methods gain importance for better, more efficient, and coordinated use of ICU resources.

Methods

Systematic review, multistep searches in MEDLINE, EMBASE, Cochrane, HTA Database, web searches, informal searches through planning and HTA networks; microplanning for an Austrian region.

Written by Dr Claudia Wild, ITA, Austria

INAHTA Briefs

Issue 2002/65

Title **Promoting Physical Activity in South Asian Muslim Women Through 'Exercise on Prescription'**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
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Reference Health Technol Assess 2002;6(08). April 2002. www.ncchta.org/execsumm/summ608.htm

Aim

To review the literature relating to EoP schemes and South Asian Muslim women to provide the theoretical framework for investigation, to carry out a national survey of health authority districts with large South Asian populations to find out what schemes exist and what provision is made for these women, to undertake case studies of schemes in which provision is made for South Asian Muslim women and to note good practice and issues arising, to undertake and evaluate a pilot intervention program with special provision for South Asian Muslim women, and to make recommendations for good practice in EoP schemes.

Conclusions and results

- Some EoP schemes make special provisions for South Asian Muslim women, but many make no such provisions. Perceived barriers to exercise for these women include access to facilities, cost, childcare facilities, cultural codes of conduct, and language. Some general issues in existing EoP schemes are a cause for concern, including communication and cooperation between parties and between agencies and the community, monitoring, and evaluation.
- The pilot program was seen as being successful both by the providers and the South Asian Muslim women who participated in it.
- While the research indicated that many EoP schemes have clear protocols and procedures and excellent facilities and programs, many others have shortcomings that need to be addressed, eg, communication between all participating parties and clarification of procedures.
- Consideration should be given to needs of South Asian Muslim women, in the form of the use of local community facilities and employment of bilingual, sympathetic staff. Costs to the women should be kept as low as possible and consideration should be given to providing childcare facilities. To be effective, EoP programs should be long rather than short term.

Recommendations

To measure and evaluate the effectiveness of EoP schemes, various methods and measures should be used including health outcomes (physiological, behavioral) and process (procedures, cooperation between parties). An investigation into the cost implications of EoP schemes set against cost benefits would be useful, including ways of funding such schemes. There is also a need to investigate the best ways in which exercise programs could be promoted in different communities, including exercise as part of a holistic program.

Methods

A review was undertaken of selected literature related to activity and health, EoP schemes, South Asian communities, and activity levels of South Asian Muslim women. A questionnaire was sent to health authorities with South Asian populations of at least 0.5% to identify EoP schemes, agencies involved, and key contacts. Questionnaires were then sent to general practitioners and leisure centers in areas where such schemes existed. Quantitative analysis of the replies was undertaken. In 5 selected areas, interviews were conducted with each of the parties to the EoP schemes.

Title	**Promoting Physical Activity in South Asian Muslim Women Through 'Exercise on Prescription'**
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Reference	Health Technol Assess 2002;6(08). April 2002. www.ncchta.org/execsumm/summ608.htm

An EoP pilot intervention program was introduced in one area, and interviews were held with EoP providers and South Asian Muslim women.

Further research/reviews required

Further trials are needed with large samples, clear criteria for groups and intervention programs and with outcome measures at specific intervals up to 1 year. A further study should also be undertaken to try and establish schemes for South Asian Muslim women along the lines of the pilot program described, in which the value of specific interventions for these women are assessed.

Written by Dr Robert Carroll, School of Education, University of Manchester, UK

INAHTA Briefs

Issue 2002/76

Title The Effectiveness of Domiciliary Health Visiting: A Systematic Review of International Studies and A Selective Review of the British Literature

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Reference Health Technol Assess 2000;4(13). Sept 2000

Aim

The objectives were to: 1) systematically review the effectiveness and cost effectiveness of domiciliary health visiting [Part I], 2) selectively review the British health visiting literature [Part II], and 3) recommend future research.

Conclusions and results

Part I presented evidence suggesting that home visiting of parents and children: 1) improves parenting skills and the quality of the home environment, 2) ameliorates several child behavioral problems, including sleep behavior, 3) improves intellectual development in children, 4) reduces rates of unintentional injury and the prevalence of home hazards, 5) improves detection and management of postnatal depression, 6) enhances quality of social support to mothers, and 7) improves breastfeeding rates. The evidence suggests that home visiting to elderly people reduces mortality and admission to long-term institutional care among the frail 'at-risk' elderly population. Findings from the limited number of studies assessing cost effectiveness indicate a potential for net cost savings, particularly in hospital costs, from home visits to parents and their children and to elderly people and their carers. Part II of the report: 1) describes process issues related to identifying and meeting needs through home visiting, 2) analyzes the micro-context of health visitor/client interaction, and 3) demonstrates how health visiting highlights policy tensions in British health care.

Recommendations

Implications for health visiting [Parts I and II]

1) Several reviews of the literature support making the content, duration, and intensity of home visits appropriate and sensitive to client needs. 2) Professional judgement is considered valid for decisions about where to target home visiting resources. 3) Expectations of home visiting by health visitors should be realistic. 4) The literature suggests that nonprofessional home visitors can play a role, but that they require guidance, supervision, and support from professionals. More complex difficulties may not be suitable for nonprofessional home visiting. 5) The evidence suggests that home visiting interventions that are restricted to pursuing a narrow range of outcomes are less effective than more broadly based interventions that address multiple needs of individuals and families.

Methods

Electronic databases, relevant journals, and reference lists were searched, and key individuals and organizations were contacted. Studies assessing the outcomes of home visiting by British health visitors were included, as were non-British studies where home visits were made by personnel with responsibilities within the remit of British health visitors. Part II discussed studies that assessed the home visiting process of British health visitors and that analyzed policy issues. In Part I, data were extracted from each study using an agreed procedure. Study quality was assessed using a standardized checklist. Where appropriate, quantitative data were entered into a meta-analysis. Data were also discussed in a narrative manner.

Title The Effectiveness of Domiciliary Health Visiting: A Systematic Review of International Studies and A Selective Review of the British 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, www.ncchta.org/execsumm/summ413.htm

Reference Health Technol Assess 2000;4(13). Sept 2000

Further research/reviews required

Part I. There is a need:

1. For studies with rigorous experimental designs to evaluate the effectiveness of home visiting by British health visitors.
2. To undertake further studies comparing the effectiveness and cost effectiveness of professional and non-professional home visitors.
3. For full economic evaluation of home visiting by health visitors using an RCT design.
4. To establish a substantial British knowledge base.

Part II. There is a need for:

1. Sociolegal, policy, and ethical studies that explore and analyze the tensions and dilemmas in health visiting identified in this review.
2. A comprehensive survey of the roles and functions currently being undertaken by British health visitors.

Written by Ms Ruth Elkan, Queens Medical Centre, University of Nottingham, UK

INAHTA Briefs

Issue 2002/78

Title Assessment of Videoconferencing in Telehealth in Canada

Agency CCOHTA, Canadian Coordinating Office for Health Technology Assessment
865 Carling Avenue, Suite 600, Ottawa, ON, K1S 5S8 Canada;
tel: +1 613 226 2553, fax: +1 613 226 5392, http://www.ccohta.ca

Reference CCOHTA Technology Report, Issue 14, May 2001. ISBN 1-894620-00-3.
http://www.ccohta.ca/ccohta_production/entry_e.html

Aim

To provide Canadian health care decision makers with information about the use of telehealth videoconferencing (VC), including:

- Broad-based information about the collective experience of eight VC programs in Canada
- Evidence of efficacy with respect to patient care, distance education and training, user and provider satisfaction, and communication patterns
- Suggestions for future directions for using VC technology.

Conclusions and results

Survey results indicated that VC for telehealth applications in Canada is in transition between pilot project and program status. While VC telehealth activity is undergoing rapid growth, few patients are seen at present. All 8 programs surveyed report some positive results, including improved communication among colleagues, better access to care, and high-level patient satisfaction. Barriers to widespread adoption and implementation include organizational change, medico-legal concerns, insufficient infrastructure, lack of standards for user training and education, and unresolved issues on reimbursing practitioners. Of over 270 articles and reports found, 40 were selected as primary outcome studies. These studies suggest it is feasible to establish patient care systems using VC technology, but there is little evidence of clinical or economic benefit, especially on cost effectiveness compared to face-to-face care. VC is well suited to the unique geography and unevenly distributed population of Canada and will continue to expand.

Recommendations

- Encourage orderly development of VC by developing nationally approved standards and guidelines for planning, implementation, user training, and program sustainability.
- Recognize that planning strategies and long-term funding are vital to sustain VC programming.

Methods

According to predetermined criteria, representatives from the participating healthcare agencies and federal, provincial, and territorial governments identified telehealth programs across Canada in which VC was used to provide health care and distance learning in health/medical programs. Responses to a mail questionnaire and project evaluations from 8 VC programs (reaching approximately 150 sites) were synthesized. Literature published from 1998 to October 2000 was reviewed to evaluate the efficacy of VC.

Further research/reviews required

The findings of this study suggest a need for quality outcome studies on clinical and cost effectiveness of VC.

Written by Noorani H and Picot J, CCOHTA, Canada

INAHTA Briefs

Issue 2002/92

Title A Systematic Review of Discharge Arrangements for Older People

Agency NCCHTA, National Coordinating Centre for Health Technology Assessment
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom
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Reference Health Technol Assess 2002;6(4). May 2002. http://www.ncchta.org/execsumm summ604.htm

Aim

To test the following hypotheses: a) there are too few comparable randomized controlled trials (RCTs) to allow definitive analysis; b) hospital discharge process, outcome, and cost effectiveness can improve with certain interventions; c) some interventions are more effective than others; and d) there are priority areas for future research.

Conclusions and results

Overall, 6972 articles were identified, whereof 320 proceeded to relevance and quality assessment. Data were extracted from 76 papers. Final synthesis was based on 71 articles representing 54 RCTs, 10 of which were from the UK (5 trials were excluded). Four types of intervention were identified: discharge planning, comprehensive geriatric assessment, discharge support, and educational interventions. The intervention types were not mutually exclusive.

No significant effect was seen on mortality at 3 months (10 trials), 6 months (14 trials), or 12 months after discharge (14 trials). Index length of stay was not significantly affected by the interventions (19 trials).

Intervention significantly reduced the risk for hospital readmission (readmission risk ratio (RRR) 0.851; 95% confidence interval (CI), 0.760 to 0.953; p = 0.005; 35 trials). This effect was preserved where a single professional, instead of a team, provided the intervention. The effect on readmission risk was most apparent in interventions both in hospital and in the patient's home. A similar trend was seen for interventions in the patient's home only. Little effect was seen for interventions provided only in hospital or by telephone.

None of the 4 intervention types showed major effects on mortality or length of hospital stay. Only educational interventions had an effect on RRR, but the trials were limited.

The evidence does not show that discharge arrangements affect mortality or length of hospital stay. This review suggests that arrangements for discharging older people from hospital can favorably affect readmission rates. Interventions in both hospital and the patient's home had the largest effect.

No evidence from RCTs supports the general adoption of discharge planning, geriatric assessment, or discharge support schemes as means to improve discharge outcomes.

Recommendations

More research is needed, particularly in the UK. Models that provide intervention across the hospital-community interface and/or education are worth considering. Future studies should record mortality, index length of stay, and readmission rates and should measure patient health outcomes, patient/carer satisfaction, and costs. To facilitate data pooling, trials should follow agreed standards with harmonized outcome measures. Economic analysis should be integral to future studies, which should be large and inclusive enough to detect important effects and ensure generalizability of results. Research to explore cross-national comparability of studies would be worthwhile.

Methods

Literature retrieval focused on RCTs. A research assistant scanned the titles and abstracts to exclude irrelevant studies. Two reviewers independently assessed the material, and disagreements were resolved by discussion. Reprints of potentially relevant studies were obtained and checked for relevance and quality before data were extracted from RCTs.

Title A Systematic Review of Discharge Arrangements for Older People

Agency NCCHTA, National Coordinating Centre for Health Technology Assessment
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom
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Reference Health Technol Assess 2002;6(4). May 2002. http://www.ncchta.org/execsumm summ604.htm

The initial synthesis of results, built on a tabular summary of trial characteristics, comprises a qualitative overview. Where quantitative data and comparable studies were sufficient, standard approaches were used to combine the study results. Estimates of pooled effect sizes on all relevant outcome measures were obtained from the study-specific estimates using random effects models, allowing for between-study variations.

Further research/reviews required

See recommendations above.

Written by Professor Stuart Parker, Sheffield Institute for Studies on Ageing, University of Sheffield, UK

INAHTA Briefs

Issue 2003/06

Clinical Medication Review by a Pharmacist of Patients on Repeat Prescriptions in General Practice: A Randomized Controlled Trial

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Reference Health Technol Assess 2002; 6(20). Aug 2002. www.ncchta.org/execsumm/summ620.htm

Aim

To determine whether a suitably trained clinical pharmacist can effectively review the repeat clinical medications of elderly patients in general practice, and to: 1) assess whether clinical medication review by a pharmacist is a cost effective way to improve the extent, cost, and quality of clinical control of repeat prescribing compared with normal procedures; 2) evaluate the effect of medication review clinics on the number of practice consultations, outpatient consultations, hospital admissions, and deaths; 3) identify the types of interventions.

