INAHTA Briefs

INAHTA

International Network of
Agencies for Health
Technology Assessment

INAHTA Briefs Compilation

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INAHTA Briefs

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

The views expressed in each overview are those of the authors alone and do not necessarily reflect the position of INAHTA.

INAHTA asks readers to direct your personal medical and health questions to your family physician. Information found in INAHTA publications should not be used as a substitute for consulting with your doctor.

Please refer to the *INAHTA Health Technology Assessment (HTA) Glossary* on INAHTA's website for descriptions of the terms used.

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This is INAHTA

Many organizations throughout the world assess healthcare technology. There is an evident need to cooperate and share information from different cultures. The International Network of Agencies on Health Technology Assessment (INAHTA) serves this purpose.

INAHTA was established in 1993 and has now grown to 50 member agencies in 26 countries. The network includes members from North and Latin America, Europe and Australasia.

Aims:

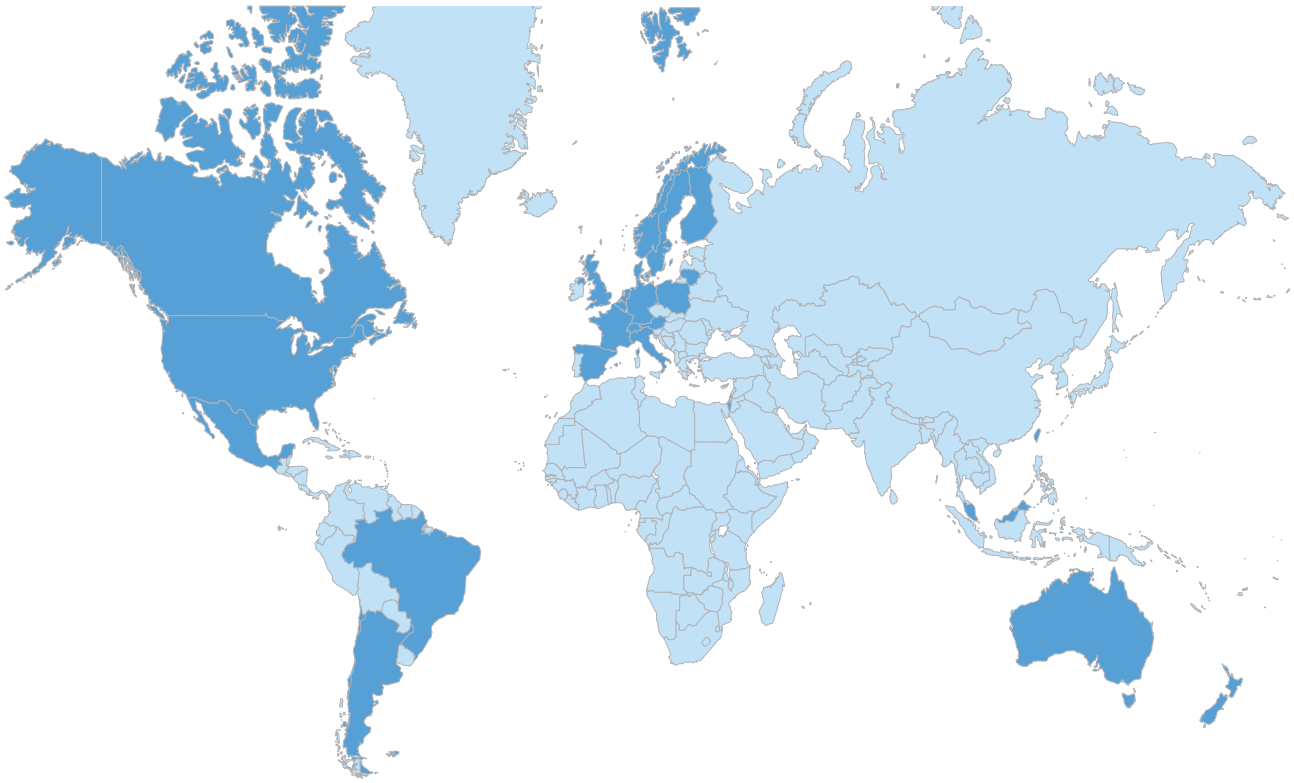
» To accelerate exchange and collaboration among HTA agencies

» To create a forum for the identification and pursuit of interests common to HTA agencies

» To promote information sharing and comparison among HTA agencies

» To create a forum for joint projects, developement of new guidelines and learning new metods

» To prevent unnecessary duplication of activities among agencies



Who can become a member?

Membership is open to any organization which fulfill the following criteria:

» Assesses technology in healthcare
» Is a non-profit organization
» Relates to a regional or national government
» Is funded at least 50% by public sources
» Provides members free access to reports
» Shares information within network

Activities of working groups:

» Solutions for improvement within the network
» Identifying processes of decision making
» Impact of HTAs
» Improvement of quality of HTA reports
» Education and Training programs
» Clarification of Ethical approaches in HTA
» Creating awareness of INAHTA

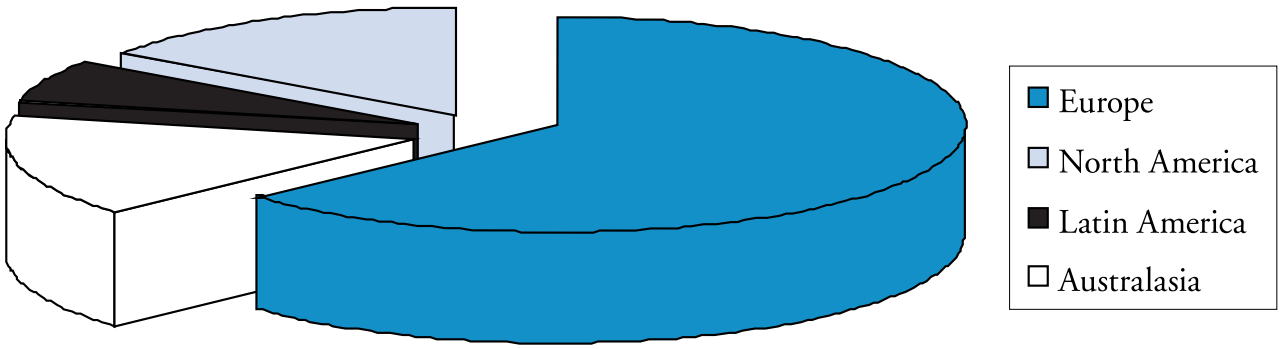
INAHTA Collaborating partners:

» HTAi – Memorandum of Understanding (MoU)
» WHO – Collaborating Centers, MoU
» HEN – technical member
» PAHO – collaborating partner
» EUnetHTA – collaborating partner
» EuroScan collaboration
» World Bank cooperation
» Industry – awareness, HTAi Policy Forum

INAHTA activities:

» HTA Database – Library of HTAs
» Annual Meetings – Networking opportunities
» Working groups – Joint projects
» Surveys – Sharing practices
» ListServ – Communication strategy
» E-learning courses – human resources
» Articles in Medical Journals

INAHTA – A Global Network:



Dissemination activities

INAHTA's key communication form is Internet. The INAHTA website and Members-only section provides the best source of regularly updated information about ongoing activities and member agencies.

Please visit **www.inahta.org**.

The Brief series is intended as a forum for member agencies to present overviews of recently published reports. Information in the INAHTA briefs is developed and submitted by the member, regularly published, and placed on the INAHTA website.

Joint projects involve the member agencies in collaborative efforts to evaluate medical technologies of mutual interest. The INAHTA/HTAi Working Group on Ethical Issues has recently published "Ethics manual".

The HTA Database contains information on healthcare technology assessments and is managed by INAHTA in collaboration with our UK member Centre for Reviews and Dissemination (CRD). New records are continually added, and INAHTA publications and on-going reviews are sent to CRD by the INAHTA Secretariat every six months. All titles of current projects and publications from INAHTA agencies are also available in Spanish.

Other means of dissemination include participation in international conferences, workshops, exhibitions, and educational activities and seminars. The INAHTA exhibition is presented yearly at the HTAi conference. INAHTA and most member agencies distribute reports and other information at the exhibition. There is also an opportunity to meet and exchange experience on HTA related issues with representatives from the INAHTA agencies during the Meet the Agencies initiative.

HTA Glossary gives the HTA community, both producers and users of assessment information, a common vocabulary for work in this field.

For more information, please visit www.inahta.org or contact the INAHTA Secretariat via e-mail: secretariat@inahta.org, tel +46 8 412 3200, or fax +46 8 411 3260.

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INAHTA Briefs

Issue 2009/048

Title **Rehabilitation of Breast Cancer Patients**

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Reference Report no. 02 - 2009. ISBN 978-82-8121-253-4, ISSN 1890-1298.
www.kunnskapssenteret.no/Publikasjoner/5763.cms

Aim

To evaluate different rehabilitation interventions for breast cancer patients.

Conclusions and results

Limited documentation addresses the efficacy of rehabilitation interventions for breast cancer patients. The documentation from this review indicates that physical activity after primary cancer treatment may increase quality of life (QoL) and reduce fatigue. Patients might also have some benefits in QoL from cognitive behavior therapy (CBT) interventions. More documentation is needed on the effects of physiotherapy, psychoeducation, and social and emotional support.

We identified 9617 references and assessed 191 full-text articles. We included 46 randomized controlled trials (RCTs) of moderate or high quality. Seven studies addressed physiotherapy, 11 studies investigated dif ferent types of physical activity, and 18 studies examined different psychosocial interventions. Two studies addressed nutrition, 5 studies addressed complemenary interventions as rehabilitation, and 3 studies evaluated a complex rehabilitation program. Meta-analyses were not possible due to variations in interventions and outcomes. The studies on physical activity after primary cancer treatment showed effects on improving QoL and reducing fatigue. Inconsistencies made it difficult to draw conclusions from the studies on physical activity during primary treatment. Three studies showed that early physical activity was not associated with aggravated lymphedema. Four studies showed that CBT intervention after primary cancer treatment will increase overall QoL.

Methods

A group of experts in areas related to generic medical rehabilitation and more specific breast cancer treatment was organized to evaluate the literature. Systematic searches were carried out in relevant databases, eg, Cochrane Library, Centre for Reviews and Dissemination, MEDLINE, EMBASE, CINAHL, PsycINFO, AMED, and PEDro until September 2008. Two separate reviewers selected relevant studies. One person retrieved and another person checked the data from included studies.

Further research/reviews required

Further research should examine the effect of rehabilitation interventions in breast cancer patients. Few studies in the present review include patients undergoing new, long-term medical treatment regiments for breast cancer; new studies should address this. Additional research might profitably assess whether some interventions are more effective in certain subgroups of breast cancer patients.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/049

Title **The Clinical Effectiveness and Cost Effectiveness of Treatments for Children with Idiopathic Steroid-Resistant Nephrotic Syndrome: A Systematic Review**

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Reference Volume 11.21. ISSN 1366-5278. www.ncchta.org/project/1497.asp

Aim

To systematically review the clinical and cost effectiveness of treatments for children with idiopathic steroid-resistant nephrotic syndrome.