Conclusions and results

The mean numbers of individual medication changes per patient were 2.2 in the intervention group and 1.9 in the control group. The numbers of repeat medication items rose in both groups, but the rise was significantly less in the intervention group. Medication costs rose in both groups, but the rise was significantly less in the intervention group. The cost saving on medication in the intervention group compared with the control group was £4.75 per 28-day month. Extrapolated for 1 year, the saving is £61.75 per patient. No difference was found between the groups in the numbers of outpatient consultations, hospital admissions, or practice consultations over the 12-month period. The intervention group had fewer deaths than the control group, but the difference was not statistically significant. Over the 12 months, 97% of the intervention group had medication reviews vs 44% in the control group. A recommendation was made in 258 of the 591 (44%) patient consultations. Only 28 patients (5%) needed referral to a GP, and 25 patients (4%) needed referral for a test. The pharmacist handled all other medication-related problems. A recommendation was made for 603 of the 2927 repeat medications (21%). Recommendations were 'stop the medicine' (118 medicines, 4% of all medicines) and 'technical', eg, a generic switch or removal of a 'redundant item' from repeat list (177, 6%). Of the 603 medication interventions, 395 (65%) were handled by the pharmacist alone without a GP. Recommendations and permission were sought from a GP for 208 interventions (34%). The pharmacist's advice was accepted and acted upon in 179 instances (86%).

Recommendations

A suitably trained pharmacist can consult with elderly patients to review them, their medications, and conditions for which drugs were prescribed. This resulted in more medication review and intervention than if the pharmacist was not involved. Pharmacist intervention led to fewer drugs used in the intervention group than in the control group, and thus to major net financial savings. There was no evidence on adverse effects on use of health services.

Methods

RCT of clinical medication review in elderly patients on repeat medication in general practice. The control group received normal GP care. Patients in the intervention group were invited to consult with the pharmacist at the surgery. The pharmacist assessed the patient, the illnesses, and the medication regimen, and made recommendations.

Further research/reviews required

The study demonstrates the potential of an extended role for pharmacists, but its reproducibility as a service modality needs further testing. Only one, very experienced, pharmacist was involved, working in 4 selected Leeds practices. It is important to reproduce the results with more pharmacists in large numbers of practices over a wider geographical and socioeconomic area before fundamentally changing services and the role of the pharmacist.

Written by Dr Arnold Zermansky, School of Healthcare Studies, University of Leeds, UK

INAHTA Briefs

Issue 2003/11

Title A Randomized Controlled Crossover Trial of Nurse Practitioner Versus Doctor-led Outpatient Care in a Bronchiectasis Clinic

Agency NCCHTA, National Coordinating Centre for Health Technology Assessment
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Reference Health Technol Assess 2002; 6(27). Oct 2002. www.ncchta.org/execsumm/summ627.htm

Aim

In a specialist outpatient clinic for bronchiectasis patients, the study objectives were: 1) to assess the feasibility and safety of nurse practitioner-led outpatient clinics and their acceptability to patients and their doctors, and 2) to compare the cost effectiveness of nurse practitioner-led care with a doctor-led system of care.

Conclusions and results

Of the 80 patients recruited, 39 were randomized to nurse practitioner-led followed by doctor-led care, and 41 to doctor-led followed by nurse practitioner-led care. Baseline lung function and 12-minute walk distance were similar in the two groups.

At the final followup, the mean difference in FEV1 between nurse practitioner-led and doctor-led care was 0.2% predicted. The mean difference in 12-minute-walk distance between the two methods of service delivery was 18 meters. Of those patients who were using antibiotics and indicated their compliance, 100% were compliant while receiving nurse practitioner-led care compared with 81% of patients during doctor-led care, a difference that was statistically significant. The health-related quality-of-life analysis revealed no significant mode of care effects. However, patients reported less vitality/energy and greater levels of pain following doctor-led care, but fewer role limitations because of emotional problems. In analyzing patient satisfaction with the clinic consultations, a statistically significant difference favored the nurse practitioner. However, nurse practitioner-led care resulted in significantly higher resource use compared with doctor-led care. The mean difference per patient was £1498 and was greater in the first year (£2625) than in the second (£411).

Recommendations

Nurse practitioner-led care for stable patients in a chronic chest disease clinic is safe and as effective as doctor-led care. Patient satisfaction was significantly higher with some aspects of nurse practitioner-led care, and patient compliance with antibiotic therapy was higher. Nurse practitioner-led care used significantly more resources in admissions and antibiotic prescriptions. This may be a learning effect (difference was substantially greater in year 1.)

Methods

Two-phase study: First, the nurse practitioner completed a 6-month program to enable her to practice independently. This included tuition in the principles of bronchiectasis, its clinical presentation and management, and practical experience and skills in clinical assessment and therapeutics. The second phase used a RCT (crossover design) to compare nurse practitioner-led with doctor-led care in a bronchiectasis outpatients' clinic. Sample size was based on establishing equivalence of the two care modes.

Further research/reviews required

The design was robust and appropriate for this type of evaluation. Randomization allowed the most objective treatment assignment during of study and detected unpredicted differences in hospitalization and cost. In future studies, randomization during training and a formal evaluation of all outcomes immediately thereafter would help identify needs and minimize the learning curve effect during formal evaluation. Another option would be to lengthen the trial.

Written by Ms Noreen Caine, Papworth Hospital NHS Trust, Cambridge, UK

INAHTA Briefs

Issue 2002/35

Title **Pulmonary Thromboendarterectomy (PTE) for Chronic Thromboembolic Pulmonary Hypertension (CTEPH)**

Agency **MSAC, Medicare Services Advisory Committee**
Commonwealth Department of Health and Ageing,
GPO Box 9848 Canberra ACT 2601 Australia;
tel: +61 2 6289 6811, fax: +61 2 6289 8799, http://www.msac.gov.au

Reference MSAC reference 05. Assessment report ISSN 1443-7120

Aim

To assess the safety and effectiveness of the procedure and under what circumstances public funding should be supported for this procedure to be performed in Australia.

Conclusions and results

Safety: Limited available information suggests significant morbidity and mortality associated with the procedure.

Effectiveness: Although comparisons with medical therapy and lung transplants were not available, there is evidence the procedure improves survival, functional status, quality of life, and hemodynamic outcomes.

Cost effectiveness: Providing PTE in Australia would have cost benefits relative to sending patients overseas for treatment. Compared to medical management of patients in Australia PTE, may cost less than $13 500 per life-year gained.

Recommendations

There is sufficient evidence regarding the safety and effectiveness of PTE for CTEPH to support public funding for the procedure in Australia.

Methods

MSAC conducted a systematic review of the biomedical literature from 1966 to 2000 using biomedical electronic databases, the Internet, and international health technology agency websites to identify relevant studies. Textbooks and reference lists of publications were also considered. Cost effectiveness measures compared the cost of funding PTE for 6 patients in Australia with current practice (sending 3 patients overseas and treating 3 medically in Australia) and treating all 6 medically in Australia. This analysis relied upon published estimates of increased survival from PTE compared to medical treatment. PTE in Australia was assumed to cost the same as a heart transplant. Data deficiencies, including lack of consistency, meant that cost effectiveness was assessed according to cost per life-year gained rather than quality-adjusted life-years.

Prepared by the Centre for Clinical Effectiveness, Australia

INAHTA Briefs

Issue 2002/83

Title The Challenges of Early Assessment: Leukotriene Receptor Antagonists

Agency CCOHTA, Canadian Coordinating Office for Health Technology Assessment
865 Carling Avenue, Suite 600, Ottawa, ON, K1S 5S8 Canada;
tel: +1 613 226 2553, fax: +1 613 226 5392, http://www.ccohta.ca

Reference CCOHTA Technology Report, Issue 19, October 2001. ISBN 1-894620-16-X (print); ISBN 1-894620-15-1 (online): http://www.ccohta.ca/ccohta_production/entry_e.html

Aim

– To evaluate the efficacy and safety of leukotriene receptor antagonists (LTRAs) as compared to inhaled corticosteroids (ICs) in the treatment of mild-to-moderate chronic or recurrent asthma.

Conclusions and results

Reviewers discovered that most of the evidence from 22 relevant randomized controlled trials was reported exclusively in the form of abstracts or conference posters. Drug manufacturers responsible for funding the trials were asked to clarify vague, missing, or problematic information and data, but did not respond. Given the sparsity of information, reviewers could not establish with any degree of confidence the methodological soundness of at least 65% of the included studies and the population(s) to which results of trials could be generalized. Meta-analysis was therefore considered inappropriate, and only a qualitative synthesis was possible. Reviewers also could not determine whether the low overall quality of the studies retrieved was due to major methodological shortcomings, publication status of trial reports, or both. Because the collective evidence for the efficacy and safety of the two LTRAs is not yet satisfactory, their value as monotherapy or as an adjunct to ICs cannot be determined at present.

Methods

This systematic review planned to compare LTRAs and ICs by identifying four basic definitions and concomitant research designs: three designs using LTRAs as an add-on to ICs, and the fourth comparing LTRAs and ICs head-to-head. Most of the studies identified (64.6%) fell into the latter design category, including 6 of 8 montelukast studies and 8 of 14 zafirlukast studies. Due to the sparsity of information, reviewers relaxed the inclusion criteria to include studies with vague or ad hoc definitions of "mild-to-moderate, chronic or recurrent asthma" to describe the trial populations, as well as studies with ambiguous information about participants' pre-trial symptom status while on ICs. However, the minimum, symptom-controlling IC dose had to be established before randomization.

Further research/reviews required

Most of the investigation comparing the utility of LTRAs in relation to ICs is currently in progress; full evaluation of the evidence concerning the value of these drugs awaits public availability of this information.

Written by Schachter HM, Kovesi T, Ducharme F, Langford S, Clifford T, and Moher D, CCOHTA, Canada

INAHTA Briefs

Issue 2002/94

Title **Long-acting ß2-agonists for Maintenance Therapy of Stable Chronic Obstructive Pulmonary Disease: A Systematic Review**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
865 Carling Avenue, Suite 600, Ottawa, ON, K1S 5S8 Canada;
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Reference CCOHTA Technology Report, Issue 27, September 2002. ISBN 1-894620-54-2 (print); ISBN 1-89462-53-4 (online): http://www.ccohta.ca

Aim

To assess the efficacy and safety of salmeterol and formoterol for maintenance treatment of patients with stable, non-reversible chronic obstructive pulmonary disease (COPD), as compared to:

- Placebo (with or without the additional use of short-acting ß2-agonists)
- Anticholinergics (with or without the additional use of short-acting ß2-agonists).

Conclusions and results

A systematic review identified 58 potentially relevant studies. Of these studies, 9 described trials that satisfied the eligibility criteria (6 were of moderate quality and 3 of low quality as assessed on the Jadad scale). The trials reviewed compared salmeterol and formoterol both to placebo and to the older alternative agent, ipratropium bromide. Because of differences in trial design and reporting, meta-analysis of quantitative outcome measures was not possible. Rather, a best-evidence-synthesis approach was used. Among patients with less than 15% improvement in FEV1 (forced expiratory volume in one second) after a single dose of short- or long-acting bronchodilator, reviewers found that the long-acting ß2-agonists were superior to placebo in decreasing the use of a rescue inhaler. Although an increase in FEV1 was also observed, there was no improvement in functional outcomes such as distance traveled in a 6-minute walking test. Reviewers found little evidence regarding the effects of these agents on COPD exacerbations and on health-related quality of life. The two studies, both of moderate quality that compared the new agents with ipratropium bromide did not show salmeterol and formoterol to be more efficacious. Safety data were not reported in any of the studies reviewed.

Methods

Published and unpublished reports were identified by three methods: 1) searching multiple databases and web sites; 2) hand searching selected journals, documents, and bibliographies of selected papers; and 3) contacting the manufacturers of salmeterol and formoterol. Regardless of publication status, studies using both parallel and cross-over designs were included as long as the duration of therapy was at least 4 weeks. The eligibility criteria for trial participants included non-asthmatic, stable COPD, an FEV1 of 75% or less than predicted, an FEV1 /FEV (forced vital capacity) ratio less than 70% predicted, and less than 15% improvement in FEV1 after a dose of a short- or long-acting ß2-agonists. Two reviewers independently made decisions about study inclusion, quality, and data extraction.

Written by Shukla VK, Husereau DR, Boucher M, Mensinkai S, Dales R, CCOHTA, Canada

INAHTA Briefs

Issue 2002/42

Visual Electrodiagnosis, April 2001

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Reference MSAC application 1005. Assessment report ISSN 1443-7120

Aim

To assess the safety and effectiveness of several visual electrodiagnostic tests for diagnosing retinal disease, optic nerve damage, and visual field defects and under what circumstances public funding should be supported for these tests.

Conclusions and results

Safety: No significant consumer risks were identified.

Effectiveness: There was no rigorous evidence to support diagnostic effectiveness for the following five tests considered in detail: focal electroretinography (ERG), multifocal ERG, visual evoked potentials (VEP), scotopic threshold response (STR), and intensity response function (IRF). Studies were generally of a poor quality, did not identify diagnostic characteristics, and offered little discussion of patient management outcomes. All of the studies considered were ranked only as level IV evidence. In the case of focal ERG, some studies provided diagnostic characteristics, but were flawed due to selection of patients who were already diagnosed with the disease or by failing to provide a reference test. This would have tended to overestimate the accuracy of focal ERG as a diagnostic test.

Electroretinography, pattern electroretinography, dark adaptometry, electrooculography, and visual evoked responses are recognised tests by the International Society of Clinical Electrophysiology of Vision.

Cost effectiveness: This could not be evaluated due to insufficient evidence regarding accuracy of the tests and usefulness of patient outcomes.

Recommendations

1. Public funding should be supported for electroretinography, pattern electroretinography, dark adaptometry, electrooculography, and visual evoked responses, but should
2. not be supported for focal or multifocal ERG, VEP, STR, or IRF.

Methods

MSAC conducted a systematic review of the biomedical literature from 1966 to October 2000 by accessing biomedical databases, the Internet, and international health technology websites to identify the accuracy and precision of the tests and their usefulness in terms of patient outcomes.