Conclusions and results

The systematic review of clinical effectiveness included 2 systematic reviews and 11 trials. Seven different therapies were included, but only ciclosporin and cyclophosphamide were assessed by more than one study. The quality of reporting and methodology of the included studies was generally poor. No economic evaluations were identified. Ciclosporin significantly increased remission rates compared with placebo or supportive treatment (RR 7.66, 95% CI 1.06, 55.34), but not for a subgroup with FSGS (RR 5.83, 95% CI 0.75, 45.09). No significant difference in remission rates was found with cyclophosphamide plus prednisone versus prednisone, but the time to response was significantly less with cyclophosphamide (38.4 days [range 6-80] versus 95.5 days [range 61-129], $p<0.05$). No significant differences were found between azathioprine versus placebo, 6-month versus 18-month regimen of methylprednisolone, intravenous dexamethasone versus intravenous methylprednisolone, or tuna fish oil versus placebo. A difference in the urine albumin to creatinine ratio reduction percentage between high-dose and low-dose enalapril was found, but this was statistically significant in the period before crossover only. Studies varied in the extent of reporting adverse events. Limited literature was found on costs associated with steroid-resistant nephrotic syndrome in children. The cost of pharmacotherapy varies considerably, eg, an 8-week course of cyclophosphamide costs less than 6 pounds (GBP) while a course of ciclosporin costs almost GBP 900 per year. Children who fail to respond to treatment are at high risk of developing end stage renal failure, the costs of which are considerable. No published evidence on the cost effectiveness of treatments for children was identified. Subsequent searches were undertaken to identify economic evaluations and economic evidence for treatments in adults. Data are sparse, and modeling the cost effectiveness of current treatments is not feasible at present.

Recommendations

Evidence is limited as regards the clinical and cost effectiveness of treatments for idiopathic steroid-resistant nephrotic syndrome in children. The evidence suggests a beneficial effect of ciclosporin on remission rates and of cyclophosphamide on time to remission; but poor-quality studies limit the strength of the conclusions. No economic evaluations were identified. Data on costs and outcomes are sparse and do not permit reliable modeling of the cost effectiveness of treatments for steroid-resistant nephrotic syndrome. A modeling framework is suggested should more relevant data become available.

Methods

See Executive Summary link at www.ncchta.org/project/1497.asp.

Further research/reviews required

See Executive Summary link at www.ncchta.org/project/1497.asp.

Written by Dr Jill Colquitt, SHTAC, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/050

Title **The Birmingham Rehabilitation Uptake Maximization Study (BRUM). Home-Based Compared With Hospital-Based Cardiac Rehabilitation in a Multi-Ethnic Population: Cost Effectiveness and Patient Adherence**

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Reference Volume 11.35. ISSN 1366-5278. www.hta.ac.uk/project/1210.asp

Aim

To evaluate the relative effectiveness and cost effectiveness of a home-based program of cardiac rehabilitation (using the Heart Manual) with center-based (predominantly hospital) programs in patients who had suffered myocardial infarction (MI) or undergone percutaneous coronary artery angioplasty (PTCA) or coronary artery bypass graft (CABG) within the previous 12 weeks; and to explore the reasons for nonadherence to cardiac rehabilitation programs.

Conclusions and results

We evaluated: 1) differences at 6 months, 1 year, and 2 years following center- and home-based cardiac rehabilitation in: objective cardiac risk factors, patient reported uptake and adherence, and whether these differed between patient groups (the elderly, women, and ethnic minority groups); 2) the relative costs of hospital- and home-based cardiac rehabilitation from the NHS and patients' perspectives; 3) qualitative insights into the reasons for nonparticipation in cardiac rehabilitation programs; 4) differences in cardiac clinical events (MI/death from cardiac cause) at 2 years following hospital- and home-based cardiac rehabilitation.

At all three follow-up points no clinically or statistically significant differences appeared in any of the primary outcome measures between the home-based and center-based groups, or in secondary outcomes. Significant improvements in total cholesterol, smoking prevalence, HADS anxiety score, self-reported physical activity, and diet were observed in the home and center-based arms between baseline and 6-month follow-up. From 6 to 24 months follow-up there were no significant changes for most outcomes. Five or more contacts with a cardiac rehabilitation nurse were received by 96% of participants in the home-based arm, while only 56% of participants in the center-based arm attended this many rehabilitation classes ($P<0.001$).

Recommendations

For low/moderate risk patients (post-MI/PTCA/CABG) a home-based cardiac rehabilitation program produces similar outcomes when compared to center-based programs. With the level of home visiting in this trial, the home program was more costly to the health service, but this difference disappeared when including travel costs borne by patients attending center-based programs. As patients cited a range of individualistic reasons for nonadherence to cardiac rehabilitation, a range of options to fit individual needs might improve adherence and maximize participation.

Methods

See Executive Summary link at www.hta.ac.uk/project/1210.asp.

Further research/reviews required

See Executive Summary link at www.hta.ac.uk/project/1210.asp.

Written by Dr Kate Jolly, University of Birmingham, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/051

Title **A Systematic Review of the Clinical, Public Health and Cost Effectiveness of Rapid Diagnostic Tests for the Detection and Identification of Bacterial Intestinal Pathogens in Feces and Food**

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Reference Volume 11.36. ISSN 1366-5278. www.hta.ac.uk/project/1445.asp

Aim

1. To identify studies on rapid diagnostic methods for food poisoning due to *Salmonella* spp., *Campylobacter*, *Escherichia coli* O157, *Clostridium perfringens, Staphylococcus aureus,* and *Bacillus cereus* relevant to both the food chain and clinical samples
2. To assess and summarize the sensitivity and specificity each diagnostic test for each organism compared to a gold standard
3. To assess usefulness for transfer to clinical testing of tests designed and/or currently applied only to food samples
4. To assess the time for full laboratory analysis and reporting for each diagnostic test
5. To develop a decision analytic model to assess the cost and cost effectiveness of each diagnostic test in a clinical setting and in managing outbreaks
6. To make recommendations for future research based on this systematic review of evidence.

Conclusions and results

Good test performance levels are observed with rapid test methods, especially for polymerase chain reaction (PCR) assays. The estimated levels of diagnostic accuracy using the area under the curve (the summary receiver operating characteristic curve) were high. Although traditional culture is the natural reference test to use for comparative statistical analyses, in many instances the rapid test outperforms culture, detecting additional potentially true positive cases of foodborne illness. The economic model suggests that adoption of rapid tests in combination with routine culture is unlikely to be cost effective. Nominal group analysis identified priorities as: the exclusion of infection due to organisms causing severe disease; and meticulous organization to reduce the interval between sample collection and reporting of results to the clinician.

Recommendations

Despite the relatively poor-quality reporting of studies evaluating rapid detection methods, the reviewed evidence shows that PCR for *Campylobacter, Salmonella,* and *E coli* O157 is potentially very successful in identifying pathogens, possibly more than the number currently detected through culture. Less is known about the benefits of testing for *B. cereus, C. perfringens,* and *S. aureus.* It is unclear how clinical outcomes may change if test results are available more quickly and with greater precision than the current practice of bacterial culture.

Methods

See Executive Summary link at www.hta.ac.uk/project/1445.asp.

Further research/reviews required

Further research is needed on the effectiveness and cost effectiveness of emerging tests for more than one organism at a time, eg, multiplex PCR and DNA microarray technologies.

Written by Dr Ibrahim Abubakar, University of East Anglia, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/052

Title **A Randomized Controlled Trial Examining the Longer-Term Outcomes of Standard Versus New Antiepileptic Drugs; The SANAD Trial**

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Reference Volume 11.37. ISSN 1366-5278. www.hta.ac.uk/project/1031.asp

Aim

To compare the effectiveness and cost effectiveness of standard and new antiepileptic drugs.

Conclusions and results

Participants: 1721 patients were recruited to Arm A; 716 to Arm B.

Arm A

Lamotrigine had the lowest incidence of treatment failure and was statistically superior to all drugs for this outcome with the exception of oxcarbazepine. At 1 and 2 years after remission 12% and 8% fewer patients, respectively, experienced treatment failure on lamotrigine than on carbamazepine (the standard drug). Lamotrigine's superiority over carbamazepine was due to its better tolerability, but satisfactory evidence indicates that lamotrigine is not clinically inferior to carbamazepine for measures of its efficacy (treatment failure due to inadequate seizure control and time to achieving 12-month remission). No consistent differences in quality-of-life outcomes were found between treatment groups, although patients achieving a 12-month remission by 2 years after randomization had quality-of-life outcomes superior to those who had not, and patients who had experienced treatment failure exhibited poorer quality of life than those who remained on their randomized treatment. Health economic analysis supported lamotrigine being preferred to carbamazepine for both cost per seizure avoided and cost per QALY gained. Probability is high that lamotrigine is a cost-effective alternative to carbamazepine.

Arm B

As regards time to treatment failure, valproate (the standard drug) was preferred to both topiramate and lamotrigine. Valproate was the drug least likely to be associated with treatment failure for inadequate seizure control and was the preferred drug for time to achieving a 12-month remission. Quality-of-life assessments did not show any between-treatment differences, although patients achieving a 12-month remission by 2 years after randomization had superior quality-of-life outcomes to those who had not, and patients who had experienced a treatment failure outcome exhibited poorer quality of life. Health economic assessment supported the conclusion that valproate should remain the drug of first choice for idiopathic generalized or unclassified epilepsy, although topiramate is suggested as a cost-effective alternative to valproate.

Recommendations

The study provides evidence that lamotrigine may be a clinical and cost-effective alternative to carbamazepine (the standard drug treatment) for patients diagnosed with partial seizures. For patients with idiopathic generalized epilepsy, or difficult-to-classify epilepsy, valproate remains the most effective drug clinically, but topiramate may be a cost-effective option for some patients.

Methods

See Executive Summary link at www.hta.ac.uk/project/1031.asp.

Further research/reviews required

See Executive Summary link at www.hta.ac.uk/project/1031.asp.

Written by David Chadwick OBE, the Walton Centre for Neurology and Neurosurgery, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/053

Title **Taxanes for the Adjuvant Treatment Early Breast Cancer: Systematic Review and Economic Evaluation**

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Reference Volume 11.40. ISSN 1366-5278. www.hta.ac.uk/project/1516.asp

Aim

To estimate the clinical and cost effectiveness of docetaxel and paclitaxel compared with non-taxane, anthracycline-containing chemotherapy regimens for adjuvant treatment of women with early-stage breast cancer.

Conclusions and results

Eight of the 11 selected trials (6 docetaxel and 5 paclitaxel) reported a significant improvement in disease-free survival (DFS) or time to recurrence (TTR) for taxanes over comparator regimens. Docetaxel was associated with more adverse events than paclitaxel, most notably febrile neutropenia. Taxanes produced cardiotoxicity, although this was not reported to be greater than for anthracycline comparator arms in all trials. Treatment-related deaths were uncommon. Where reported, all chemotherapy regimens caused health-related quality of life (HRQoL) to deteriorate during treatment. Following treatment, no clinically significant differences were found between taxane and comparator treatment groups. Scant data compared licensed regimens of taxanes with chemotherapy regimens commonly used in the United Kingdom (UK). The three trials selected as the basis for economic analysis were those that used the taxanes in accordance with current UK marketing authorization and had also reported in full. The estimated incremental cost-effectiveness ratio (ICER) for docetaxel compared to FAC6, based on the BCIRG 001 study, is 12 000 pounds sterling (GBP) (7000-39 000 GBP) and for paclitaxel compared with AC, based on the NSABP B28 and CALGB 9344 studies, is 43 000 GBP (16 000 GBP – dominated) and 39 000 GBP (12 000 GBP – dominated) respectively. However, the comparators used in these trials restrict the generalizability of the results, as they do not conform to current standard care in the UK, typically FEC6 and E4-CMF4. An exploratory indirect comparison shows that the benefits of taxane-containing regimens compared to regimens in current use in the UK is subject to large uncertainty due to the lack of direct trial comparisons between these interventions. Assumptions regarding the benefits in the taxane arm after the trial follow-up period and the annual rate of recurrence in this period have the most significant influence on the ICER.

Recommendations

See Executive Summary link at www.hta.ac.uk/project/1516.asp.

Methods

See Executive Summary link at www.hta.ac.uk/project/1516.asp.

Further research/reviews required

More research is needed, comparing taxanes used in line with their current UK marketing authorization and with anthracycline-containing regimens commonly used in the UK. The ongoing TACT trial is expected to provide useful data. Scant data are available on the effectiveness of taxanes for the over-70s. Further research is required into the long-term outcomes of taxane therapy, eg, whether there are any long-term adverse events that significantly impact on overall survival or quality of life and whether the increases in DFS will translate into increases in overall survival.

Written by Sue Ward, University of Sheffield, NETSCC, United Kingdom

INAHTA Briefs

Issue 2009/054

Title **The Clinical Effectiveness and Cost Effectiveness of Screening for Open Angle Glaucoma: A Systematic Review and Economic Evaluation**

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Reference Volume 11.41. ISSN 1366-5278. www.hta.ac.uk/project/1446.asp

Aim

To assess the extent to which screening for open angle glaucoma (OAG) would meet the United Kingdom (UK) National Screening Committee criteria for a screening program.

Conclusions and results

The criteria address the condition, test, treatment, and screening program. The specific objectives were to: 1) identify risk factors for developing OAG and determine the prevalence and incidence of OAG; 2) review the accuracy of screening tests for OAG; 3) review treatment effectiveness and extrapolate these effects to long-term visual outcome; 4) identify potential benefits and harms of screening and subsequent management; 5) determine the relative clinical and cost effectiveness of alternative screening strategies; 6) describe the impact on the NHS and other groups of screening for OAG; and 7) identify and prioritize areas for future research.

The prevalence of OAG in the UK is estimated at 2% (95% CI 1.6 to 2.3), ranging from 0.3% to 3.2% in people aged 40 to 70 years respectively. Incidence is estimated to be between 30 and 181 per 100 000 person-years for ages 50 and 70 years respectively. Of an estimated half million people affected, about 65% have not been identified; certain groups are at increased risk of developing OAG. For ages 40 to 75 years, OAG prevalence estimates are: myopics 2.7%, diabetics 3.3%, and family history in a first-degree relative 6.7%. The risk is 4 times higher among those of black ethnicity. For a low-prevalence disease, a screening test should be highly specific. Most potential screening tests reviewed had an estimated specificity of 85% or higher. However, due to the strongly heterogeneous nature of the data, and the relatively small number of studies, it was not possible to conclude whether any one test was clearly superior. Prevalence was the main determinant of cost effectiveness. The prevalence level would have to be about 3% to 4% in 40-year-olds, with a screening interval of 10 years, before it might be considered cost-effective to screen. Screening might be cost effective in a 50-year-old cohort at a prevalence of 4% with a 10-year screening interval. General population screening at any age appears unlikely to be cost effective. Selective screening of groups with higher prevalence (black ethnicity and family history) might be worthwhile, although 6% of the population would be eligible.

Recommendations

See Executive Summary link at www.hta.ac.uk/project/1446.asp.

Methods

See Executive Summary link at www.hta.ac.uk/project/1446.asp.

Further research/reviews required

Further research should aim to develop and provide quality data to populate the economic model; by conducting a feasibility study of interventions to improve detection, by obtaining further data on costs of blindness, risk of progression, and health outcomes, and by conducting a randomized controlled trial of interventions to improve the uptake of glaucoma testing.

Written by Dr Jennifer Burr, University of Aberdeen, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/055

Title **Acceptability, Benefit, and Costs of Early Screening for Hearing Disability: A Study of Potential Screening Tests and Models**

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Reference Volume 11.42. ISSN 1366-5278. www.hta.ac.uk/project/1025.asp

Aim

To assess the acceptability, benefit, and cost of early detection for adult hearing impairment.

Conclusions and results

The four main objectives were to: 1) find the prevalence of reported hearing problems in the United Kingdom (UK) population, to compare with other reported ear, nose, and throat (ENT) problems, and to assess attitudes toward screening, particularly hearing screening; to examine the extent to which the population might benefit from amplification and the factors that influence this benefit and to examine what screening techniques might be best to identify those who would benefit from amplification; to examine the extent to which benefit might be realized in the real world by providing a hearing aid; 2) examine the acceptability, benefits, and performance of differently organized screening programs; 3) examine the compliance of patients in long-term use of hearing aids after early identification and to determine the extent to which people with early identified hearing impairments have better outcomes; and 4) examine the costs and cost effectiveness of different potential screening programs.

About 12% of people aged 55 through 74 years have a hearing problem that causes moderate or severe worry, annoyance, or upset. Although 14% have a bilateral hearing impairment of at least 35 dB hearing level (HL), only 3% currently receive intervention (through use of hearing aids). The mean reported duration of hearing problems, which mainly affect the ability to hear speech in noise, is about 10 years. Over 90% of people interviewed felt that hearing screening was acceptable, especially if associated with the GP practice. Good amplification was shown to benefit about 1 in 4 of the population. In a population intervention trial, less benefit was measured with a single hearing aid than in the laboratory-based, speech-in-noise test, but a strong correlation was found between benefit from amplification and from using hearing aids. Questionnaires and audiometric screens yielded good performance relative operating characteristic (ROC) curves with otoacoustic emissions, but speech-in-noise tests were not as good. One- and two-stage screening programs were examined in systematic and opportunistic forms. The systematic screening program was more acceptable and yielded a better response.

Recommendations

See Executive Summary link at www.hta.ac.uk/project/1025.asp.

Methods

See Executive Summary link at www.hta.ac.uk/project/1025.asp.

Further research/reviews required

1) Prospective pilot study of 2-stage hearing screen to identify bilateral 35+ dB HL hearing impairment in people aged 60 to 70 years in a primary care trust (PCT) setting using current NHS hearing aids; 2) development and trial of simple audiometric screening device (target price LOW); 3) trial of a *Hearing Direct* telemedicine alternative to a questionnaire and low-cost audiometric screen device; 4) workforce review modeling of different screening programs and their cost and financial impact.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/056

Title **Overview of the Clinical Effectiveness of Positron Emission Tomography Imaging in Selected Cancers**

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Reference Volume 11.44. ISSN 1366-5278. www.hta.ac.uk/project/1487.asp

Aim

To evaluate the clinical effectiveness of positron emission tomography using 2-[^{18}F]-fluoro-2-deoxy-D-glucose (FDG-PET) in 8 cancers (breast, colorectal, head and neck, lung, lymphoma, melanoma, esophageal, and thyroid).

Conclusions and results

For each cancer, the study evaluated the use of FDG-PET and FDG-PET + computed tomography (CT) to aid management decisions relating to diagnosis, staging/restaging, recurrence, treatment response, and radiotherapy (RT) planning. For non-small cell lung cancer (NSCLC), FDG-PET was cost effective in CT node-negative patients, but not in CT node-positive patients. A model indicated that FDG-PET was also cost effective in RT planning, but this model was based on sparse evidence. In late-stage Hodgkin lymphoma (HL), FDG-PET was cost effective for restaging after induction therapy. Robust evidence shows that FDG-PET changed patient management in staging/restaging colorectal cancer and when characterizing a solitary pulmonary nodule (SPN). FDG-PET had an impact on patient management across pediatric lymphoma decisions, but this indication requires further study of individual management decisions. For other cancer management decisions, the evidence on patient management is weak. In terms of diagnostic accuracy, FDG-PET was accurate in detecting distant metastases across several sites, but sensitivity was varied in detection of lymph node metastases and was poor for small lesions, or when biopsy or sentinel lymph node biopsy were the alternatives. FDG-PET also showed improved diagnostic accuracy over alternatives in the following cancers: a) colorectal recurrence; b) detection of occult and synchronous head and neck tumors where other tests have failed; c) staging regional lymph nodes in clinically N+ necks; d) restaging/recurrence in head and neck; e) staging SCLC; f) staging lymphoma; g) restaging non-Hodgkin lymphoma; h) staging esophageal; and i) recurrent epithelial thyroid cancer, where elevated biomarkers are not confirmed by ^{131}I scintigraphy.

Recommendations

The strongest evidence for the clinical effectiveness of FDG-PET is in staging NSCLC, restaging HL, staging/restaging colorectal cancer, and characterization of SPN. Some of these may still require clinical audit to augment the evidence base.

Methods

See Executive Summary link at www.hta.ac.uk/project/1487.asp.

Further research/reviews required

This report details the type of studies required to augment the evidence for each cancer management decision, but these must be considered alongside UK clinical priorities, taking account of the recent work of the National Cancer Research Institute. For treatment response and RT planning, the need for larger studies using consistent methods across the UK is highlighted as a priority for all cancers.

Written by Dr Karen Facey, Drymen, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/057

Title **The Clinical Effectiveness and Cost Effectiveness of Cardiac Resynchronization (Biventricular Pacing) for Heart Failure: Systematic Review and Economic Model**

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Reference Volume 11.47. ISSN 1366-5278. www.hta.ac.uk/project/1518.asp

Aim

To assess the clinical and cost effectiveness of cardiac resynchronization therapy (CRT) for people with heart failure and evidence of dyssynchrony by comparing CRT devices, CRT-P and CRT with defibrillation (CRT-D), each with optimal pharmaceutical therapy (OPT), and with each other.