INAHTA Briefs

Issue 2002/47

Title Accuracy and Reliability of Using Computerized Interpretation of Electrocardiograms for Routine Examinations

Agency AHFMR, Alberta Heritage Foundation for Medical Research
Alberta Health Technology Assessment Unit, Suit 1500,
10104-103 Avenue NW, Edmonton, Alberta T5J 4A7, Canada;
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Reference ISBN-1-896956-46-7 HTA 25: Series A (English), January 2002

Aim

To determine the available published evidence on the diagnostic accuracy and reliability of computerized interpretation of electrocardiograms (ECGs). Computerized interpretation of ECGs is an automated laboratory test for screening ECGs in asymptomatic adults. The intent was to inform health policy makers, medical practitioners, and other interested parties about the current status concerning the use of computerized ECG interpretation for detecting normal heart activity. This review is confined to the use of computerized ECG interpretation during routine examinations of resting ECG performed in ambulatory settings.

Conclusions and results

No primary research studies were found that addressed the question of whether computerized interpretation of resting ECG can be considered an accurate and reliable automated laboratory test for screening heart conditions in asymptomatic adults as part of their routine clinical examination.

The available evidence (weak and limited) suggested that computer programs with best diagnostic performance may be as accurate as the human reader. Results showed that these programs confirm normality (in terms of heart condition) as established by non-ECG clinical evidence (the gold standard for type A diagnosis) in more than 90% of cases.

The available evidence did not permit conclusive answers on the diagnostic accuracy and reliability of computerized interpretation of resting ECG in asymptomatic adults. The question whether it can replace interpretation by a skilled professional in an ambulatory clinical environment for this application has yet to be answered.

Recommendations

Computerized interpretation of ECGs should be used with an awareness of the potential risk of false positive and false negative findings. Complete reliance on computerized ECG interpretation may result in incorrect diagnoses and could lead to inappropriate management decisions. Computerized interpretation of resting ECG in primary care has future potential. The immediate availability of computerized ECG interpretation has been viewed as a significant improvement for practicing clinicians. Those considering the use of computerized ECG interpretation for this indication should be aware that:

- The ECG test is only one of the tests used to detect/exclude possible heart conditions and is of limited value as a stand-alone screening tool in an apparently healthy population.
- It remains to be determined whether the use of computerized ECG interpretation actually increases physician's accuracy in ECG interpretation, saves physician time, improves quality of patient care, and leads to a reduction in the costs.
- There are different applications of computerized ECG interpretation. The computer programs available on the market apply different approaches to diagnostic classification of ECGs and use different terminology.

Methods

Systematic review of the research published from 1994 to April 2001. The following databases were searched: PubMed MEDLINE, HealthSTAR, EMBASE, ECRI database, The Cochrane database of Systematic Reviews, Best Evidence database and the NHS (UK) Centre for Reviews and Dissemination databases (HTA, EED, and DARE), National Guideline Clearinghouse, CCOHTA publications, and the WWW. Two well renowned experts externally reviewed this report.

Written by Paula Corabian, ADHFMR, Canada

INAHTA Briefs

Issue 2002/50

Organization of Services for Diabetic Retinopathy Screening

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Reference Health Technology Assessment Report 1; ISBN 1-903961-12-2

Aim

To determine the most effective and efficient approach to achieving, implementing, and sustaining a quality assured screening program for diabetic retinopathy in Scotland that takes account of patient requirements.

Conclusions and results

A national screening program should be organized within current health service structures in Scotland and must be integrated with routine diabetes care as outlined in the Scottish Diabetes Framework. NHS boards should have the responsibility for implementing the program in their area. Digital retinal photography has been shown to achieve high sensitivity and specificity for sight-threatening disease. Indirect opthalmoscopy has also proven to be sensitive and specific enough to be viable as a model for a national screening program. Mydriasis may be required in some cases prior to screening. Patients should be informed about the screening process.

Recommendations

A national systematic diabetic retinopathy screening program for Scotland should be established to detect referable retinopathy. The screening program should:

- Utilize a three-stage process based on non-mydriatic digital cameras, with the use of mydriasis and slit lamps where necessary.
- Be performed by appropriately trained, accredited, and competent professionals.
- Enhance existing schemes to achieve the approved quality assured specifications.
- Ensure screening is accessible to all diabetic patients, whether they receive community and/or hospital based diabetic care. Local implementation may include services in diabetes centers, primary healthcare facilities, mobile vans, or community optometrists.
- Be evaluated as the screening program is implemented and reviewed in the light of further research to enable optimal service provision.

Methods

Clinical effectiveness, organizational issues, and patient issues were appraised, and an economic evaluation was performed. Systematic literature searching was used to identify evidence published in the scientific literature. Evidence was submitted from professional and patient groups, manufacturers, other interested parties, and experts. The views and preferences of patients were elicited and considered.

Produced by HTBS, UK

INAHTA Briefs

Issue 2002/66

Title **Ultrasound Screening in Pregnancy: A Systematic Review of the Clinical Effectiveness, Cost Effectiveness and Women's Views**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
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Reference Health Technol Assess 2000;4(16). Sept 2000. www.ncchta.org/execsumm/summ416.htm

Aim

- To update the pre-existing Cochrane review, to compile new Cochrane reviews of routine ultrasound in late pregnancy and routine Doppler® ultrasound in pregnancy, and to compile literature reviews of women's views on undergoing routine ultrasound examination with estimates of costs and cost effectiveness of routine ultrasound examinations.
- To conduct a primary study to assess the consequences of a routine two-stage ultrasound regimen in pregnancy in a teaching hospital (clinical pathways) and to conduct a primary study of costs of a routine two-stage ultrasound regimen in early or mid-pregnancy in a UK teaching hospital.
- To refine/update a decision model of cost effectiveness of options for routine scanning for fetal anomalies.

Conclusions and results

- Evidence shows that routine ultrasound in early pregnancy (<24 weeks gestation) provides (1) better gestational age assessment, and hence fewer inductions of labor for 'post-term pregnancy; (2) earlier detection of multiple pregnancies, but not shown to have an important impact on outcome in multiple pregnancies; (3) detection of clinically unsuspected fetal malformation while termination of pregnancy is possible, and hence reduces perinatal mortality rate if detection of fetal malformations is an important objective, if a high level of diagnostic expertise exists, and if termination of pregnancy for fetal abnormality is widely accepted in the population screened. No convincing evidence of benefit from routine examination in late pregnancy (>24 weeks) was found, whether using imaging or Doppler ultrasound.
- Ultrasound is attractive to women and partners; perhaps because it provides early visual confirmation of pregnancy and contact with their babies, and reassures about fetal well being. Such features may augment the potential for anxiety, shock, and disappointment when the scan shows a problem. Recent changes in the use of ultrasound may lead to more findings of uncertain clinical significance, which is likely to have psychological and social consequences for women. Trials comparing ultrasound/no ultrasound have not considered its psychological/social impact on parents and babies.
- There are few good quality economic evaluations and primary cost studies of ultrasound scanning in pregnancy. Only one economic evaluation conducted alongside an RCT was included in the review. Routine scanning in the second trimester was shown to be relatively cost effective. However, the costs to women of attending ultrasound examinations were significant compared with NHS service costs.
- Several inefficiencies in the routine ultrasound screening program were identified (including the need for repeat scans and that not all women book at early gestations), some of which are unavoidable, but which have implications for both its clinical and cost effectiveness.

Recommendations

The authors provide a summary of implications for policy and practice to guide clinicians, women, and health planners based on available evidence from the systematic reviews, primary studies, and decision model.

Title **Ultrasound Screening in Pregnancy: A Systematic Review of the Clinical Effectiveness, Cost Effectiveness and Women's Views**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
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Reference Health Technol Assess 2000;4(16). Sept 2000. www.ncchta.org/execsumm/summ416.htm

Methods

Systematic reviews of the literature were conducted as fully described in the main report. The systematic review findings were augmented by primary research of clinical pathways and costs, the methods of which are described in individual sections of the report.

Further research/reviews required

The authors describe the implications of their findings for research in the report covering: guidelines on research methods; priorities for research; documenting current practice; clinical pathways; costs and outcomes; defining options for screening; ethical and cultural issues; and cost effectiveness.

Written by Dr Leanne Bricker, Dept of Obstetrics and Gynaecology, University of Liverpool, UK

INAHTA Briefs

Issue 2002/72

Mammography Screening

Agency SMM, The Norwegian Centre for Health Technology Assessment
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Reference SMM Report No. 4/2002. ISBN 82-14-02788-8

Aim

To undertake a critical and systematic review of the clinical effectiveness of mammography screening for groups aged 40 to 49 years and 50 to 59 years. The effect of mammography screening is controversial. This controversy is mainly related to the balance between supposed reduced mortality and possible negative consequences of screening.

Conclusions and results

This technology assessment on mammography screening is based on systematic reviews and meta-analyses of 7 (8) randomized controlled trials (RCT) published from 1995 and later, including results of population-based screening programs.

Women in the relevant age groups must be informed about all aspects of mammography screening as a health offer. This information must address the benefits and also the negative consequences of screening. The knowledge presented in this report includes the following elements:

- Mammography screening reduces breast cancer mortality in the group aged 50 to 69 years. The scientific documentation has some weaknesses, and the estimated relative risk reduction in mortality is estimated to range between 6% and 27%. Other documentation reports a risk reduction of 20% to 25%.
- The effect in the group aged 40 to 49 years is less, and uncertain, with even weaker evidence.
- Mammography screening does not protect against developing breast cancer between screening rounds. Interval cancer is a reality, and more than one fifth of the women who are diagnosed with breast cancer receive their cancer diagnosis between screening rounds. Women must be made aware of this phenomenon.
- There is a cumulative risk of false positive mammograms for each screening round and, thereby, a need for new mammograms and other examinations (including biopsies or surgery).
- Mammography screening increases the incidence of breast cancer findings by also detecting early stages (Ductal Carcinoma in Situ (DCIS)). It is uncertain if all DCISs require treatment. The problem is that we do not know which DCISs need treatment and which ones do not.

Methods

Studies were identified by searching MEDLINE, EMBASE, Cinahl, PsychInfo, Cochrane Library, DARE, INAHTA, and The National Guideline Clearinghouse. The draft report was peer reviewed by Norwegian and Nordic experts.

Written by Dr Berit Mørland, SMM, Norway

INAHTA Briefs

Issue 2002/79

Title A Population-Based Cohort Study of Surveillance Mammography After Treatment of Primary Breast Cancer

Agency CCOHTA, Canadian Coordinating Office for Health Technology Assessment
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Reference CCOHTA Technology Report, Issue 15, July 2001. ISBN 1-894620-03-8 (print); ISBN 1-894620-04-6 (online): http://www.ccohta.ca/ccohta_production/entry_e.html

Aim

- To describe the rates of use of annual surveillance mammography (SM) following treatment of primary breast cancer in women in Ontario, Canada
- To describe the rates of subsequent breast surgery following annual SM.

Conclusions and results

Although practice guidelines in the United States and Canada have recommended annual surveillance, this study found the median interval between consecutive surveillance mammograms to be 14.7 months. Women diagnosed at age 70 or older, and women treated by lumpectomy without radiation therapy, were less likely to use SM compared to other women treated for breast cancer. Ironically, these two groups are also at highest risk for recurrence. The data show, but do not explain, long intervals between the date of SM and the dates of breast biopsies (median 2.97 months), lumpectomies (median 2.55 months), and mastectomies (median 2.50 months). The consequences of this delay are unknown. The data also show that two-thirds of subsequent breast surgery performed for women previously treated for breast cancer occurs more than 4 months following SM. This finding suggests a hypothesis that SM does not detect all recurrences or all new primary contralateral breast cancers.

Recommendations

- Monitor the rate of SM use among the women at highest risk for recurrence.
- Monitor the interval between SM and subsequent breast surgery.
- Monitor the number of women who use SM and undergo subsequent lumpectomy or mastectomy, and compare that number with the number of women who undergo surgery without previous SM.

Methods

The first part of this two-part project, published in June, 2000, was a systematic literature review by L. McGahan and H. Noorani titled "Surveillance mammography after treatment for primary breast cancer" which evaluated the practice and its impact on disease outcomes. The second part of the project, described in this brief, identified 12 279 women with new cases of invasive breast cancer diagnosed in Ontario between July 1, 1991, and December 31, 1993. Of these women, those who underwent lumpectomy and mastectomy procedures within 4 months after diagnosis were followed for surveillance mammography, subsequent diagnostic procedures on the breast, subsequent breast surgery, and death from any cause, up to December 31, 1998.

Written by Paszat L, Grunfeld E, van Walraven C, Coyle D, Sawka C, Yun J, McGahan L, Noorani H, CCOHTA, Canada

INAHTA Briefs

Issue 2002/91

Title **Screening for Gestational Diabetes: A Systematic Review and Economic Evaluation**

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Reference Health Technol Assess 2002; 6(11). Nov 2002. www.ncchta.org/execsumm/summ611.htm

Aim

To review current knowledge, clarify research needs, and assist with policy making in the interim, pending future research.

Conclusions and results

Debate continues on the definition of GDM (gestational diabetes millitus). GDM is usually defined by divergence from normal glucose levels. Since glucose levels are usually raised in pregnancy, this may lead to misclassification and unnecessary intervention. Ideally, GDM should be defined by the incidence of adverse effects. However, the most common reported complication of GDM is 'macrosomia' in the baby, usually defined by arbitrary weight cut-offs that fail to distinguish the abnormal growth patterns associated with high insulin levels in the womb.