Conclusions and results

Five randomized controlled trials met the inclusion criteria, recruiting 3434 participants. Quality was good to moderate. Meta-analyses showed that both CRT-P and CRT-D devices significantly reduced the mortality and level of heart failure hospitalizations, and they improved health-related quality of life in people with NYHA (New York Heart Association) class III and IV heart failure and evidence of dyssynchrony (QRS interval >120 ms) who were also receiving OPT. A single, direct comparison indicated that the effects of CRT-P and CRT-D were similar, with the exception of an additional reduction in sudden cardiac death (SCD) associated with CRT-D. Implanting a CRT device in 13 people would result in an average saving of one additional life over a 3-year period compared with OPT. The NHS device and procedure cost of implanting a new CRT-P system was estimated to be 5074 pounds sterling (GBP) and that of a CRT-D system 17 266 GBP. The discounted lifetime costs of OPT, CRT-P, and CRT-D were estimated as 9375 GBP, 20 804 GBP, and 32 689 GBP, respectively. One industry submission to NICE used a discrete event simulation model that gave estimated incremental cost-effectiveness ratios of CRT-P vs OPT of 15 645 GBP per quality-adjusted life-year (QALY).

Recommendations

The study found that CRT-P and CRT-D devices reduce mortality and hospitalizations due to heart failure, improve quality of life, and reduce SCD in people with heart failure NYHA classes III and IV, and evidence of dyssynchrony. When measured using a lifetime time horizon and compared with optimal medical therapy, the devices are estimated to be cost effective at a willingness-to-pay (WTP) threshold of 30 000 GBP per QALY; CRT-P is cost effective at a WTP threshold of 20 000 GBP per QALY. When the cost and effectiveness of all three treatment strategies are compared, the estimated net benefit from CRT-D is less than with the other two strategies, until the WTP threshold exceeds 40 160 GBP/QALY.

Methods

See Executive Summary link at www.hta.ac.uk/project/1518.asp.

Further research/reviews required

Further research is needed into the identification of those patients unlikely to benefit from this therapy, the appropriate use of CRT-D devices, the differences in mortality and heart failure hospitalization for NYHA classes I and II, and the long-term implications of using this therapy.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/058

Title **Cost Effectiveness of Functional Cardiac Testing in the Diagnosis and Management of Coronary Artery Disease: A Randomized Controlled Trial. The Cecat Trial**

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Reference Volume 11.49. ISSN 1366-5278. www.hta.ac.uk/project/1217.asp

Aim

To assess: the feasibility and utility of functional cardiac tests as a gateway to angiography in diagnosing coronary artery disease; the ability of diagnostic strategies that include functional tests to identify patients who gain most from revascularization; outcomes for patients who underwent 4 alternative diagnostic strategies; and the most cost-effective diagnostic strategy for patients with suspected coronary artery disease.

Conclusions and results

Initial diagnostic tests were completed successfully with unequivocal results for 98% of angiography patients, 94% of single photon emission computed tomography (SPECT) sestamibi (MIBI) patients (p=0.05), 78% of cardiac magnetic resonance imaging (MRI) patients (p<0.001), and 90% of stress echocardiography patients (p<0.001). Claustrophobia and large size were the most common reasons for failure to complete tests. 22% of MIBI patients, 20% MRI patients, and 25% stress echo patients avoided angiogram. For patients who had positive functional tests, diagnoses were confirmed by angiography (50% stenosis in LAD or 70% stenosis in any other major vessel) in 83% of MIBI patients, 89% of MRI patients, and 84% of stress echo patients. Negative functional tests were followed by positive angiograms in 31% MIBI patients, 52% MRI patients, and 48% stress echo patients. Proportions that had coronary artery bypass grafting (CABG) were similar at 10% (angiography), 11% (cardiac MRI), and 13% (SPECT MIBI and stress echo). Proportions who had percutaneous transluminal coronary angioplasty (PTCA) were 25% (angiography), 18% (SPECT MIBI), and 23% (MRI and stress echo). At 18 months, comparing SPECT MIBI and stress echo with angiography we can rule out clinically significant difference in total exercise time since the upper limit of the confidence interval was less than 1. The cardiac MRI group had significantly shorter mean total exercise time of 35 seconds and the upper limit of the confidence interval was 1.14 minutes less than angiography group. Hence, we cannot rule out a difference of at least 1 minute with 95% confidence.

Recommendations

20%/25% of patients can avoid invasive testing by use of functional cardiac testing as gateway to angiography, without substantial effects on outcomes. Patients allocated to the MIBI group had similar results to the angiography group, and we ruled out clinically significant differences. At 18 months the group had more patients with significant improvement in CCS compared with angiography patients.

Methods

See Executive Summary link at www.hta.ac.uk/project/1217.asp.

Further research/reviews required

Further research, using blinded re-assessment of functional test results and angiograms, is required to formally assess diagnostic accuracy of functional tests. Longer-term, cost-effectiveness analysis is planned to assess whether decisions based on functional tests have significant impact up to 2 years post treatment.

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INAHTA Briefs

Issue 2009/059

Title **Systematic Reviews of the Clinical Effectiveness and Cost Effectiveness of Proton Pump Inhibitors in Acute Upper Gastrointestinal Bleeding**

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Reference Volume 11.51. ISSN 1366-5278. www.hta.ac.uk/project/1385.asp

Aim

1) To evaluate clinical and cost effectiveness of proton pump inhibitors (PPIs) in preventing and treating acute upper gastrointestinal (GI) hemorrhage. 2) To evaluate clinical and cost effectiveness of PPI therapy vs H_2-receptor antagonist (H_2RA), *Helicobacter pylori (H. pylori)* eradication, or no therapy for preventing first and /or subsequent bleeds in patients who continue to use nonsteroidal anti-inflammatory drugs (NSAIDs). 3) To evaluate clinical effectiveness of PPI therapy vs H_2RA, *H. pylori* eradication, or no therapy for preventing subsequent bleeds in patients with previous peptic ulcer (PU) bleeding.

Conclusions and results

1a) PPI treatment initiated after endoscopic diagnosis of PU bleeding significantly reduced re-bleeding (Odds ratio, OR 0.49; 95% confidence interval, CI 0.37 to 0.65) and surgery (OR 0.61; 95% CI 0.48 to 0.78) compared with placebo or H_2RA. No evidence of an overall effect of PPI treatment on all-cause mortality (OR 101; 95% CI 0.74 to 1.40). PPIs significantly reduced mortality among studies conducted in Asia (OR 0.35; 95% CI 0.16 to 0.74) or among patients with high-risk endoscopic findings (OR 0.53; 95% CI 0.31 to 0.91). 1b) PPI treatment initiated prior to endoscopy in upper GI bleeding significantly reduced the proportion of patients with stigmata of recent hemorrhage (SRH) at index endoscopy compared with placebo or H_2RA (OR 0.67; 95% CI 0.54 to 0.84). No evidence that PPI treatment affected mortality, re-bleeding, or need for surgery. 1c) Oral PPI before and after endoscopy, with endoscopic hemostatic therapy (EHT) for those with major SRH, is likely to be the most cost-effective strategy.

Recommendations

See Executive Summary link at www.hta.ac.uk/project/1385.asp.

Methods

See Executive Summary link at www.hta.ac.uk/project/1385.asp.

Further research/reviews required

Regarding PPIs in the acute hospital management of patients with upper GI bleeding: i) The issue of PPI administration prior to endoscopic diagnosis needs to be explored further in large randomized controlled trials that randomize patients with acute upper GI bleeding to PPI therapy before endoscopy. ii) A large, multicenter trial is needed in Europe and North America that would randomize patients to high-dose intravenous PPI or control treatment after any appropriate endoscopic intervention and address mortality as the primary endpoint. Unfortunately, such a trial faces major obstacles. iii) Randomized trials directly comparing different doses of PPIs and/or oral and intravenous administration of PPIs in patients with PU bleeding are also needed. iv) Evidence is very limited on head-to-head clinical outcome comparisons between different PPIs in PU bleeding, so such trials may be relevant.

Written by Professor David Forman, University of Leeds, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/060

Title **'Cut Down to Quit' with Nicotine Replacement Therapies in Smoking Cessation: A Systematic Review of Effectiveness and Economic Analysis**

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Reference Volume 12.02. ISSN 1366-5278. www.hta.ac.uk/execsumm/summ1202.shtml

Aim

To systematically review the clinical effectiveness of 'cut down to quit' (CDTQ) with nicotine replacement therapy (NRT) in smoking cessation; and to review published economic evaluations and undertake a *de novo* cost-effectiveness analysis of CDTQ with NRT in smoking cessation.

Conclusions and results

No systematic reviews of the effectiveness of CDTQ and no randomized controlled trials (RCTs) specifically addressing CDTQ were identified. Seven randomized placebo-controlled smoking reduction trials were included; six of these were industry sponsored. However, sustained smoking cessation was only reported as a secondary outcome in these trials and required commencement of cessation within the first 6 weeks of treatment. Meta-analyses of the study-level results demonstrated statistically significant superiority of NRT compared with placebo. Individual patient data from unpublished reports of five RCTs were used to calculate sustained abstinence of at least 6 months starting at any time during the treatment period (generally 12 months). From this, the meta-analysis indicated statistically significant superiority of NRT versus placebo [relative risk 2.06, 95% confidence interval (CI) 1.34 to 3.15]. The proportions achieving this outcome across all five RCTs were 6.75% of participants receiving NRT and 3.29% of those receiving placebo. The number-needed-to-treat was 29. This measure of sustained abstinence was used for economic modeling. No existing economic analyses of CDTQ were identified.

Recommendations

Meta-analysis of RCT evidence of quit rates in NRT-supported smoking reduction studies indicates that NRT is an effective intervention in achieving sustained smoking abstinence for smokers who declare unwillingness or inability to attempt an abrupt quit. The 12-month sustained abstinence success rate in this population (approximately 5.3% with NRT versus approximately 2.6% with placebo) is considerably less than that documented for an abrupt quit NRT regime in smokers willing to attempt an abrupt quit with NRT (which according to other systematic reviews is around 16% with NRT vs 10% with placebo). Most of the evidence of effectiveness of CDTQ came from trials that required considerable patient–investigator contact.

Methods

See Executive Summary link at www.hta.ac.uk/execsumm/summ1202.shtml.

Further research/reviews required

Randomized trials in recalcitrant smokers allowing head-to-head comparison of CDTQ delivered with various NRT modalities (eg, inhalator, nasal spray, lozenge, gum, and patch) would be informative. Research is also needed into the best ways of implementing a CDTQ strategy and integrating this with abrupt quit options in the context of all UK smoking services.

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INAHTA Briefs

Issue 2009/061

Title **Exhaled Nitric Oxide Measurement Using Niox or Niox Mino**

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Reference Health Technology Assessment Report, MOH/P/PAK/178.09 (TR).
www.moh.gov.my/MohPortal/htaDetail.jsp?action=view&id=57

Aim

To assess the safety, effectiveness, and cost effectiveness of exhaled nitric oxide (FE_{NO}) measurement using NIOX or NIOX MINO in managing respiratory diseases, especially asthma.