GDM screening fails to meet certain UK National Screening Committee (NSC) criteria. Several screening tests have been used but some, eg, glycosylated hemoglobin and fructosamine, have proved unsatisfactory and can be discarded. Others, eg, urine testing or random blood glucose, are far from satisfactory, but inexpensive. There is marked international variation. Risk factors, eg, weight, age, and family history are useful in selective screening, but miss some cases of GDM. Fasting plasma glucose (FPG) is convenient and reliable, but some cases would be missed by FPG screening alone. Glucose challenge tests (GCTs) also have shortcomings. Definitive diagnosis is usually by oral glucose tolerance test (OGTT), but glucose load and timing vary in different countries, and reproducibility of the test is poor. More natural methods, eg, test meals, have been used, but not widely.

Recommendations

In some pregnant women, glucose levels rise sufficiently to harm the baby. However, many women with lower levels of glucose intolerance, whose babies are not at risk, may suffer anxiety and inconvenience from being classed as abnormal. Presently, the best test is probably the GCT, preferably combined with FPG. The benefits of followup OGTT are doubtful.

Methods

A literature review focused on screening methods and costs, and an appraisal of screening for GDM against the criteria for assessing screening programs used by the NSC.

Further research/reviews required

1) The 'disease' needs to be better defined by documenting the rate of adverse events in population-based epidemiological surveys (should include ethnic groups, as risks appear to vary). This work would relate outcomes of pregnancy to maternal blood glucose and other factors to determine the glucose level at which outcomes worsened significantly. Data on other factors, eg, overweight, would be used to determine if glucose intolerance was an independent cause, and if so at what level. 2) If the research showed a continuum of risk rather than distinct normal and abnormal groups, economic analysis should examine the cost effectiveness of intervention at different levels. 3) Trials of the marginal costs and benefits of different screening tests (eg, FPG vs GCT, and whether if these are positive a followup OGTT is necessary). 4) Trials of intervention in key groups, eg, those with normal FPG but elevated postprandial levels. 5) Further analysis of the cost effectiveness of screening.

It is recommended to await the results of the two main trials, the Hyperglycaemia and Pregnancy Outcome Study (HAPO) and the ACHOIS trial (a collaborative trial of treatment for screen-detected GDM) before further research is commissioned by the HTA Programme.

Written by Prof Norman Waugh, SHTAC, University of Southampton, UK

INAHTA Briefs

Issue 2003/10

Title **Screening for Hepatitis C Among Injecting Drug Users and in Genitourinary Medicine Clinics: Systematic Reviews of Effectiveness, Modeling Study and National Survey of Current Practice**

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Reference Health Technol Assess 2002; 6(31). Dec 2002. www.ncchta.org/execsumm/summ631.htm

Aim

To review the clinical effectiveness and cost effectiveness of screening for hepatitis C virus (HCV) in injecting drug users (IDUs), and genitourinary medicine (GUM) clinic attenders in the UK.

Conclusions and results

Six relevant studies of screening strategies were revealed. Only one study addressed screening in the UK. The other studies were of limited scope/relevance to the UK. The response rate for the study of current practice in HCV screening was 65% overall, and 26% of drug services reported screening compared to 92% of GUM clinics. In the modeling study, screening for HCV in IDUs was estimated to yield benefits over no screening at a cost of £28,120/ QALY. This estimate was reasonably stable in a wide range of one-way sensitivity analyses. The cost effectiveness of universal screening in GUM clinics was estimated to be £84,570/QALY and was subject to considerable uncertainty. Selective screening in GUM clinics is likely to be more cost effective than universal screening.

Recommendations

Screening objectives for HCV need to be clarified. Screening for HCV in IDUs in contact with services is moderately cost effective. Universal screening in GUM clinics is less cost effective and subject to greater uncertainty than screening IDUs in contact with services. Due to insufficient information on the epidemiology of HCV in groups other than IDUs, it is uncertain whether seeking people other than IDUs for screening is cost effective.

Methods

To review economic evaluations of screening programs, electronic databases were searched (1996–2001) using a broad strategy to identify evaluations of screening programs for HCV. Articles were appraised using a standard framework. To study practices in HCV screening, all GUM clinics, health authorities, and prisons, and 50% of drug services in England were surveyed by questionnaire (October 2001). Participants were asked about screening, diagnosis, and treatment in their organization. The cost-effectiveness model examined the progress of hypothetical cohorts through the stages of screening, diagnosis, and treatment in two separate populations: IDUs in contact with drug services and GUM clinic attenders. Screening was compared to a no-screening scenario and cost utility (£/quality-adjusted life-year (QALY)) was estimated. Literature searches identified values for the parameters in the model. Costs were discounted at 6% and benefits at 1.5%. Sensitivity analyses and multi-way analyses were conducted. Electronic databases were searched (1981–2002) for studies on behavioral changes associated with gaining knowledge of HCV status. Further relevant studies were searched through citations, scrutiny of references, and from experts.

Further research/reviews required

These are detailed fully in the report.

Written by Dr Ken Stein, Peninsula Technology Assessment Group, Exeter, UK

INAHTA Briefs

Issue 2003/12

Title **Positron Emission Tomography (PET) Imaging in Cancer Management**

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Reference Health Technology Assessment Report 2, November 2002, ISBN 1-903961-31-9

Aim

- To determine the role of fluorine-18 deoxyglucose (FDG)-PET imaging in cancer management by evaluating clinical and cost effectiveness in terms of impact on patient morbidity and mortality.
- To consider the best configuration of PET facilities and cyclotrons to serve Scotland, if PET was found to be clinically and cost effective.

This assessment focused primarily on non-small cell lung cancer (NSCLC) and lymphoma.

Conclusions and results

An economic model indicates that FDG-PET imaging is cost effective compared with computed tomography (CT) in restaging Hodgkin's disease at the completion of induction chemotherapy, saving up to 30% of patients from unnecessary radiotherapy. FDG-PET is also potentially cost effective in NSCLC if used before mediastinoscopy in CT-negative patients. Information from other INAHTA-published HTAs indicates evidence of clinical effectiveness in solitary pulmonary nodule, malignant melanoma, recurrent head and neck cancer and lymphoma. From a patient perspective it was found that communication of the process and possible outcomes could be improved, but some patients valued the reassurance offered by the PET image compared with other diagnostic techniques.

Recommendations

- A PET imaging facility including a cyclotron, dedicated to clinical use and specific health services research, should be set up in Scotland and linked to a specialist cancer center.
- All patients who require restaging of Hodgkin's disease should receive FDG-PET imaging to select those for surveillance or radical radiotherapy.
- PET research should be undertaken in other cancers, eg, lung cancer (NSCLC and single pulmonary nodule), malignant melanoma and recurrent head and neck cancer, to inform economic modeling and patient outcome.
- All patients undergoing FDG-PET should have their outcomes recorded, either through participation in a national or international trial to confirm and extend current applications of FDG-PET imaging or through health services research designed to allow costs and patient outcomes to be recorded for economic modeling.

In the 2 years anticipated to build a PET facility, the Scottish Executive Health Department and NHSScotland will work together to consider interim solutions for provision of PET imaging services from current research facilities in the UK.

Methods

The scientific literature was searched systematically to identify published evidence. Experts, professional groups, patient groups, manufacturers, and other interested parties were invited to submit evidence. Clinical effectiveness evidence was critically appraised, economic evaluations were performed, and a review of evidence on patient and organizational issues was carried out. Patient needs' and preferences were also considered focus group work.

Written by Prof Karen M Facey, NHS QIS, UK

INAHTA Briefs

Issue 2003/15

Title **Digital Mammography versus Film-Screen Mammography: Technical, Clinical, and Economic Assessments**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
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Reference CCOHTA Technology Report, Issue 30, October 2002. ISBN 1-894620-62-3 (print); ISBN 1-894620-61-5 (online): http://www.ccohta.ca

Aim

- To compare the technical aspects of digital mammography (DM) and film-screen mammography (FSM)
- To compare the clinical effectiveness of DM and FSM
- To model the potential costs and effects of DM and FSM within the context of the Canadian health system.

Conclusions and results

Technical Benefits: This report considered two digital mammography (DM) systems: digital radiography-mammography (DR-M) and computed radiography-mammography (CR-M). Operational and technical benefits of DM over FSM include improved diagnostic accuracy; ease of image manipulation, transmission, and archiving; and suitability for computer-aided diagnosis.

Clinical Effectiveness: Although DM offers some potential clinical benefits over FSM, including shorter examination time and lower radiation dosage, these benefits have not been demonstrated in a clinical setting. The ability to detect cancer is comparable for DR-M and FSM; there is insufficient data on the clinical effectiveness of CR-M.

Economic Analysis: DR-M was found to have significantly higher annualized costs than either FSM or CR-M. Assuming that DR-M and CR-M are, at best, clinically equivalent to FSM, the minimum-cost system is preferred. Therefore, conventional FSM is preferable to DM at this time. As the costs of CR-M are comparable to those of FSM, CR-M may be preferable to DR-M once acceptable clinical performance has been demonstrated.

Recommendations

Not applicable.

Methods

For each of the three aims of this study, relevant studies were independently selected by two reviewers from the results of a systematic search of multiple electronic databases. The technical review was based on 37 relevant articles; the clinical review on 7; and the economic analysis on 17. Since only a few heterogeneous studies were available for the clinical review, the literature was summarized qualitatively rather than analyzed quantitatively. Cost minimization analysis compared the costs of providing mammography using conventional (FSM), digital (DR-M), or hybrid (CR-M) systems.

Further research/reviews required

Large studies are needed to demonstrate any clinical advantages of DM.

Written by Ho C, Hailey D, Warburton R, MacGregor J, Pisano E, Joyce J, CCOHTA, Canada

INAHTA Briefs

Issue 2002/33

Title **Predictive Genetic Testing for Hereditary Breast and Colorectal Cancer**

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Reference ITA-Report April 2002. The assessment is available in German only at www.oeaw.ac.at/ita/hta/

Aim and Method

The aim of this assessment was to analyze the current scientific knowledge and the situation of genetic counseling on predictive genetic testing for hereditary breast and colorectal cancer. Predictive genetic testing will be available for several common diseases in the near future, and questions related to reimbursement and quality assurance will be raised.

This report is based on a nonsystematic literature search using several databases (eg, EMBASE, MEDLINE, Cochrane Library), a CCOHTA assessment, and a US review (American Gastroenterological Assoc.). In addition to the scientific basis on genetic testing, the authors describe and analyze the different diagnostic testing methods and the benefits of early detection methods and prophylactic interventions in the context of individual/familial and social consequences.

Background

Breast and colorectal cancer are among the most frequent cancer diseases. Most are based on random accumulation of risk factors, 5% to 10% show a familial determination. A hereditary modified gene is responsible for the increased cancer risk. In these families, the high tumor frequency, young age at diagnosis, and multiple primary tumors are striking.

Results and Conclusion

Genetic diagnosis: The sequence analysis is the gold standard. Denaturing high performance liquid chromatography/DHPLC is a fast alternative method. The identification of the responsible gene defect in an affected family member is important. If the test result is positive, it is still uncertain if the disease will occur, when and to what degree founded in the geno-/phenotype correlation. The individual risk estimate is based on empirical evidence. The test results have effects on the entire family.

Prevention/early detection: Currently, primary prevention is not possible except for familial adenomatous polyposis (FAP). The so-called preventive medical checkups are – in reality – early detection examinations. The evidence on early detection methods is better for colorectal cancer than for breast cancer.

Prophylactic surgical interventions: Prophylactic mastectomy (PM) reduces the relative breast cancer morbidity risk by approximately 90%. The question is whether PM influences mortality. Acceptance of PM depends on culture. Colectomy can be used as a prophylactic (FAP) and therapeutic method. After surgery, the cancer risk remains high. Hence, early detection examinations are still necessary.

Counseling: The clinical evidence is often fragmentary and of limited quality. The patient is exposed to so-called objective scientific data. The presentation of the data and the interpretation of the genetic information on sensitivity, specificity, positive predictive value, and number needed to screen or treat are important to understand and to use in making personal decisions.

Reflections: New identification of mutations and demand stimulated by false/inappropriate understanding of genetics will result in an increase in predictive genetic testing and counseling. The gap is wide between predictive genetic diagnosis and prevention, early detection, and therapeutic interventions. These circumstances require a basic strategy. Since predictive genetic diagnosis is a sensitive societal issue, it is important to deal with it carefully to avoid inappropriate hopes and/or discrimination.

Written by Dr. Susanna Jonas, ITA, Austria

INAHTA Briefs

Issue 2002/60

Genetic Test for Fragile X Syndrome – January 2002

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Reference MSAC Application 1035. Assessment Report ISBN 0 642 82123

Aim

To assess the safety and effectiveness of nucleic acid amplification for fragile X testing and under what circumstances public funding should be supported for the procedure.

Conclusions and results

Safety: An extensive literature search did not identify any studies reporting adverse events associated with i) testing individuals suspected of having fragile X syndrome, or ii) cascade testing of relatives of affected individuals. Similarly, no adverse events specific to prenatal diagnosis of fragile X (ie, amniocentesis or chrionic villus sampling) were identified in the literature, although the potential adverse events of these procedures are well documented.

Effectiveness: Evidence of the accuracy of the tests from the published literature indicates that cytogenetic testing is not as accurate as molecular techniques (ie, PCR and Southern blot) in detecting the fragile X full mutation. With regard to a fragile X premutation, cytogenetic testing was unable to detect such a mutation. The sensitivity of cytogenetic testing varied across studies, although specificity was consistently high with few false positive results reported. Studies comparing PCR to Southern blot reported high sensitivity and specificity. It should be noted, however, that PCR may not reliably amplify full mutations, and Southern blot is usually necessary to reliably demonstrate a full mutation.

Cost effectiveness: A cascade testing program is estimated to cost up to $4 million annually, and would result in a cost per initial case detected of between $14 000 and $28 000.

Recommendations

Public funding should be supported for Nucleic Acid Amplification (NAA) in those with specific clinical features of Fragile X (A) syndrome, including intellectual disabilities and in first and second degree relatives of individuals with Fragile X (A) mutation and Southern blot where the results of NAA testing are inconclusive.