Conclusions and results

The evidence shows that FE_{NO} measurement is safe and noninvasive. A good level of evidence shows good correlation between FE_{NO} values as measured by using the two devices (NIOX and NIOX MINO). FE_{NO} measurement provides superior diagnostic accuracy compared to conventional tests for diagnosing asthma. It can be used as a predictor of steroid response and loss of control in asthma following steroid withdrawal. There was limited evidence to establish the relationship between FE_{NO} and compliance with inhaled corticosteroids and its role in diagnosing and monitoring other respiratory diseases. The evidence shows that the use of FE_{NO} in treatment decisions is less costly than asthma management based on standard guidelines.

Recommendations

Based on the review mentioned above, FE_{NO} measurement can be recommended for use in Ministry of Health facilities having chest physicians (adult and pediatric), particularly for diagnosing asthma.

Methods

PubMed, Ovid, ProQuest, Cochrane, Food and Drug Administration (FDA), and HTA databases were searched, among others. Additional articles were identified from reviewing the bibliographies of retrieved articles. No limitations were placed on language. We used the Critical Appraisal Skills Program (CASP) to appraise relevant articles. Using the Oxford Centre for Evidence-based Medicine Levels of Evidence (May 2001) we graded evidence according to the levels of evidence for assessing diagnosis.

Further research/reviews required

Effectiveness in management of other respiratory diseases.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/062

Title **Bio Magnetic Therapy**

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Reference Technology Review Report, 002/08.
http://medicaldev.moh.gov.my/uploads/tr_2008/biomagnetic.pdf

Aim

To determine the safety and effectiveness of biomagnetic therapy.

Conclusions and results

Biomagnetic therapy, eg, in the form of a band or bracelet, is not a registered medical device with the US Food and Drug Administration. Evidence found by the review showed that biomagnetic therapy is not effective in treating chronic low back pain and pressure ulcers. However, poor quality evidence showed improved leg ulcer healing and some pain reduction in the treatment of knee pain.

Recommendations

Based on the above review, biomagnetic therapy in the form of a band or bracelet cannot be recommended. It is not a replacement for standard medical treatment. Further clinical research is warranted to provide evidence of its effectiveness in treating any medical condition.

Methods

The literature was systematically reviewed. PubMed, ProQuest, and MEDLINE, via Ebsco, were searched. HTA agency websites and society websites were searched, and retrieved articles were cross-referenced according to topic. One systematic review, five randomized controlled trials, and one experimental study were reviewed.

Further research/reviews required

Further clinical research is warranted to provide evidence on the effectiveness of biomagnetic therapy in treating any medical condition.

Written by Noormah Mohd Darus, MaHTAS, Malaysia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/063

Title **Hydroxyapatitite Granular Bone Graft – GranuMaS™**

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Reference Health Technology Review Report, 003/2008.
http://medicaldev.moh.gov.my/uploads/tr_2008/granumas.pdf

Aim

To assess the safety, effectiveness, and cost effectiveness of hydroxyapatite granular bone graft –GranuMaS™– as a synthetic bone graft substitute.

Conclusions and results

GranuMaS™ is derived from pure commercial chemicals and Malaysian limestone. It has passed all the required criteria for the American Society for Testing and Materials (ASTM) F1185-88 (1993) Standards and has undergone many in vitro and in vivo tests and two clinical trials. A fair level of evidence shows that using GranuMaS™ as a synthetic bone graft substitute is safe and effective for preservation of alveolar ridge post tooth extraction and is suitable for use in patients with traumatic fractures and bone loss. However, further randomized controlled trials (RCTs) involving larger numbers of subjects should be conducted. No evidence could be retrieved on the cost effectiveness of GranuMaS™. However, it is priced lower than imported synthetic bone graft.

Recommendations

Based on the above review, GranuMaS™ can be used as a research tool in research environments, eg, Phase 3 RCTs with larger numbers of subjects, to provide better quality evidence before it can be used widely in Malaysia. The research should include its other applications, eg, fusion of joints and vertebra, augmentation of osteoporotic bone defects, and augmentation, correction, and rectification of malpositioned bone.

Methods

Databases searched included PubMed, Ovid, ProQuest, EBSCOhost, CINAHL, Cochrane Systematic Reviews, Cochrane Central Register for Controlled Trials, HTA Databases, Health Business Full Text Elite, Food and Drug Administration (FDA) website from 2000-2007, and Google. Additional articles were identified from reviewing the bibliographies of retrieved articles and from documents provided by GranuLab (M) Sdn. Bhd. No limitations were placed on language. Personal communication included telephone calls. Relevant articles were appraised and evidence graded according to the US/Canadian Preventive Services Task Force.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/064

Title **Medic Strapping Pad**

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Reference Technology Review Report, 004/08.
http://medicaldev.moh.gov.my/uploads/medical_strapping_pad.pdf

Aim

To determine the safety, effectiveness, and cost effectiveness of Medical Strapping Pad (MSP) to reduce bleeding in emergency cases.

Conclusions and results

Evidence was insufficient as regards the safety, effectiveness, and cost effectiveness of MSP. No published articles on MSP were retrieved. Hence, the results and discussion were based on information provided by the distributor. Since no journal articles or research findings were provided, only anecdotal claims suggested that MSP could be applied to the wound site in less time, as compared to gamgee and bandage.

Recommendations

Although evidence was insufficient as regards the safety, effectiveness, and cost effectiveness of MSP, it has potential in the emergency management of wounds and bleeding. Further research is recommended to evaluate this product.

Methods

Electronic databases searched for relevant literature included PubMed, Ovid, ProQuest, EBSCOhost, EBM Reviews of controlled trials, Cochrane database on systematic reviews, Cochrane Clinical Trial Registry, Science Direct, Springer Link, and general databases such as Google and Yahoo. This study included all primary papers, systematic reviews, or meta analyses pertaining to safety, effectiveness, and cost effectiveness of MSP. All relevant literature was critically appraised and the evidence level graded according to the US/Canadian Preventive Services Task Force (Harris 2001).

Further research/reviews required

Clinical research is warranted to provide evidence on the safety and effectiveness of the product.

Written by Izzuna MMG, MaHTAS, Malaysia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/065

Title **MassARRAY Compact System**

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Reference Technology Review Report, 005/08.
http://medicaldev.moh.gov.my/uploads/massarray.pdf

Aim

To determine effectiveness in terms of reliability, accuracy, sensitivity, specificity, and cost effectiveness of MassARRAY as a technique for gene analysis.

Conclusions and results

Retrievable, fair-level evidence showed that using MassARRAY as an assay to detect gene variants and genotyping materials is effective in terms of accuracy, sensitivity, specificity, and high sample throughput levels, and cost effective compared to the other conventional genotyping methods.

Recommendations

- MassARRAY Compact System may be the best choice for a core facility due to its expensive consumables.
- MassARRAY Compact System provides high-throughput SNP genotyping for identifying specific genes for diseases, eg, myocardial infarction, prostate cancer, human papilloma virus, diabetes, and drug-resistant malaria.

Training

- Training should be provided for those who use array technologies in their own laboratory.
- Training should cover RNA/DNA preparations, probe generation and purification, hybridizations, and scanning. Additional sessions should include bioinformatics and microarray data analysis.

Methods

A search of electronic databases included PubMed, Ovid search engine, full text journals covered by MEDLINE, CINAHL, and HTA databases, FDA website, and Google search engine for published reports. Additional articles were identified from reviewing bibliographies in retrieved articles. No limitations were placed on the search.

The search strategy included the following terms, alone or in various combinations: Mass Array, effectiveness, accuracy, sensitivity, specificity, cost effectiveness, cost, mass spectrometry, cancer, MassARRAY MALDI-TOF MS methods and genotyping, and genotyping methods. All relevant literature was systematically reviewed, and the evidence was graded according to the modified Oxford scale.

Written by Mariammah Krishnasamy, MaHTAS, Malaysia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/066

Title **FibroScan**

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Reference Technology Review Report, 006/08.
http://medicaldev.moh.gov.my/uploads/fibroscan.pdf

Aim

To determine the safety and effectiveness (diagnostic accuracy) of FibroScan.

Conclusions and results

Good evidence shows that FibroScan correlates better with fibrotic area than existing liver fibrosis markers, suggesting that FibroScan can be used as an alternative to liver biopsy in assessing liver fibrosis, as it is safe and offers sufficient diagnostic accuracy.

Real-time elastography is a new and promising sonography-based noninvasive method for assessing liver fibrosis in patients with chronic viral hepatitis. In combination with simple laboratory values, real-time elastography can further improve the discrimination of different fibrosis stages, which plays a decisive role in managing patients with viral hepatitis.

The review showed good evidence of effectiveness in using FibroScan. Since these are early results, more research is needed. Most of the studies conducted to date were small, focused on a subset of patients with chronic liver disease, failed to consider the full range of noninvasive tests, and arrived at differing thresholds for discriminating among the degrees of fibrosis. It was also unclear whether the studies were independent of industry involvement. Future studies on larger patient cohorts are necessary for improvement and to validate the elasticity scores and discriminating power of the FibroScan.

Recommendations

The potential for noninvasive fibrosis staging is promising, but it remains unclear which technology or combination of technologies will be most useful. It could be compelling to use FibroScan more frequently based on its rapid and noninvasive nature. However, the degree to which FibroScan can replace liver biopsy remains unclear.

Methods

The literature was systematically reviewed. PubMed, ProQuest, and MEDLINE via EBSCO were searched as were websites of HTA agencies and societies, and the articles retrieved were cross-referenced accordingly. Cross-sectional studies and studies on diagnostic accuracy were assessed.

Further research/reviews required

Further clinical research is warranted to provide additional evidence of effectiveness in using FibroScan to diagnose liver fibrosis and to validate the elasticity scores and discriminating power of FibroScan.

Written by Noormah Mohd Darus, MaHTAS, Malaysia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/067

Title **Portable Oxygen Generator System - Gastec® System**

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Reference Technology Review Report, 007/08.
http://medicaldev.moh.gov.my/uploads/oxygen.pdf

Aim

To assess the safety, effectiveness, and cost effectiveness of the portable oxygen generator system – Gastec® System.

Conclusions and results

No scientific evidence is available on the safety or effectiveness of the portable oxygen generator system – Gastec® System.

Recommendations

Oxygen therapy is an established technology, although no scientific evidence is available on the safety and effectiveness of Gastec® System. It was proposed that the Engineering Division of the Ministry of Health in Malaysia carry out a technical evaluation of this technology.

Methods

The following electronic databases were used to search the literature: HTA sites, including INAHTA, ANZHSN, EUROScan, and ARSNEPS; EBM reviews; Cochrane Database of Systematic Reviews; MEDLINE (1966 - 17th April, 2008), Current Contents, Cochrane Controlled Trials Registry, and general databases, eg, Google and Yahoo. The manufacture's website was also searched for further information.

These databases were initially searched using the search terms: oxygen generator, onsite oxygen generator, portable oxygen generating system, oxygen gas generator, GASTEC, pressure swing adsorption OR vacuum swing adsorption. No limitations were imposed on the search.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/068

Title **Sterybox Air Disinfectant**

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Reference Technology Review Report, 008/08.
http://medicaldev.moh.gov.my/uploads/sterybox.pdf

Aim

To assess the effectiveness, safety, and cost effectiveness of Sterybox and other airborne disinfectants using the ultraviolet irradiation technique.

Conclusions and results

No evidence was retrievable on the effectiveness, safety (including FDA approval), and cost effectiveness of Sterybox. However, evidence on other airborne disinfectants using UVGI (similar technology adopted by Sterybox) was found in four experimental studies, two technology reviews, one cross-sectional study, and one narrative review. In conclusion, limited, low-level evidence was found on the technology in controlling/eliminating certain pathogens, eg, MDR Mycobacterium tuberculosis, Legionella sp, and measles virus, feasible in application and with small avoidable side effects.

Recommendations

Additional, high-quality scientific evidence is required to support the effectiveness, safety, and cost effectiveness of Sterybox and other air disinfectants using ultraviolet germicidal irradiation. The application of such devices depends on the purpose to control the type of airborne pathogens with proper installation. The UVGI may be used as a supplement to other essential engineering control methods, but not as their substitution.

Methods

Literature was searched through electronic, scientific databases, specifically: PubMed, MEDLINE, Cochrane, INAHTA, Proquest, Horizon Scanning, and other relevant websites, eg, the US FDA website, and general search engines. The search strategy used the following terms alone or in combination: Sterybox, airborne infection, airborne disinfectant, ultraviolet irradiation, UVGI, UV-CHRIS, and Ultraviolet High Reflecting Coil Irradiation System. No limits were imposed on the search.

Further research/reviews required

Additional research is warranted to obtain evidence on the effectiveness, safety, and cost effectiveness of Sterybox and other airborne disinfectants using the ultraviolet irradiation technique.

Written by Yusof MAM and Bakri R, MaHTAS, Malaysia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/069

Title **Circumcision Clamps**

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Reference Technology Review Report, 009/2008.
http://medicaldev.moh.gov.my/uploads/sunathron1.pdf

Aim

To assess the safety, effectiveness, and cost effectiveness of circumcision clamps.

Conclusions and results

Many types of nondisposable and disposable circumcision clamps are available on the market. A fair level of evidence supported the safety of Gomco, Mogen, Plastibell, and Tara KLamp. The evidence to support the safety of Sunathrone™ remains insufficient. A fair level of evidence also supported the effectiveness of Gomco, Mogen, Plastibell, and Tara KLamp. However, more randomized controlled trials should be conducted involving larger numbers of subjects. A poor level of evidence supported the effectiveness of Sunathrone™. No evidence was retrievable regarding the cost effectiveness of circumcision clamps.

Recommendations

Based on the above review, disposable circumcision clamps such as Tara KLamp and Sunathrone™ can be used as a research tool (to be used in research environments). Further clinical research, eg, randomized clinical trials, is warranted to provide better quality evidence.

Methods

The databases searched included: PubMed, Ovid, ProQuest, EBSCO Host, CINAHL, Cochrane database for systematic reviews, HTA Databases, Horizon scanning databases, the Food and Drug Administration (FDA) website, and MHRA. Additional articles were identified by reviewing the bibliographies of retrieved articles and from documents provided by Sunatrone Bio-medical Sdn. Bhd and Taramedic Corporation Sdn. Bhd. No limitations were imposed on the search. Personal communication was carried out by telephone. Relevant articles were appraised and evidence graded in accordance with the US/Canadian Preventive Services Task Force.

Written by Dr Junainah Sabirin, MaHTAS, Malaysia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/070

Title **Sonotron**

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Reference Technology Review Report, 010/08.
http://medicaldev.moh.gov.my/uploads/sonotron.pdf

Aim

To determine the safety, effectiveness, and cost effectiveness of Sonotron in treating patients with diabetic wounds, arthritis, and post stroke.

Conclusions and results

No published papers on Sonotron were retrieved. According to the Sonotron distributor in Malaysia, in 1999-2000 nine doctors from various parts of Malaysia conducted a pilot study involving 555 patients. In 2003-2004, after the pilot study, a larger study reviewed 1054 clinical cases treated with Sonotron.

The 2003-2004 study reported no adverse events pertaining to Sonotron, and all respondents viewed Sonotron to be a safe procedure. Regarding musculoskeletal disorders, all 225 patients who received a single session reported at least 50% improvement, where 40% reported 91% to 100% improvement. Trends in reported improvement were similar for other disorders studied, ie, neurologic disorders, ENT disorders, dermatologic disorders, gastrointestinal disorders, ophthalmologic disorders, dental and oral disorders, gynecologic/genitourinary disorders, and pulmonary disorders. However, the number of cases in each group (disorders) was small, ranging from 4 cases to 33 cases.

In conclusion, evidence is insufficient as regards the safety, effectiveness, and cost effectiveness of Sonotron.

Recommendations

Based on this review, Sonotron is not recommended as standard treatment for patients with diabetic wounds, arthritis, and post stroke.

Methods

Literature was searched through electronic databases, including: PubMed, Cochrane Library, Ovid, Science Direct, ProQuest, and general databases such as Google and Yahoo.

This study included all primary papers, systematic reviews, or meta-analyses pertaining to the safety, effectiveness, and cost effectiveness of Sonotron. Critical Appraisal Checklist Project (CASP) checklists were used to appraise all relevant literature, and evidence was graded according to the US/Canadian Preventive Services Task Force Level of Evidence.

Further research/reviews required

Further clinical research, eg, randomized clinical trials, is warranted to provide good quality evidence for each indication as claimed by the manufacturer and Sonotron users.

Written by Izzuna MMG, Norkiah U, MaHTAS, Malaysia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/071

Title **Atmosphere Air Purifier**

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Reference Technology Review Report, 011/08.
http://medicaldev.moh.gov.my/uploads/air_purifier.pdf

Aim

To determine the safety and effectiveness of a portable device that utilizes high efficiency particulate arrestor (HEPA) filters to purify air.

Conclusions and results

Sufficient scientific evidence was retrievable to support the claim that HEPA filters have a minimum efficiency exceeding 90% for particles of 0.3 microns in diameter. Evidence showed that air purifiers or air cleaners with HEPA filters could remove air pollutants and particulates such as molds, bacteria, smoke contaminant, and cat- and dog-associated allergens. Scientific evidence was insufficient as regards the efficacy of HEPA filters in capturing viruses, gaseous pollutants, or radon and its progeny.

Recommendations

The following is recommended:

- Portable air purifiers may be considered for use in a recommended room size for residential areas, taking into account the capacity of the equipment.
- The ATMOSPHERE air purifier is not recommended for Ministry of Health facilities.

Methods

The search for published reports included the following electronic databases: PubMed, Ovid search engine, full text journal which covers MEDLINE, CINAHL, HTA Databases, FDA website, and Google search engine. Additional articles were identified by reviewing the bibliographies of retrieved articles. No limitations were imposed on the search. The search strategy used the following terms, alone or in combination: HEPA filter, high efficiency particulate air filter, portable air filter, air cleaner, effectiveness, safety, smoke, dust, mites, virus, microorganisms, fungus, bacteria, micro particles, and particulates.

All relevant literature was systematically reviewed, and the evidence was graded according to the modified Oxford scale.

Written by Mariammah Krishnasamy, MaHTAS, Malaysia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/072

Title **Multidisciplinary Combined Treatment in Peritoneal Neoplasms**

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Reference ISBN 978-84-393-8004-7

Aim

To assess the efficacy and safety of the Sugarbaker procedure in treating peritoneal carcinomatosis secondary to colorectal cancer, ovarian cancer, pseudomyxoma peritonei, abdominal sarcoma, malignant mesothelioma, and gastric cancer.

Conclusions and results

Of the 1619 publications identified, 43 verified the overview inclusion criteria. Evidence from randomized clinical trials (RCTs) proves that the Sugarbaker procedure is superior to conventional treatment in terms of survival for peritoneal carcinomatosis secondary to colorectal or gastric cancer. Evidence of the intervention's efficacy for peritoneal carcinomatosis secondary to ovarian cancer, pseudomyxoma peritonei, or malignant peritoneal mesothelioma emerges from uncontrolled case series and is inconclusive. A small, randomized trial of peritoneal sarcomatosis failed to show a benefit of the Sugarbaker procedure. Scant data are available on quality of life, and the results are difficult to assess.

Methods

A bibliographic search was conducted for the most recent systematic reviews and the studies that update them. Sources searched were MEDLINE (accessed through PubMed), EMBASE (accessed through Ovid) and CENTRAL, up to 2007. We assessed methodological quality and level of evidence of the identified systematic reviews (AMSTAR tool), clinical trials, and case series (SIGN scale) and described the study results.

Further research/reviews required

International multicentric RCTs with adequate sample size are needed to gain a deeper understanding of some important therapeutic issues related to carcinomatosis secondary to colorectal and gastric cancer and to assess the efficacy of the Sugarbaker procedure in the remaining conditions.

Written by Pedro Barrios, Hospital de la Santa Creu i Sant Pau, CAHTA, Spain

ISSN 1654-501X

INAHTA Briefs

Issue 2009/073

Title **Pharmaceutical and Non-Pharmaceutical Interventions for Alzheimer's Disease, a Rapid Assessment**

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Reference Report no. 111 (A), 2009. www.kce.fgov.be/index_en.aspx?SGREF=5212&CREF=13587

Aim

To study the effectiveness and cost effectiveness of current pharmaceutical and nonpharmaceutical interventions targeting Alzheimer's disease (AD) patients and analyze AD drug prescriptions for 2002 to 2006.

Conclusions and results

No single diagnostic instrument is adequate for population screening, but neuropsychological tests and new disease-specific markers make diagnosis more accurate. Studies of nonpharmacological interventions often have methodological issues, but several promising patient-targeted interventions were identified: cognitive stimulation with or without acetylcholinesterase inhibitors (ChEIs), activities of daily living (ADL) rehabilitative care, music therapy, massage/touch, and physical activity. Most promising are support programs for informal caregivers, which lower depression in caregivers and delay the time to institutionalization of patients.

Regarding pharmacotherapy, the efficacy data for Ginkgo biloba are not robust. For memantine monotherapy, the effects on cognitive function and Clinician's Interview-based Impression of Change (CIBIC+) are weak (to absent), improvements of ADL and psychopathology are minor. RCT data on degree of care and effect on institutionalization were not made public. For ChEIs, the number needed to treat is 10 for cognitive function and CIBIC+; benefits on ADL and psychopathology are minor. For institutionalization, RCT results are negative, or not available. Gastrointestinal side effects are frequent.