Methods

MSAC conducted a systematic review of the biomedical literature (Cochrane Library, EBM-Reviews-ACP Journal Club, MEDLINE, PreMedline, Current Contents, Biological Abstracts and PsychINFO) from commencement to June 2001. The above sources were searched for cross-sectional studies which evaluated the diagnostic characteristics of at least two tests (PCR, Southern blot or cytogenetic test) for the diagnosis of fragile X (full or premutation).

Prepared by Ornella Clavisi, Monash Institute of Health Services Research, Australia

INAHTA Briefs

Issue 2003/05

Title A Comparative Study of Hypertonic Saline, Daily and Alternate-day rhDNase in Children with Cystic Fibrosis

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Reference Health Technol Assess 2003; 6(34). Jan 2003. www.ncchta.org/execsumm/summ634.htm

Aim

The objective of this study is to compare the efficacy and cost effectiveness of daily recombinant human deoxyribonuclease (rhDNase), alternate-day rhDNase and hypertonic saline in the treatment of children with cystic fibrosis.

Conclusions and results

Forty-eight children were recruited to the study. Following 12 weeks of treatment, there was a mean increase in FEV1 over baseline of 16%, 14%, and 3% with daily rhDNase, alternate-day rhDNase, and hypertonic saline, respectively. Comparing daily rhDNase with alternate-day rhDNase, there was no evidence of difference between the treatments. However, daily rhDNase showed a significantly greater increase in FEV1 compared with hypertonic saline. The mean difference in total cost between daily rhDNase and alternate-day rhDNase was £513 over the 12-week treatment period, and between daily rhDNase and hypertonic saline it was £1409. None of the other secondary outcome measures showed significant differences between the treatments.

Recommendations

Alternate-day rhDNase appears to be as effective as daily rhDNase in cystic fibrosis and, on average, reduces health service costs. It appears that 7% hypertonic saline is not as effective as daily rhDNase, although there was some variation in individual response.

Methods

This was an open-label, active-treatment, randomized crossover trial. Each patient was allocated consecutively to 12 weeks of treatment with once-daily 2.5 mg rhDNase, alternate-day 2.5 mg rhDNase, or twice-daily 5 ml of 7% hypertonic saline, in random order. There was a 2-week washout period between treatments.

Further research/reviews required

To support the results, a followup long-term parallel trial comparing daily rhDNase with alternate-day rhDNase, which includes a health economic analysis, should be performed.

Written by Dr Colin Wallis, Respiratory Unit, Great Ormond Street Hospital for Children, NHS Trust, London, UK

INAHTA Briefs

Issue 2002/63

Title **A Design and Use of Questionnaires: A Review of Best Practice Applicable to Surveys of Health Service Staff and Patients**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
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Reference Health Technol Assess 2001;5(31). Dec 2001. www.ncchta.org/execsumm/summ531.htm

Aim

To identify current best practice with respect to the design and conduct of questionnaire surveys, including theories of respondent behavior, expert opinion, and high-quality evidence from experimental studies.

Conclusions and results

The two principal modes of administration are self-completion and interviewer administration. Evidence from identified studies provided no consistent picture of the superiority of any one mode in terms of the quantity or quality of the response, or the resources required. Evidence supported the notion that question wording and framing, including the choice and order of response categories, can have an important impact on the nature and quality of responses. Evidence from several primary studies supports the assertion that general questions should precede specific questions.

Potential respondents must have both the means and will to complete the questionnaire; the perceived costs of responding must not exceed the benefits. The apparent relevance, importance, and interest of the survey to the respondent have an important influence on response rates. The number of contacts made with sampled individuals is another powerful factor. Other factors shown to influence response rates include making a self-interest/utility appeal to the respondent and the use of incentives. Anonymity has not been demonstrated to have any consistent effects on the rate or quality of response.

There can be no universal recommendations on best practice in respect of questionnaire design and survey conduct. Researchers need to consider the aims of the particular study, the population under investigation, and the resources available. In choosing a mode of questionnaire administration, consideration needs to be given to the availability of an appropriate sampling frame, anticipated response rates, the potential for bias from sources other than non-response, acceptability to the target population, the time available, the financial budget, and the availability of other resources.

The "task analysis" model, the theory of social exchange, and theories of perception and cognition should inform decisions regarding the physical design of questionnaires and strategies for delivering and returning them. The aim should be to enhance the perceived and actual benefits of responding and to minimize the perceived and real costs. The effort required to interpret questions and provide responses should be made as easy as possible.

Recommendations

Through careful attention to the design and layout of questionnaires, the risk of errors in posing and interpreting questions and in recording and coding responses can be reduced, and potential inter-rater variability can be minimized. Questionnaire appearance can influence respondents' decisions at several stages, from arousal of interest in questionnaire completion, through task evaluation, to initiation and monitoring of the process of completion. There is a need for consistency in the presentation of visual information and an understanding and application of "graphic non-verbal language".

Title **A Design and Use of Questionnaires: A Review of Best Practice Applicable to Surveys of Health Service Staff and Patients**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom
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Reference Health Technol Assess 2001;5(31). Dec 2001. www.ncchta.org/execsumm/summ531.htm

Methods

The starting point for this review was expert opinion from key textbooks. High-grade evidence was then sought from experimental and quasi-experimental studies to support or refute the experts' recommendations. In addition, information was sought on the theoretical underpinnings of survey response. The PsycLIT electronic database was used in addition to MEDLINE, and the search was confined to articles published in the English language between 1975 and 1996. However, because of the heterogeneity of studies, no attempts at meta-analysis were made. Findings are presented as relative risks with associated 95% confidence intervals (for differences in percentages), or as differences in means with associated 95% confidence intervals (for continuous data).

Further research/reviews required

Both quantitative research (in the form of experimental manipulations of various aspects of questionnaire design and administration) and qualitative research (in the form of cognitive interviews addressing the processes by which respondents react to questionnaire stimuli) are required.

Written by Ms Elaine McColl, Centre for Health Service Research University of Newcastle, UK

INAHTA Briefs

Issue 2002/64

A Study of the Methods Used to Select Review Criteria for Clinical Audit

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Reference Health Technol Assess 2002;6(01). Jan 2002. www.ncchta.org/execsumm/summ601.htm

Aim

To develop a clear definition of the desirable characteristics of review criteria and their selection for clinical audit. To create and use a valid questionnaire, the Audit Criteria Questionnaire (ACQ), to identify the degree to which review criteria that have those characteristics are selected or developed. To identify obstacles to the selection or development of review criteria and recommend methods of overcoming such obstacles. To advance our understanding of how review criteria for clinical audit are selected.

Conclusions and results

Reported methods of selecting review criteria for clinical audit were often less systematic than desirable. Of the respondents, 71% based their review criteria on the research literature. Only 27% recorded whether the validity of the research was appraised, and 25% recorded the methods used to appraise it. Furthermore, 29% had not reported using the research literature to select their review criteria. Consultation with colleagues was the most common basis for selecting review criteria, as an alternative or supplement to evidence from the literature. Patients or carers were rarely consulted. Assessing the validity of review criteria is impeded by the lack of information on how review criteria were developed, even in published audit protocols. About half of respondents used audit review criteria that had been piloted. Of the respondents, 81% had prioritized their review criteria. Clinical and non-clinical audits did not differ significantly on ACQ scores. Reporting of national or regional audits was extremely rare in the current study. The ACQ scores for unpublished review criteria were even lower than for published ones. The most commonly noted problems focused on organizing the audit and gathering literature upon which to base criteria. Audit leads reported the need for training to enhance skills in literature searching and critical appraisal. The organization has an important role to provide such training, and to ensure that library facilities are of a high standard and individuals are assisted by electronic or staff services in searching for relevant evidence.

Recommendations

To ensure that review criteria are valid, it is essential to have details of the evidence they are based on, the quality of the evidence, the reasons behind any prioritization, and information on how they could be used. All published audit protocols should include a detailed, transparent account of how the review criteria were selected. Training to enhance levels of skill in literature searching and critical appraisal is important for those selecting their own evidence-based review criteria.

Methods

A definition of the important and feasible characteristics of review criteria was developed through an iterative questionnaire process to generate consensus among an international panel of experts in the field of quality improvement in healthcare. Their consensus on the desirable characteristics of review criteria was used to develop an ACQ to assess how well review criteria were selected or developed. This was then used to measure how well review criteria have been selected or developed for use in clinical audits in the NHS in England and Wales. After piloting and revisions, the questionnaire was distributed to leads of clinical audits in NHS trusts and general practices. Following the questionnaire study, a sample of respondents was selected for interview.

INAHTA Briefs

Issue 2002/64

Title A Study of the Methods Used to Select Review Criteria for Clinical Audit

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
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Reference Health Technol Assess 2002;6(01). Jan 2002. www.ncchta.org/execsumm/summ601.htm

Further research/reviews required

Trials of interventions designed to improve the selection of review criteria for clinical audit. The questionnaire (ACQ) developed in this study could be used as an outcome measure for such trials. One such intervention could be the creation of a library of review criteria that have all the desirable characteristics. The development and validation of a simple tool by which review criteria can be assessed. This should be based on an expert consensus of the desirable characteristics of review criteria. Testing the relative effects on the quality of patient care of national or regional audits compared with local audits. Case studies of organizations, where the selection of review criteria is given appropriate importance and resources, would identify the organizational policies that enable and maintain this.

Written by Dr Hilary Hearnshaw, Centre for Primary Health Care Studies, University of Warwick, UK

INAHTA Briefs

Issue 2002/96

Title **Subgroup Analyses in Randomized Controlled Trials: Quantifying the Risks of False-positives and False-negatives**

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Reference Health Technol Assess 2001;5(33) Oct 2001 www.ncchta.org/execsumm/summ533.htm

Aim

To quantify the extent to which subgroup analyses may be misleading and to compare the relative merits and weaknesses of the two most common approaches to subgroup analysis: separate (subgroup-specific) analyses of treatment effect and formal statistical tests of interaction. To establish what factors affect the performance of the two approaches. To provide estimates of the increase in sample size required to detect differential subgroup effects and to provide recommendations on the analysis and interpretation of subgroup analyses.

Conclusions and results

With simulated simplest case data with no differential subgroup effects, the formal tests of interaction were significant in 5% of cases as expected, while subgroup-specific tests were less reliable and (incorrectly) identified effects in 7%–66% of cases depending on whether there was an overall treatment effect. The most common type of subgroup effect identified in this way was where treatment effect was significant in one subgroup only. When a differential subgroup effect was included, the performance of the formal interaction test was generally superior to that of the subgroup-specific analyses, with more differential effects correctly identified using interaction tests. The ability of formal interaction tests to (correctly) identify subgroup effects improved as the size of the interaction increased relative to the overall treatment effect. When the size of the interaction was twice the overall effect or greater, the interaction tests had at least the same power as the overall treatment effect, but was considerably reduced for smaller interactions more likely to occur in practice. The inflation factor required to increase the sample size to detect the interaction with the same power as the overall effect varied with the size of the interaction. For an interaction of the same magnitude as the overall effect, this inflation factor was four. This increased dramatically for more subtle interactions to 100 or greater for interactions smaller than 20% of the overall effect. Formal interaction tests were generally robust to alterations in the number and size of the treatment and subgroups and, for continuous data, the variance in the treatment groups; the only exception being a change in the variance in one of the subgroups. In contrast, the performance of the subgroup-specific tests was affected by almost all of these factors with only a change in the number of treatment groups having no impact at all. While it is generally recognized that subgroup analyses can produce spurious results, the extent of the problem is almost certainly underestimated. This is particularly true for subgroup-specific analyses. In addition, the increase in sample size required to identify differential subgroup effects may be substantial, and the previously used 'rule of four' may not always be sufficient, especially when interactions are relatively subtle.

Recommendations

Trials should ideally be powered with subgroup analyses in mind. Subgroup analyses should be restricted to those proposed before data collection, Any subgroups chosen after this time should be clearly identified. Subgroup-specific analyses are particularly unreliable and are affected by many factors. Subgroup analyses should be based on formal tests of interaction, but even these should be interpreted with caution. Results from subgroup analyses should not be over-interpreted, and unless there is strong supporting evidence, they are best viewed as a hypothesis-generation exercise. Any apparent lack of differential effect should be regarded with caution unless the study was specifically powered with interactions in mind.

Title **Subgroup Analyses in Randomized Controlled Trials: Quantifying the Risks of False-positives and False-negatives**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
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Reference Health Technol Assess 2001;5(33) Oct 2001 www.ncchta.org/execsumm/summ533.htm

Methods

Subgroup-specific and formal interaction tests were assessed, firstly, by simulating data with no differential subgroup effects and determining the extent to which the two approaches (incorrectly) identified such an effect. Secondly, data were simulated with a range of types and magnitudes of subgroup effect (sample size determined by the nominal power (50%–95%) for the overall treatment effect) and the extent to which the two approaches were able to (correctly) identify the subgroup effect determined. Initially, data were simulated to represent the 'simplest case' of two equal-sized treatment groups and two equal-sized subgroups. Additional simulations were used to explore the impact of various trial specifications.

Further research/reviews required

Implications of considering confidence intervals rather than p-values could be considered. The same approach could be applied to contexts other than randomized controlled trials, eg, observational studies and meta-analyses.

Written by S Brookes, Lecturer in Medical Statistics, Dept Social Medicine, Univ Bristol, UK

INAHTA Briefs

Issue 2003/08

Title How Important Are Comprehensive Literature Searches and the Assessment of Trial Quality in Systematic Reviews? Empirical Study

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Reference Health Technol Assess 2003; 7(1). Jan 2003. www.ncchta.org/execsumm/summ701.htm

Aim

1) To examine the characteristics of difficult-to-locate clinical trials and lower-quality trials. 2) To compare, within meta-analyses, the treatment effects reported in difficult-to-locate trials with those in more accessible trials, and of trials of lower quality with trials of higher quality. 3) To assess the impact of excluding difficult-to-locate trials and lower-quality trials on pooled effect estimates, p-values, and the shape of funnel plots.

Conclusions and results

In total, 159 systematic reviews met the inclusion criteria, but not all included difficult-to-locate trials. Comparisons of treatment effects were based on: unpublished vs published; other languages vs English; non-indexed vs MEDLINE-indexed. Analyses of trial quality were based on: inadequately concealed/unclear vs adequately concealed; not double-blind vs double-blind. The importance of difficult-to-locate trials appears to vary across medical specialties. Unpublished trials show less beneficial effects than published trials whereas non-English language trials and non-indexed trials tend to show larger treatment effects. Trials that are difficult to locate tend to be smaller and of lower methodological quality than trials that are easily accessible and published in English. Trials with inadequate or unclear concealment of allocation show more beneficial effects than adequately concealed trials. Similarly, open trials tend to be more beneficial than double-blind trials. In most meta-analyses, exclusion of trials with inadequate or unclear concealment and trials without double-blinding led to a change (often substantial) toward less beneficial treatment effects. Including unpublished trials reduces funnel plot asymmetry whereas including trials published in languages other than English and non-indexed trials increases the degree of asymmetry in the funnel plot. The impact of trials of lower methodological quality on the funnel plot is substantial for trials with inadequate or unclear concealment of allocation.

Recommendations

Systematic reviews based on searching the English language literature accessible in major bibliographic databases will often produce results close to those obtained from reviews based on more comprehensive searches that are free of language restrictions. The finding that difficult-to-locate trials are often of lower quality raises the worrying possibility that rather than preventing bias through extensive literature searches, bias could be introduced by including trials of low methodological quality. The results confirm that the funnel plot and the regression method to assess funnel plot asymmetry are useful to detect the tendency for smaller studies in a meta-analysis to show larger treatment effects.

Methods

Eight medical journals that regularly publish systematic reviews, the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effectiveness and the Health Technology Assessment database were searched for relevant articles. Meta-analyses of therapeutic or preventive interventions based on comprehensive literature searches and which combined the binary outcomes of at least 5 controlled clinical trials were included. Language was assessed using the SERLINE journals database, and published trials were classified according to whether or not they had been published in a MEDLINE-indexed journal. Quality assessment was restricted to trials included in Cochrane reviews.

Further research/reviews required

Four main areas are described fully in the report

Written by Professor Matthias Egger, Department of Social Medicine, University of Bristol, UK

INAHTA Briefs

Issue 2002/68

Tobacco Smoking and Oral Health

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Reference SBU Report 157, 2002, ISBN91-87890-74-7, Available in Swedish at http://www.sbu.se

Aim

This report reviews the scientific literature on smoking as a risk factor for periodontal disease, oral and pharyngeal cancer, and issues related to dental implant treatment.

Conclusions and results

- Periodontal disease rates are higher in smokers than in non-smokers.
- Periodontal disease is more severe in smokers than in non-smokers.
- The risk for contracting periodontal disease is 3 to 5 times higher in smokers than in non-smokers.
- Periodontal disease is less common in former smokers than in current smokers. However, former smokers remain more susceptible to periodontal disease than do non-smokers.
- Smoking is related to oral and pharyngeal cancer. The risk increases with the number of cigarettes smoked and the duration of the habit. Alcohol use further increases the risk.
- Smoking cessation, in comparison to current smoking, will substantially decrease the risk for contracting oral and pharyngeal cancer.
- Smoking may impair the outcome of dental implant treatment, but the evidence is conflicting.

Methods

A computer-aided, systematic search of MEDLINE and the Cochrane Library (1966 to November 2001) was conducted to identify the relevant literature, using a combination of keywords for smoking and outcomes of oral health. The references from all retrieved articles were also screened.

Further research required

The evidence on smoking as a risk factor in dental implant treatment is limited and contradictory. Studies of high methodological quality are lacking.

Written by Dr Susanna Axelsson, SBU, Sweden

INAHTA Briefs

Issue 2002/34

Title **Photodynamic Therapy With Verteporfin (PDT-V) for Agerelated Macular Degeneration, July 2001**

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Reference MSAC application 1039. Assessment report ISSN 1443-7120

Aim

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

Conclusions and results

Safety: Randomized controlled trials indicate a relatively high and precise number of adverse events (1 in 7) including visual disturbance (22%), injection site events (16%), infusion-related back pain (2.5%), allergic reactions (2%), and photosensitivity reactions (3.5%). Incidence of adverse events with fluorescein angiography (which is used to assess eligibility PDT-V) is measured at 4.5% (case studies, surveys, and other studies of lower evidence levels).

Effectiveness: PDT-V was more effective than placebo in patients with classic choriodal neovascularisation (CNV) in reducing loss of less than 15 letters after an average of 5.6 treatments over 24 months. Four patients with classic CNV need to be treated to produce one positive result (only 2 where there is no evidence of occult CNV). PDT-V did not reverse visual loss. PDT-V was not more effective than placebo for less typical lesions, patients with occult CNV and patients who were current smokers.

Cost effectiveness: Modeling suggests a cost per vision year gained of $6100 to $35 400 based on assumed clinical advantages and associated offsets. PDT-V funding is estimated to cost $10M to $30M in the first year, $16M to $36M in the second year and $13.6M per annum in subsequent years when testing only new patients. This assumes diagnosis is accurate. However, the difficulty of diagnosing patients may mean additional costs.

This draft report does not include recommendations.

Method

MSAC conducted a systematic review of the biomedical literature from 1966 to April 2001 accessing biomedical electronic databases, the Internet, and international health technology agency websites. Effectiveness was assessed using a randomized controlled trial of 609 patients that compared verteporfin with placebo in PDT for patients with neovascular AMD. Cost effectiveness assessment is based on modeling by the applicant of cost per vision-year gained for different clinical scenarios that compare PDT-V and placebo (and includes sensitivity analysis). Aggregate costings assume that the stock of current patients would be cleared in 2 years.

INAHTA Briefs

Issue 2002/90

Title Photodynamic Therapy in the Treatment of Age-related Macular Degeneration

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Reference CAHTA evaluation report. March 2002. 59 pages and 68 references. Full text available in Spanish at http://www.aatm.es/cas/informes/i.html

Aim

Scientific evidence related to the efficacy, effectiveness, and safety of photodynamic therapy in treating age-related macular degeneration was assessed. The report also addresses the clinical application of this technology in Spain and its impact at organizational, legal, and economic levels. It also describes alternative treatments and levels of scientific knowledge.

Conclusions and results

Age-associated macular degeneration (AMD) progressively damages the sensitive center of the retina (macula) and hence the center of the visual field. There are two types of disease: atrophic or dry and exudative, neovascular or wet. Exudative cases account for 10% of total AMD and affect approximately 2% of those aged above 60 years. It is characterized by a severe, progressive loss of vision, and 90% of the cases of blindness could present this neovascular form.

The scientific evidence suggests that photodynamic therapy may be efficacious and safe in patients with a classic subfoveal pattern (CNV) equal to or greater than 50% of the total surface of the lesion and secondary to AMD over the time analyzed (2 years). Evidence is insufficient to justify the systematic use of this therapy in patients with lesions of less than 50%.

Studies identified in this overview differ in terms of patient selection criteria. The first included patients with evidence of a classic pattern of choroidal neovascularization CNV secondary to AMD and with an extension of this pattern equal to or greater than 50% of the total surface of the lesion. The second included patients with occult CNV without the classic component and secondary to AMD and to pathological myopia.

Recommendations

Controlled and randomized clinical studies with a longer followup are required to confirm that the effects last more than 2 years and to determine important aspects that were not addressed, particularly on the patients' health-related quality of life.

Cost effectiveness

A cost-effectiveness study of photodynamic therapy applied to the second eye suffering from exudative AMD, but with better sight and with classical subfoveal CNV, was also identified. The results suggest that it is minimally cost effective in patients with AMD with classic subfoveal CNV in the second eye (better sight) and an initial visual acuity of 20/40. If the initial visual acuity of the second eye (in the same conditions) was worse, photodynamic therapy was not cost effective.

Methods

The bibliographic search strategy identified two controlled and randomized multicenter clinical trials (2 years of followup) and a systematic review. The methodological quality of the original studies and the scientific evidence they presented was regarded as high based on the scale for evaluating scientific evidence produced by CAHTA.

Written by Antoni Parada, CAHTA, Spain

INAHTA Briefs

Issue 2003/16

Title **Photodynamic Therapy with Verteporfin for the Treatment of Neovascular Age-Related Macular Degeneration: A Clinical Assessment**

Agency **CCOHTA, Canadian Coordinating Office for Health Technology Assessment**
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Reference CCOHTA Technology Report, Issue 31, November 2002. ISBN 1-894620-63-1 (print); ISBN 1-894620-64-X (online): http://www.ccohta.ca

Aim

- To assess the potential harms and benefits of verteporfin photodynamic therapy (PDT) in treating neovascular age-related macular degeneration (AMD)
- To discuss the economic implications of this new therapy.

Conclusions and results

Clinical Effectiveness: Two reports describing three randomized, controlled trials involving 948 participants met the eligibility criteria when rated using the Jadad scale. Compared with placebo, 2 years of treatment with verteporfin PDT reduced the number of cases of central blindness by slowing disease progression. However, most treated individuals will continue to lose visual acuity. Long-term therapy can result in complications, most commonly visual disturbances and injection site events. Compared to placebo, verteporfin PDT did not cause an overall increase in serious adverse events and appears to be reasonably well tolerated. The use of verteporfin PDT will likely increase the need for angiographic screening to determine eligibility for treatment. The direct impact of this treatment on quality of life and visual function is not known. Its impact on individuals with poorer vision is also unknown.

Economic Implications: Four cost effectiveness analyses were identified. These studies suggest that verteporfin PDT will modestly increase patient quality-adjusted life-years. However, the two-year incremental costs for this procedure in Canada are estimated to be between $10,625 and $14,250.

Recommendations

Not applicable.

Methods

This systematic review looked at randomized controlled trials comparing verteporfin PDT with placebo or current therapy in adults with wet AMD. Two independent reviewers identified relevant reports from the results of database searches, bibliographic searches, hand searches of reviews and conference abstracts, and information gathered from experts in the field and from the drug manufacturer. Outcome measures included:

- Number of individuals with legal blindness or changed visual acuity
- Impact on quality of life
- Impact on visual function
- Morbidity.

Further research/reviews required

Further research is needed to assess the direct impact of verteporfin PDT on quality of life and visual function.

Written by Husereau DR, Shukla VB, Skidmore B, Maberley D, CCOHTA, Canada

INAHTA Briefs

Issue 2003/20

Title Phakic Intraocular Lenses

Agency CEDIT, Committee for Evaluation and Diffusion of Innovative Technologies
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Reference CEDIT Report (in French) No. 02.05/Ra1/02/Recommendation 02.05/Re-1/02

Aim

Phakic intraocular lenses (IOLs) are designed to correct myopia, hyperopia, presbyopia, and, in the future, astigmatism. In contrast to corneal ablation, implantation of phakic intraocular lenses is reversible. The technology is long-standing. Innovations in design make the new generation of intraocular lenses more effective and simpler to position surgically. Anterior and posterior chamber phakic IOLs comprise a lens (which is concave in the case of myopia and convex in the case of hyperopia) together with a system for positioning and fixating the lens. Angle-fixated anterior chamber IOLs (of the GBR type by Ioltech, and Vivarte by CIBA-vision) are supported by the angle where the iris and cornea meet. The iris-fixated anterior chamber IOLs (ARTISAN® by OPHTEC) and posterior chamber IOLs supported on 4 points of the ciliary sulcus (ICL™ by STAAR Surgical) are 1-piece lenses.

Conclusions and results

Several generations of anterior chamber phakic intraocular lenses have been introduced since 1986. The first generation of intraocular lenses (ZB IOL) were discontinued due to complications. Newer models were designed to avoid contact with the iris while maintaining sufficient distance from the natural lens and the cornea. Results obtained with ZB5M (not used since 1997), NuVita, and ZSAL-4 intraocular lenses have been published. Several complications have been described: pupil ovalization, halos, glare, retinal detachment, uveitis and endothelial cell loss. The new, foldable, anterior chamber IOLs are not assessed in the literature due to insufficient data.

Iris-fixated lenses were designed in 1991 (named ARTISAN® in 1998). After 2 years of followup, endothelial cell loss was reported also with this type of intraocular lens. Posterior chamber phakic intraocular lenses can cause cataracts because of contact between the implant and the natural lens. Cases of retinal detachment have also been reported. Endothelial alteration is less of a problem for these IOLs than for anterior chamber IOLs.

The unit price for a phakic IOL varies between 381 and 640¸ depending on manufacturer. The cost for implanting intraocular lenses depends on the type of establishment (public, private) and on the surgical practice of the ophthalmologist (ambulatory or inpatient).

Recommendations

Phakic IOLs are an alternative to ablative surgery to correct mild refractive error. They appear to be the only technology capable of treating severe, disabling myopia. CEDIT considers this technology to be insufficiently evaluated, particularly as regards long-term tolerance. Furthermore, followup of patients via a registry does not seem feasible. CEDIT recommends setting up a clinical research protocol within the framework of a multicenter evaluation. The study should consider patients suffering from high ametropia who are intolerant to contact lenses and willing to comply with medium- and long-term followup. The study would be a means to define the criteria for choosing a particular type of implant (iris-fixated, anterior chamber angle-fixated or posterior chamber).