More data are needed on ChEI + memantine. Most economic models extrapolate an improvement in cognitive function to a delay in institutionalization, but RCTs did not confirm this. Over 40 000 patients in Belgium (pop.10 million) used ChEIs in 2008, 34% of the 34 000 AD patients in elderly homes and 69% of the 41 000 AD patients at home (treatment duration over 3 years if ChEI started at home). Frequent concomitant use of antipsychotics: 21% (at home) and 45% (elderly home), and antidepressants: 26% to 52%. About 5000 patients used memantine in 2008.

Recommendations

Limit antipsychotics use in AD. Care needed when ChEIs started in medically instable AD. Public financing questioned for Ginkgo biloba and memantine monotherapy. Impact on behavior of AD treatments is important, mainly in geriatric patients. Fund RCT of caregiver support program.

Methods

We limited our search to HTA reports and systematic reviews and did not formally score the quality of the reviews. Full economic evaluations were included if published after 2004. Belgian drug prescription data were analyzed for 2002 to 2006.

Further research/reviews required

Cost-effectiveness analyses of magnetic resonance imaging, neuropsychological tests, and the proposed AD markers. Standardization of nonpharmaceutical interventions. Reasons why ChEIs are first started after institutionalization. Accurate prevalence data for dementia, future needs for elderly homes and home care.

Written by Frank Hulstaert, KCE, Belgium

ISSN 1654-501X

INAHTA Briefs

Issue 2009/074

Title **Policies for Orphan Diseases and Orphan Drugs**

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Reference Report no. 112 (C), 2009. www.kce.fgov.be/index_en.aspx?SGREF=5212&CREF=13651

Aim

To describe the regulatory processes for orphan drugs from orphan designation to reimbursement and explore whether and how to improve the policy on orphan drugs.

Conclusions and results

European legislation defines a rare disease as a life-threatening or chronically debilitating condition with a prevalence of 5 patients per 10 000 people or less. EU has created incentives for development of orphan drugs, eg, fee reductions, protocol assistance, and 10 years of market exclusivity.

The European Medicines Agency (EMEA) grants the orphan designation, after which marketing authorization can be requested. Upon authorization, a European Public Assessment Report (EPAR) is prepared and published on the EMEA website. The EPARs generally reflect the information from clinical files submitted to EMEA, but more could be done to improve the utility of the EPARs for national drug reimbursement committees (DRCs).

To obtain product reimbursement, companies must send the DRC a budget impact analysis and evidence on the drug's efficacy, preferably, and effectiveness.

Recommendations

Some of the recommendations formulated for the European and national levels include:

- For high priority orphan diseases, Europe should set up registries as early as possible; preferably before a drug is being developed for the disease.
- HTA agencies could help design patient registries to ensure that useful data are collected on the effectiveness and cost effectiveness of novel drugs.
- Aggregated data from the registries should publicly available.
- Registries should be funded and governed independently from the company developing an orphan drug.
- Evidence from RCTs with clinically relevant endpoints should remain the standard for granting marketing authorization.
- HTA agencies may provide valuable input at the EMEA level to define the endpoints and level of clinical improvement needed in phase-3 studies to qualify the product for reimbursement.

Methods

Definitions for orphan diseases and orphan drugs were based on a narrative review of regulatory documents and published articles. Descriptions of regulatory processes were based on regulatory documents and interviews with experts, key actors, and stakeholders involved at the national and European levels.

We compared the clinical files submitted to EMEA for marketing authorization, the resulting EPARs, and clinical evidence submitted to the Belgian National Institute for Health and Disability Insurance as part of a drug reimbursement request for 15 specific, drug-indication combinations.

Clinical and economic evidence submitted to the Belgian DRC was critically appraised for 8 cases, looking at the type and level of evidence and the methodological standards applied to drug reimbursement files for orphan drugs.

Six countries were included in comparing orphan drug reimbursement procedures: Belgium, France, Italy, the Netherlands, Sweden and the United Kingdom.

Written by Irina Cleemput, KCE, Belgium

ISSN 1654-501X

INAHTA Briefs

Issue 2009/075

Title **Endobronchial Valves in the Treatment of Severe Pulmonary Emphysema: a Rapid Health Technology Assessment**

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Reference Report no. 114 (C), 2009

Aim

To systematically review the cost effectiveness of endobronchial valves (EBVs) as an additional modality to optimal noninvasive therapy in patients with severe pulmonary emphysema.

Conclusions and results

No data from randomized controlled trials (RCTs) have been published. The available evidence indicates that the efficacy of EBVs on the outcome measures important to patients is, on average, limited. Subgroups of patients that are to be identified may benefit more substantially from the procedure, but future research needs to resolve such issues.

The findings indicate that the safety of EBV insertion in patients with severe emphysema remains a concern. The procedure may induce pneumothorax, and the presence of a foreign object in the bronchial tree seems to induce chronic obstructive pulmonary disease (COPD) exacerbations and lead to more hospitalizations during follow-up.

Recommendations

Reimbursement of EBVs in patients with end-stage pulmonary emphysema cannot be supported due to poorly demonstrated clinical benefit, potential adverse effects, and high costs for limited efficacy.

Assignment of a CE-label to a medical device does not guarantee its effectiveness or clinical safety, and such labeling may mislead patients and physicians. KCE recommends inclusion of this issue on the agenda of the Belgian presidency of the European Union in 2010.

Methods

A systematic literature search identified no RCT on the efficacy of EBV, but found 9 case series in peer-reviewed journals. A search of ClinicalTrials.gov, revealed 5 registered trials. Contact with manufacturers and principal investigators of these studies and a search of the grey literature identified data on some of the registered trials. Minutes from an FDA meeting presented some results from the yet unpublished VENT trial.

A cost-effectiveness sub-study of the VENT trial was set up to gather utilization and quality of life information on patients enrolled in the clinical VENT study (ClinicalTrials.gov identifier NCT00137956) to analyze the relative cost effectiveness of the EBV procedure. This sub-study was stopped prematurely because "Emphasys Medical decided to discontinue the study due to resources and cost required to execute the study as compared to the amount of additional data being received."

Further research/reviews required

The devices may provide a larger benefit in subgroups of patients, but it is unclear how these subgroups can be identified and whether the clinical improvement would outweigh the potential harms. The possible benefit of EBVs in such subgroups should be proven in a prospective RCT including patient-oriented endpoints.

Written by Van Brabandt H, KCE, Belgium

ISSN 1654-501X

INAHTA Briefs

Issue 2009/076

Title **Positron Emission Tomography (PET) in Belgium: an Update**

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Reference Report no. 110 (C), 2009

Aim

To answer the following research questions: What is the diagnostic accuracy and clinical effectiveness of PET and PET/CT? What are the clinical indications for PET and PET/CT? Which programming criteria are used in other countries? Can the number of patients requiring a PET scan be estimated in Belgium?

Conclusions and results

During the past 4 years, the body of evidence for new indications currently not reimbursed in Belgium (eg, primary staging of head and neck cancer and cervical cancer) has increased, although the quality of this evidence did not improve. By allowing reimbursement of PET scans through the nomenclature code *scintigraphy double tomography*, the programming of PET scanners had only a minor influence on the real number of PET examinations in Belgium. Two methods are available to align the number of PET scanners to the clinical needs: (i) programming and (ii) accreditation criteria and reimbursement modalities. In Belgium, a programming of PET scanners based on a calculation of the needs is impossible in the short run.

Recommendations

- Calculating the number of PET scans needed is impossible in the short run and is therefore not recommended as a means of programming PET scanners in Belgium.
- An alternative to programming would be to regulate the number of PET scanners:
  - by setting accreditation criteria that are strict enough, and strictly monitored the application to assure the quality of examinations;
  - by determining reimbursement criteria that limit the reimbursable indications to those that are based on scientific evidence.
- Reimbursement of PET examinations is conditional upon registration of the indication in a unique, authorized, and standardized registry. This mandatory registration should allow for follow-up of whether the proposed system corresponds to the actual needs.
- The list of reimbursed indications for PET and PET/CT should be updated every 3 years, with special attention to new tracers and new imaging modalities. For this update, the research question should be expanded to other imaging techniques, to allow a systematic positioning of PET and PET/CT towards these techniques.
- If an oncological indication supported by inconclusive scientific evidence is added to this list, reimbursement should be linked to the multidisciplinary oncological consult.
- Compliance with these reimbursement criteria should be checked systematically.
- Reimbursement of PET scans through the nomenclature code *scintigraphy double tomography* should be abandoned to allow transparent and controlled follow-up of the number of PET investigations.

Methods

We systematically reviewed HTA reports, systematic reviews, meta-analyses, RCTs, and diagnostic and prognostic studies. Search dates: January-May 2009. Databases: CRD database (HTA database, DARE, NHS EED), MEDLINE, EMBASE, and websites of HTA agencies.

Written by Joan Vlayen, KCE, Belgium

ISSN 1654-501X

INAHTA Briefs

Issue 2009/077

Title **Effectiveness of Protocols Sedo Analgesia in Adult Patients in Intensive Care Units: A Review of Literature of Scientific Evidence**

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Reference Report no. 22.
www.redsalud.gov.cl/portal/url/item/6e5acd9c633eb319e0400101f017966.pdf

Aim

To review sedation protocols in critically ill adult patients.

Conclusions and results

The outcomes measured in this review are the length of stay for patients in the intensive care unit (ICU) and the number of days involving mechanical ventilation.

Recommendations

- Use a guide or protocol to assess sedation of the patient on a regular basis, using this validated measurement scale to make the daily dose adjustments necessary to avoid sedation.
- The choice of drugs used and the level of sedation and analgesia desired should be decided at the outset, individually for each patient according to their history, clinical condition, etc.
- Assessment of sedo-analgesia protocols requires valid and reliable scales to ensure the quality and safety of patient care in the intensive care unit.

Methods

The literature review covered material from the past 10 years in MEDLINE, Cochrane Collaboration, Controlled Clinical Trial Register, DARE of York University, LILACS, International Network of Agencies for Health Technology Assessment, Chilean Society of Anesthesiology, Society of Intensive Care (Chile), Society of Anesthesiology (USA), and Intensive Medicine Society (USA).

Further research/reviews required

Consideration of variability in the management of patients in the ICU is necessary to identify a larger number of randomized clinical trials that can provide scientific evidence to support decision-making in this field.

Written by Luis Vera, Patricia Kraemer, ETESA, Chile

ISSN 1654-501X

INAHTA Briefs

Issue 2009/078

Title **Review of Evidence and Recommendations for Environmental Management in Bone Marrow Transplant Units**

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Reference Report no. 21.
www.redsalud.gov.cl/portal/url/item/6e5bfcdba13a5dcfe0400101f017d32.pdf

Aim

To search for scientific evidence to support recommendations for environmental management of bone marrow transplantation.