Methods

A literature search included several databases (MEDLINE, EMBASE, Biosis, Pascal, EBM reviews, Cochrane). Five experts were interviewed on the medical benefits of this technology.

Written by Edlinger C, Perrin J-P, Vongmany N, Charpentier E, Fery-Lemonnier E, CEDIT, France

INAHTA Briefs

Issue 2002/30

Assessments of Telemedicine Applications – An Update

Agencies

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FinOHTA, Finnish Office for Health Care Technology Assessment
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Reference Joint report by AHFMR and FinOHTA, September 2001. ISBN: 1-896956-45-9

Aim

To update the systematic review of the telemedicine evaluation literature that was included in the 1999 INAHTA report on assessment of telemedicine. The present review covers studies published since the completion of the earlier report.

Methods

Systematic literature review based on searches of the MEDLINE, EMBASE, CINAHL, HEALTHSTAR and CRD databases and the Cochrane Library from November 1998 to December 2000.

Results and Conclusions

- The review identified 38 scientifically credible studies that included comparison with a non-telemedicine alternative and which reported administrative changes, patient outcomes, or results of economic assessment.
- Nine of the studies were considered to be of good quality. Only some of these corresponded to the nine papers that described work based on randomized controlled trials. The quality of most cost and economic analyses was relatively poor.
- Nineteen of the studies concluded that telemedicine had advantages over the alternative approach, 16 also drew attention to some negative aspects or were unclear whether telemedicine had advantages and 3 found that the alternative approach had advantages over telemedicine.
- For several applications, savings and some clinical benefits were obtained through avoiding travel and associated delays. The home care studies showed convincing evidence of benefit, while those on teledermatology indicated that there were cost disadvantages to healthcare providers, but not to patients.
- Twenty-three of the studies appeared to have potential to influence future decisions on the telemedicine application under consideration. However, several of these had methodological limitations.
- The overall findings are similar to those of the review included in the 1999 INAHTA report. Useful data are emerging on some telemedicine applications, but good quality studies are still scarce and generalizability of most assessment findings may be limited.

Written by: David Hailey, AHFMR, Canada, Risto Roine, FinOHTA, and Arto Ohinmaa, Oulu University, Finland

INAHTA Briefs

Issue 2002/32

Title The Neuromate® Neurosurgical Stereotactic Robot

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Reference CEDIT Report (in French) No. 00.06/Ra1/00/Recommendation 00.06/Re1/00

Aim

CEDIT was consulted for an evaluation of the NeuroMate® neurosurgical robot. The NeuroMate® system from the company ISS is a computer-controlled, image-guided neurosurgery multijointed arm with five degrees of freedom. It allows the stereotactic positioning of an instrument holder usually guiding surgical instruments typically used in stereotactic neurosurgery. It enables, in two possible function modes (with or without stereotactic frames):

- Accurate and automatic positioning of the instrument holder
- Visualization of instrument position in real time on a workstation. The NeuroMate® then acts as a single-axis neuronavigation system, that axis being the depth of penetration in the brain.

Results

The literature in the field is mainly descriptive (feasibility studies). The neurosurgical team in Grenoble, the first to have developed the Neuromate®, is the only one to have provided information on the benefit of robotics in stereo tactic neurosurgery, such as reaching targets that are difficult to access, preoperative simulation for teaching purposes, etc. Since the goal is to reach lesions or cerebral functions without touching functional or vascular structures, this robot is used mainly in stereotactic biopsies, functional neurosurgery, and neuroendoscopic surgery. The accuracy of positioning and repositioning the NeuroMate® is shown to be crucial in small-size lesions occurring in deep and highly functional areas. This accuracy, equal to or less than 0.5 mm, is not provided by current techniques of neuro-navigation. In addition, use of the robot is part of the current development of functional neurosurgery; whether in pain surgery, deep cerebral stimulation as in Parkinson's Disease, or presurgical exploration of pharmacoresistant epilepsy.

The catalog price of the NeuroMate system is 281 K€ (VAT included) for the stereotactic frame-based version (including the robot arm NeuroMate® and its base, a central control unit for the arm, the workstation for visualization, software for planning and position simulation, and accessories). The catalog price of a stereotactic frame and its accessories is 69 K€ (VAT included). An additional amount of 183 K€ (VAT included) is required for the frameless stereotactic version (head frame and its base, specific localizers, and ultrasound system). The maintenance contract (preventive and corrective) is offered at 48 K€ (VAT included) per year. The additional cost of consumables is 174 € (VAT included) per intervention.

Recommendations

This robot is seen to meet the requirements of accuracy, innocuity, and "minimal invasion" characterizing neuro-surgical practice. No other technique of neuronavigation currently provides this degree of accuracy. CEDIT recommends the NeuroMate® stereotactic robot for centers handling a large number of patients with stereotactic neurosurgery indications, but also recommends a harnessing of expertise (neurology, neuroradiology, neurosurgery, neurophysiology) with recognized experience in the field. The neurosurgery department of the Henri-Mondor hospital corresponds to these requirements.

Methods

A systematic review of the literature was carried out. Six databases were scanned: MEDLINE, EMBASE, HEALTHSTAR, Pascal, Cochrane, and Current Contents. Also five neurosurgeons were committed as experts. They were interviewed on the innovative aspect and on the medical benefit of the aforementioned device. Three of these experts use the robot, and one of them designed it.

Written by: C. Edlinger, JP. Perrin, S. Baffert, E. Charpentier, E. Fery-Lemonnier, CEDIT, France

INAHTA Briefs

Issue 2002/37

Title Saline Infusion Sonohysterography (SIS), May 1999

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Reference MSAC application 1007. Assessment ISSN 1443-7120

Aim

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

Conclusions and results

Safety: SIS is safe with low complication rates when used with transvaginal ultrasound (TVS).

Effectiveness: SIS with TVS is more sensitive than TVS alone in detecting uterine cavity abnormalities and has similar specificity. It benefits clinical decision making by avoiding hysteroscopies in some cases.

Cost effectiveness: The cost of SIS is offset by reductions in hysteroscopies. The incremental cost-effectiveness ratio is highly sensitive to the proportion of hysteroscopies avoided by SIS (ranging from a cost of $1052 per hysteroscopy avoided to a dominant cost effectiveness ratio).

Recommendations

Public funding should be supported for SIS as a second line diagnostic method for abnormal uterine bleeding when findings of TVS are inconclusive.

Method

MSAC conducted a systematic review of medical literature using DialogWeb which sweeps numerous medical and health related databases. The databases were searched from establishment until June 1998. Cost effectiveness analysis used a range of estimates for associated reductions in hysteroscopy (9.4%, 20% and 30.6% following a study by De Crespigny in 1997). Separate figures were provided for private and public hospital patients.

INAHTA Briefs

Issue 2002/39

Title Total Ear Reconstruction, March 2000

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Reference MSAC application 1024. Assessment report ISSN 1443-7120.

Aim

To assess the safety and effectiveness of the procedure and under what circumstances public funding should be supported for the procedure.

Conclusions and results

Safety: The complication rate is relatively high, but considered acceptable due to excellent outcomes of the procedure. The most common complications are necrosis of the skin overlying the graft site, protrusion of the donor cartilage, and chest deformities where the donor cartilage was harvested.

Effectiveness: Only one case study (level IV evidence) is available, and higher level evidence is unlikely to become available. The procedure is considered to be effective in producing a more normal-looking ear than the alternative (Branemark implant), although total ear reconstruction has slightly higher complication rates. There is some uncertainty about the timing of the surgery for patients seeking the procedure to correct a congenital deformity.

Cost effectiveness: The procedure is complex, and surgery is time consuming. The data were insufficient to perform a rigorous cost-benefit analysis.

Recommendations

Public funding should be supported.

Method

MSAC conducted a systematic review of the biomedical literature from 1975 to 1999 by accessing biomedical electronic databases, the Internet, and international health technology agency websites.

Produced by the Centre for Clinical Effectiveness,Australia

INAHTA Briefs

Issue 2002/43

Title Human Stem Cells

Agency TA-SWISS, Centre for Technology Assessment at the Swiss Science and Technology Council

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Reference Interim report: TA 41-Z/2002: "Human Stem Cells", 224 pages, in German

The contents of the interim report are provisional in character and contribute to the discussion and current debate on stem cell topics that is being coordinated by the Science et Cité Foundation together with other institutions. The final report will appear in autumn 2002 after the completion of the TA study.

Interim Results: In mid-May 2002, the draft of the new Embryo Research Law is to be discussed in Switzerland. This draft proposes regulations concerning research on human embryonic stem cells (ES cells) and 'surplus' embryos from in-vitro fertilization (IVF). The new law answers the question: How stringently should Switzerland restrain research on human embryonic stem cells? The interim report of the Centre for Technology Assessment considers the use of adult stem cells as being much less problematic in contrast to embryonic stem cells that are particularly controversial - above all from ethical and legal points of view.

According to the authors' opinion, the central question from the ethical point of view is whether research on human ES cells should be done in Switzerland at all. If this question is answered in the affirmative, two legal possibilities exist. First, the lawmakers would be able to declare the extraction of human ES cells from 'surplus' IVF embryos as being permissible under certain specific conditions. Up to now this topic has not been regulated legally. For the purpose of artificial insemination about one thousand fertilized egg cells are stored in Swiss reproduction clinics. For various reasons, these eggs can no longer be used for their original purpose. To be usable as a source of stem cells, these fertilized egg cells would need to be cultivated further for some days. During the subsequent extraction of the ES cells, the embryo would be destroyed. "The further cultivation of the legal 'surplus' IVF embryos for research purposes is a delicate point from the legal point of view ", says Rainer J. Schweizer, a legal rights expert at the University of St. Gall. A second possibility would be to import human ES cells from other countries with more tolerant legislation. This option, however, not only raises the question of double morality, but also is considered by the authors of the TA study as being illegal - at least in cases in where the stem cells are taken from embryos specially bred for research purposes or produced by therapeutic cloning. As guaranteed biological and medical findings on human stem cells are not available at present, numerous other legal problems remain unresolved.

The regulations on stem cell research require a new verdict on the moral status of the human embryo. Whatever conclusion is reached, this will have consequences on dealing with human embryos and foeti in other areas. For example, in prenatal diagnostics, in the question of abortion, in preimplantation diagnostics, or in transplantation medicine and biomedical research in general. According to the opinion of the TA study's project manager, Baerbel Huesing from the Fraunhofer Institute in Karlsruhe, the decisions made within the framework of stem cell research can possibly pave the way for the crossing boundaries in the areas mentioned. Stem cell research is still in its infancy.

The medicinal-scientific interest in human stem cells is based particularly on the fact that these cells offer the potential for developing novel therapy concepts. In this way, previously incurable diseases might be treated successfully at some point in the future. Above all, researchers expect to find possible application areas in cell replacement therapy and tissue engineering.

INAHTA Briefs

Issue 2002/43

Title **Human Stem Cells**

Agency **TA-SWISS, Centre for Technology Assessment at the Swiss Science and Technology Council**

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Reference Interim report: TA 41-Z/2002: "Human Stem Cells", 224 pages, in German

As life expectancy is increasing, the development of new therapies for degenerative illnesses (eg, Alzheimer's), cardiovascular diseases, diseases of the nervous system (eg, Parkinson's, multiple sclerosis), and cancer (eg, leukemia) is becoming increasingly important.

All market estimates available at present on the potential of the use of human stem cells assume that the market will grow explosively. According to a prognosis by a German management consultant, the worldwide market volume was 400 million USD in the year 2000. This should rise to 12.9 billion USD by 2005 and to 57.7 billion USD by 2010. Other estimates are similar in magnitude. With activities at the universities in Basle and Geneva, Switzerland is particularly active as measured by the number of scientific publications on the subject of stem cells. If one compares the scientific status of stem cell research in Switzerland with its commercial implementation up till now, one gets the impression that a "commercialization gap" exists, noted Klaus Menrad, one of the TA study's authors from the Fraunhofer Institute in Karlsruhe.

Written by Walter Grossenbacher-Mansuy,TA-SWISS, Berne

INAHTA Briefs

Issue 2002/45

Systematic Review of Autologous Fat Transfer for Breast Augmentation

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Reference ASERNIP-S Report Number 21 (February 2002) ISBN 0 909844 46 1

Aim

To compare the safety and efficacy of autologous fat transfer for breast augmentation and conventional techniques of breast enlargement using saline and cohesive silicone gel implants.

Conclusions and results

No studies comparing fat injection with other techniques for breast augmentation were recovered. Of the 10 fat injection studies retrieved, only 3 were case series, the others being case studies. Only 5 studies were retrieved that reported data on saline implants, although one of these was a comprehensive review of published data. The very small amount of data available for the fat injection technique suggested that somewhere between 20% and 100% of the injected fat had been reabsorbed. Little data was available to assess the procedure's safety. A comparison with saline implants, for which there was considerably more data, was not possible.

Recommendations

The ASERNIP-S Review Group determined that the evidence base for Autologous Fat Transfer for Breast Augmentation was poor, and consequently safety and efficacy could not be determined. Furthermore, the group recommended that owing to the lack of evidence regarding patient gain from the procedure of Autologous Fat Transfer for Breast Augmentation, coupled with the theoretical dangers of obscuring carcinoma of the female breast, the ASERNIP-S Review Group could not endorse the collection of data within Australia for this procedure.

Methods

Relevant literature on autologous fat transfer for breast augmentation was identified by searching Current Contents from 1993 to 2001 (week 20), MEDLINE from 1980 to 2001 (May week 2), EMBASE from 1980 to 2001 (week 17), HEALTHSTAR from 1975 to 2000 (December), and The Cochrane Library 2001 Issue 2. After the initial literature search, papers were restricted to English if other language papers were not considered superior. Papers detailing randomized controlled trials and controlled clinical trials were included, with case series and case reports also included for the new intervention. Additional published material and other studies were included where relevant.

Written by Andrew Chapman et al, ASERNIP-S, Australia

INAHTA Briefs

Issue 2002/46

Title **Systematic Review of Methods Used to Establish Laparoscopic Pneumoperitoneum (MELP)**

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Reference ASERNIP-S Report Number 13

Aim

To test the following hypotheses concerning MELP: open peritoneal access is safer and/or more effective than closed access; the hybrid visual/closed access method is safer and/or more effective than the blind/closed methods; and the direct trocar technique is safer and/or more effective than the Veress needle/primary trocar technique.

Conclusions and results

Open access versus needle/trocar access

Safety: The number of deaths recorded in the needle/trocar access group was too low to be compared with the open group, in which no deaths were recorded. A trend toward a reduced risk of major complications for the open access group was recorded in the prospective studies, although the risk of bowel injury was higher for that group. In patients that were not obese there was a reduced risk of minor complications for the open group, along with a trend for fewer conversions to laparotomy. *Efficacy:* The total time to establish pneumoperitoneum and complete the operation was slightly reduced in open access.

Optical trocar versus needle/trocar access

There was not enough good quality information to compare these two techniques.

Direct trocar versus needle/trocar access

Safety: No deaths were reported as a consequence of direct trocar access. However, the relative risk of death and/or major complications for these two groups could not be established due to the rarity of these complications. The risk of minor complications, most of which were caused by extraperitoneal insufflation, was reduced by 81% using direct trocar access. *Efficacy:* There was not enough good quality information to compare the two techniques.

Recommendations

As all procedures had a very low rate of injury or complications overall, large studies of good quality would be needed to show definite differences in the safety and effectiveness of these access techniques. The ASERNIP-S Review Group recommended that the relevant professional societies should formulate evidence-based Training and Practice Guidelines for the various primary access techniques.

Methods

Relevant literature on MELP was identified by searching MEDLINE, Current Contents, The Cochrane Library, EMBASE, HEALTHSTAR, and the Web of Science citation index until May 2001. Randomized, quasi-randomized, and non-randomized controlled trial studies on human patients were included if they compared access methods and provided relevant safety and efficacy outcome information. Studies in languages other than English were translated fully (randomized controlled trials) or in abstract form (other studies).

Written by Ms Tracy Merlin et al, ASERNIP-S, Australia

INAHTA Briefs

Issue 2002/49

Vagus Nerve Stimulation (VNS) for Refractory Epilepsy

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Reference ISBN1-896956-41-6 HTA 24 March 2001: Series A (English)

Aim

To analyze the available published evidence on the long-term use of VNS for refractory epilepsy.

The intent was to provide an update to the health policy makers, medical practitioners, and the public on the current status of the use of VNS for this indication in both adults and children and on its use and coverage in Canada.

Conclusions and results

The reviewed literature suggests that VNS therapy is safe, well tolerated, and effective when used as adjunctive therapy in patients (≈12 years of age) with partial-onset seizures refractory to medication and who are not candidates for epilepsy surgery or failed surgery. Limited followup evidence reported by uncontrolled studies suggests that its benefits and safety do not diminish over time for those who continue to use it. However, VNS therapy is not a cure for refractory epilepsy and should be used only as a last resort after an extensive and thorough patient evaluation. The safety and efficacy of VNS in children with refractory epilepsy has yet to be established.

Eleven of the twelve Ministries of Health across Canada responding to the survey provide coverage for this procedure and the device through their medical insurance programs and hospital budgets. VNS therapy is available in seven provinces, while three provinces and one territory provide coverage for the procedure to be performed in other provinces.

Recommendations

Further research is needed to determine the mode of action of VNS; which patients are likely to respond; its effect in less severely afflicted patients and in different syndromes of epilepsy; the quality of life of treated patients and their caregivers; and the details of stimulation paradigms.

Patients considering VNS and their caregivers should be aware that:

- VNS appears to have a moderate initial efficacy that may increase over time, but it is not a cure for epilepsy.
- VNS should only be used as a last resort after an extensive and thorough patient evaluation to rule out non-epileptic conditions and exclude patients who may benefit from conventional therapy.
- VNS does not work for everyone.
- The safety and efficacy of VNS in children with refractory epilepsy has yet to be established.
- VNS appears to have a favorable safety profile when compared to conventional therapies, but the possibility of unknown adverse effects associated with its use still exists.

Methods

Systematic review of the research published from 1998 to September 2000 and a survey of the provincial/territorial Medical Directors from Health Ministries across Canada were conducted.

The following databases were searched: MEDLINE, PubMed, HealthSTAR, EMBASE, ECRI database, The Cochrane database of Systematic Reviews, Best Evidence database, and the NHS (UK) Centre for Reviews and Dissemination databases.

Two well renowned experts externally reviewed this report.

Written by Paula Corabian and Patricia Leggett

Title Obesity – Problems and Interventions

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Reference SBU Report 160, 2002, ISBN 91-87890-78-X
Available in Swedish at http://www.sbu.se

Aim

The Project Group reviewed the evidence for preventive interventions in adults and children and a range of treatment methods, including diet, exercise, behavioral therapy, medications, alternative medicine, and surgery.

Methods

MEDLINE and Cochrane Library databases were searched for literature published on obesity between 1966 and 2001. For costs, economic assessments, ethics, quality of life and alternative medicine, searches in the Cinahl, EmBase, HEED, NHS Center for Reviews and Dissemination and PsycInfo databases were added. Reference lists, international contacts, and review articles were also used.

The literature review and quality evaluation was done in several steps. Two Project Group members independently of each other, according to pre-established criteria, first selected possibly relevant studies from abstract lists. In the second step, relevant studies fulfilling the minimum requirements were included in the critical appraisal procedure. The quality evaluations were conducted using a review format with pre-established criteria. Two members from the Project Group graded all studies, and the value of the evidence presented was ranked as high, moderate, or poor. Thereafter, facts were extracted from the studies. A synthesis of the results, particularly from the studies that received a high or moderate grade, was carried out and conclusions were drawn. Only statistically significant differences in the results were reported.

Finally, the conclusions in the report were graded according to the strength of the evidence: strong scientific evidence (Grade 1), moderate scientific evidence (Grade 2), and limited scientific evidence (Grade 3).

Results

The prevalence of obesity and its complications is increasing rapidly. The number of individuals with obesity (both adults and children) has increased substantially during the past 20 years, and approximately 500 000 individuals in Sweden are now obese. Obesity - particularly when localized to the abdomen - is associated with an increased risk for several serious diseases, eg, diabetes, cardiovascular diseases, and joint disorders. The correlation between obesity and certain types of cancer is strong. Obesity - particularly severe obesity - also has a strong negative influence on the quality of life.

It is difficult to prevent obesity

Most population-based preventive programs that have been scientifically assessed have not demonstrated any favorable effects on the prevalence of obesity. However, there are examples of successful programs for both adults and children. New outreach strategies - to change dietary habits and motivate individuals, especially children to become more physically active – need to be developed and assessed. Concurrently, public policy initiatives are needed to reduce the incidence of obesity.

Scientific assessment of treatment methods

As presented in the table (see next page) it is possible to reduce body weight by almost every method for a year. The reduction is meaningful for patients and good for health. The major problem however, is that the achieved weight loss is not usually permanent. Within a few years most who had initially succeeded in losing weight had returned to

INAHTA Briefs

Issue 2001/73

Title Obesity – Problems and Interventions

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Reference SBU Report 160, 2002, ISBN 91-87890-78-X
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Treatment	Studies, no	Weight loss Kg/1 year	Degree of evidence
Diet	25	3–10	1
Physical activity	4	4	1
Fibres	3	1–2 ?	–
Very Low Calorie Diets	8	2	3
Behavioral Therapy	4	1–2 ?	–
Drugs			
Orlistat (Xenical®)	6	3	2
Sibutramin (Reductil®)	3	4–5	2
Alternative medicine	11	–	–

their original weight. Therefore, it is particularly important to develop and assess long-term treatments that aim at permanent weight loss.

Intervening against other risk factors – even when weight reduction does not succeed can also reduce the risks of obesity. Such interventions would include increased physical activity, smoking cessation, and improved control of diabetes, high blood pressure, and elevated blood lipids.

Surgical treatment, which is an option in severely obese patients, reduces weight, on average, by somewhat more than 25% (eg, from 125 to 90 kg) up to 5 years after surgery. After 10 years, a weight loss of 16% remains, on average slightly over 20 kg. This has substantial health effects especially for improving or preventing diabetes. There are also quality of life benefits for this patient group. The intervention, however, carries risks for complications.

Limited information on cost effectiveness

The cost effectiveness of preventive methods cannot be calculated due to the uncertainty surrounding their effects. In treating obesity, the costs are relatively low for the weight reduction that is achieved through dietary counselling, behavioral therapy, dietary replacement formulas with low energy content, and surgery, but substantially higher for pharmacological treatment. No studies were found that estimated cost effectiveness based on an observed reduction in morbidity or mortality, or an improvement in the quality of life.

Prejudice against obesity must be opposed

Those affected by obesity should not be treated with disrespect and prejudice – many people risk becoming obese, but no one desires it. The reduced quality of life that individuals with obesity experience is partly attributed to the attitudes of people around them. Increased understanding for the origins of obesity and how difficult it is to treat may help reduce the prejudice against obese individuals, which occurs both within the health services and in society at large.

Written by Nils-Georg Asp, Per Björntorp, Mona Britton, et al, SBU. Sweden

INAHTA Briefs

Issue 2003/13

Title The Pediatric Economic Database Evaluation (PEDE) Project

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Reference CCOHTA Technology Report, Issue 26, May 2002. ISBN 1-894620-69-0 (online); http://www.ccohta.ca

Aim

- To analyze trends pertaining to published economic evaluations in pediatric health care over a 20-year period: 1980 to 2000
- To critically appraise the quality of these evaluations, identifying gaps and areas for further research.

Conclusions and results

Trend Analysis: Over the study period, 787 papers were published, with an average annual growth rate of 22%. Cost effectiveness analysis was more commonly used than cost-benefit analysis, while cost-utility analysis was the least common technique used. Earlier studies (1980-1984) focused on infectious diseases and congenital anomalies with complications of pregnancy and perinatal conditions becoming more common. By 1995–1999, health prevention, health treatments, and detection interventions accounted for 70% of all interventions.

Quality Appraisal: Of 150 publications tested using the quality appraisal instrument developed for this project, 38% were rated as very good to excellent and 44% were rated as good or fair. Incremental analysis and sensitivity analysis were often missing, and the overall economic analysis was usually poor. The quality of the evaluations improved little over the 20-year period.

Recommendations

Peer reviewers who critique manuscripts for publication in medical journals should become familiar with quality guidelines for health economic evaluations and insist on high-quality manuscripts.

Methods

A comprehensive database of pediatric health economic evaluations published between January 1, 1980, and December 31, 1999, was created. Each citation includes year of publication, target population, ICD-9-CM disease class, age group, experimental intervention, intervention category, health outcomes, and analytical technique. As well, each citation is linked to a bibliographic database that includes an abstract.

Trends in the literature were examined by performing various one-way frequency distributions and two-way cross tabulations on variables within the database. A quality appraisal instrument was drafted, reviewed by a panel of experts, and pilot tested. Two independent appraisers used the final questionnaire to determine the quality of a random sample of 150 publications. Test-retest and inter-rater reliability of the instrument were assessed. Quality was described using descriptive statistics, correlations, and analysis of variance.

Further research/reviews required

Statistical models are needed to capture health benefits over time horizons that include development and maturation.

Written by Ungar W, Santos M, CCOHTA, Canada

INAHTA Briefs

Issue 2003/23

Title **Systematic Review of Laparoscopic Adjustable Gastric Banding for the Treatment of Obesity (Update and re-appraisal)**

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

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Reference ASERNIP-S Report Number 31. ISBN 0 909844 56 9 Full text available: http://www.surgeons.org/asernip-s/publications.htm

Aim

To compare the safety and efficacy of laparoscopic adjustable gastric banding, vertical banded gastroplasty, and gastric bypass.

Conclusions and results

Only 6 studies reported comparative results for laparoscopic gastric banding and other surgical procedures. One study reported comparative results for all three surgical procedures, and this study was only of moderate quality. In total, 64 studies were found that reported results for LAGB, and 57 studies reported results on the comparative procedures. LAGB was associated with a mean short-term mortality rate of around 0.05% and an overall median morbidity rate of around 11.3%, compared with 0.50% and 23.6% for RYGB and 0.31% and 25.7% for VBG. Overall, all three procedures produced considerable weight loss in patients up to 4 years in the case of LAGB (the maximum followup available at the time of the review), and over 10 years in the case of the comparator procedures.

Recommendations

The ASERNIP-S Review Group concluded that the evidence base was of average quality up to 4 years for LAGB. Laparoscopic gastric banding is safer than VBG and RYGB, in terms of short-term mortality rates. LAGB is effective, at least up to 4 years, as are the comparator procedures. Up to 2 years LAGB results in less weight loss than RYGB. From 2 to 4 years there is no significant difference between LAGB and RYGB, but the quality of data is only moderate. Long-term efficacy of LAGB remains unproven, and evaluation by randomized controlled trials i s recommended to define its merits relative to the comparator procedures.

Methods

Relevant literature on laparoscopic adjustable gastric banding, vertical banded gastroplasty, and gastric bypass was identified by searching Current Contents, EMBASE, MEDLINE, and the Cochrane Library until August 2001. Only studies of patients diagnosed with morbid obesity were included for review. English language papers detailing randomized controlled trials, controlled clinical trials, and case series were included.

Written by Chapman, A.E. et al, ASERNIP-S, Australia

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