Conclusions and results

This review describes an approach toward environmental safety, infections, and conditions of installation and proposes recommendation concerning the following aspects:

- Ventilation of rooms, air filtration
- Construction and/or renovation of facilities and environmental cleaning and disinfection
- Isolation precautions
- Equipment
- Precautions for health workers
- Play Areas
- Visitors

Methods

We reviewed the literature and recommendations found in MEDLINE, Cochrane Collaboration, and CDC.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/079

Title **Routine Iron Supplementation for Children Under Five Years of Age**

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Reference Technology Review Report, 015/2008.
http://medicaldev.moh.gov.my/uploads/15.iron.pdf

Aim

To assess the safety, effectiveness, and cost effectiveness of routine iron supplementation in children below 5 years of age.

Conclusions and results

Good evidence shows that routine iron supplementation in preschool children in a population with high rates of malaria can increase the risk of severe illness and death. Good evidence shows that iron supplementation reduced the prevalence of anemia in children with iron deficiency anemia and increased hemoglobin concentration in children, especially children with lower baseline Hb levels <11g/dL, on oral medication intake, and living in a non-malarial, non-hyperendemic region. Iron supplementation resulted in better effects on growth velocity of breast fed infants, especially those who were initially malnourished and anemic, or at least iron depleted. Supplementation of iron in preterm and low birth weight infants resulted in better iron status. No convincing evidence shows that iron treatment in young children (below 3 years of age) with iron deficiency anemia has an effect on psychomotor and mental development. Good evidence shows that iron supplementation did not have positive effects on any anthropometric variable; instead iron supplementation in iron-replete children may retard growth. No evidence supports the cost effectiveness of routine iron supplementation in children with iron deficiency anemia.

Recommendations

Based on the above review, iron supplementation should not be given routinely to children under 5 years of age. Instead, iron supplementation should be given to children who are iron deficient or have iron deficiency anemia. Iron supplementation is recommended for asymptomatic children who are at increased risk for iron deficiency, eg, premature and low birth weight infants or exclusively breast fed infants whose mothers are iron deficient or have iron deficiency anemia. Intermittent iron supplementation can be used instead of daily iron supplementation in children with iron deficiency anemia.

Methods

Databases searched included: PubMed, Ovid full text, ProQuest, EBSCOhost, MEDLINE, CINAHL, Cochrane database for systematic reviews, HTA Databases, Horizon scanning databases, and the Food and Drug Administration (FDA) website. Additional articles were identified from reviewing the bibliographies of retrieved articles. The search was limited to children. Studies related to multiple micronutrient supplementations were not included. Relevant articles were appraised and evidence graded according to US/Canadian Preventive Services Task Force.

Written by Dr Junainah Sabirin, MaHTAS, Malaysia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/080

Title **Compression Stockings for Prevention of Varicose Veins and Deep Vein Thrombosis Among Nurses**

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Reference Technology Review Report, 020/08.
http://medicaldev.moh.gov.my/uploads/20.stockings.pdf

Aim

To determine the safety, effectiveness, and cost effectiveness of graduated compression stockings to prevent varicose veins and deep vein thrombosis in nurses.

Conclusions and results

Compression stockings are safe, provided proper type and size are used. Evidence is insufficient on the efficacy or effectiveness of using compression stockings to prevent varicose veins or deep vein thrombosis in nurses. However, they may prevent the emergence of third-trimester, long saphenous vein reflux at the saphenofemoral junction and leg symptoms in pregnant nurses. Compression stockings may also benefit nurses with a previous history of deep vein thrombosis by preventing moderate to severe post-thrombotic syndrome, and they could benefit nurses with chronic venous insufficiency by reducing symptoms and edema.

Recommendations

Based on the evidence retrieved, compression stockings are not recommended as an item to be supplied to **all** nurses in Ministry of Health Malaysia. However, compression stockings may be considered for use by nurses who are at risk (eg, pregnant, have a history of deep vein thrombosis, or are diagnosed as having chronic venous insufficiency).

Methods

A literature search of electronic databases included: MEDLINE, Cochrane Library, Science Direct, EBSCOhost, and general databases, eg, Google and Yahoo. The search included systematic reviews, meta-analyses, and randomized clinical trials that involved the use of compression stockings to prevent or treat varicose veins and deep vein thrombosis. Studies of hospitalized patients only, or flight passengers only, were excluded.

All relevant literature was critically appraised using Critical Appraisal Skills Programme (CASP) checklists, and evidence was graded according to the US/Canadian Preventive Services Task Force Levels of Evidence (2001).

Further research/reviews required

Further clinical research is warranted.

Written by Izzuna MMG, Mohd Said M, MaHTAS, Malaysia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/081

Title **Spinal Implants: DR8™ Pedicle Screw System**

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Reference Technology Review Report, 016/08.
http://medicaldev.moh.gov.my/uploads/16.spinal.pdf

Aim

To determine the safety, effectiveness, and cost effectiveness of the DR8™ Pedicle Screw System for spinal implants.

Conclusions and results

No scientific evidence was retrieved on the DR8™ Pedicle Screw System. The titanium screws and rods conformed to a grade of Ti-6AI-4V or UNS R56401. Titanium screws underwent mechanical testing and conformed to required standards.

The evidence was insufficient to support the safety, effectiveness, and cost effectiveness of the DR8™ Pedicle Screw System.

Recommendations

Based on this review, the DR8™ Pedicle Screw System cannot be recommended for use until further evidence is obtained on its safety and effectiveness.

Methods

A literature search included the following electronic databases: MEDLINE, Cochrane Library, Science Direct, EBSCOhost, and general databases, eg, Google and Yahoo.

All relevant literature was critically appraised using Critical Appraisal Skills Programme (CASP) checklists, and evidence was graded according to the US/Canadian Preventive Services Task Force Levels of Evidence (Harris 2001).

Regarding effectiveness, this review included only human studies. Only randomized controlled trials and systematic reviews of randomized controlled trials were included. Animal studies and observational studies were excluded.

Regarding safety assessment, all studies on the DR8™ Pedicle Screw were included.

Further research/reviews required

Further clinical research is warranted.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/082

Title **Antioxidant Treatment Room**

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Reference Technology Review Report, 014/08.
http://medicaldev.moh.gov.my/uploads/14.antioxidant.pdf

Aim

To determine the safety and effectiveness of anti-oxidant treatment rooms.

Conclusions and results

No scientific evidence supports the efficacy of anti-oxidant treatment rooms for diabetic patients. All articles available on the website provided only anecdotal evidence and testimonials.

Recommendations

Based on the review, anti-oxidant room treatment cannot be recommended. It is not a replacement for standard medical treatment. More clinical research is warranted to provide evidence of effectiveness for its use in treating any medical condition.

Methods

The literature was systematically reviewed. PubMed, ProQuest, and MEDLINE via EBSCO were searched, as were websites of HTA agencies and relevant societies. Articles retrieved were cross-referenced according to topic. Articles available on the website provided only anecdotal evidence and testimonials.

Further research/reviews required

Clinical research is warranted to provide evidence of effectiveness concerning the use of anti-oxidant treatment rooms in treating medical conditions.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/083

Title **Automated Gel Permeation Chromatography (GPC)**

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Reference Technology Review Report, 21/08.
http://medicaldev.moh.gov.my/uploads/gpc.pdf

Aim

To determine the safety, efficacy, and effectiveness of automated gel permeation chromatography (GPC) for sample cleanup process.

Conclusions and results

No evidence was retrievable on the effectiveness and cost effectiveness of automated GPC as regards clinical sample preparation or sample clean up. No technology assessment report addressed this technology.

Recommendations

GPC needs to be validated and tested before considering its use for sample preparation or sample clean up for clinical samples.

Methods

Electronic databases searched for relevant articles included: PubMed, Ovid search engine, MEDLINE, CINAHL, and Cochrane database of systematic reviews, HTA Databases, Horizon scanning databases (CADTH, ASERNIP-S, Defra, Euroscan), FDA website, and Google search engine.

The search strategy used the following terms either alone or in combination: gel permeation chromatography,accuracy, precision, efficacy, sample clean up, and sample preparation. Relevant literature was critically appraised, and evidence was graded according to US/Canadian Preventive Services Task Force (Appendix 1).

Further research/reviews required

Clinical research is warranted for this device before it can be recommended for use.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/084

Title **HER2 Testing**

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Reference Technology Review Report, 012/08.
http://medicaldev.moh.gov.my/uploads/12.her2.pdf

Aim

To determine the safety, effectiveness, and cost effectiveness of HER2 (human epidermal growth factor receptor 2) testing for breast cancer.

Conclusions and results

Immunohistochemistry (IHC) results show more variability (for IHC score of 2+) than fluorescence in situ hybridization (FISH) results, particularly in FISH-negative cases. The results of most studies indicate that a high-level HER2 amplification and an IHC score of 3+ will identify HER2-positive breast carcinoma; low level amplification and/or IHC of 2+ should be carefully interpreted. There is agreement that the most (cost) effective testing strategy is to screen all patients with IHC, followed by FISH/CISH for IHC of 2+ (or of 2+ and 3+) as recommended in the HER2-testing algorithm. The exclusive use of FISH for HER2 testing could lead to misdiagnosis in some cases.

Most of the retrievable evidence shows that concordance is high between FISH and chromogenic in situ hybridization (CISH). However, evidence suggests that CISH may be a viable and potential alternative to FISH for use in the HER2-testing algorithm.

Recommendations

Due to the consequential costs (nonmonetary costs/side effects of the therapy with trastuzumab and monetary costs) we recommend that all patients be screened with IHC, followed by FISH/CISH for IHC of 2+ (or of 2+ and 3+) as recommended in the HER2-testing algorithm.

Methods

The literature was systematically reviewed. PubMed, ProQuest, and MEDLINE via EBSCO were searched, as were websites for HTA agencies and relevant societies. Articles retrieved were cross-referenced according to topic. Eight diagnostic studies and two cost-effectiveness studies (one of which was a systematic review) were assessed in this review.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/085

Title **Maggot Debridement Therapy**

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Reference Technology Review Report, 017/08.
http://medicaldev.moh.gov.my/uploads/17.maggot.pdf

Aim

To determine the safety and effectiveness of maggot debridement therapy.

Conclusions and results

Many questions remain unanswered, and a large prospective evaluation is warranted. Although maggot debridement therapy (MDT)-debrided wounds decrease in size, which prepares them for closure more rapidly than with conventional therapy, the rate of wound closure was not significantly higher than that associated with conventional/standard therapy. A larger study, preferably with subjects whose disease is not as advanced, might better demonstrate the impact of maggot therapy in complete wound closure. In addition to issues of efficacy and safety, future studies must also address the cost effectiveness of MDT.

Recommendations

Based on the review, more pragmatic trials are warranted to provide further evidence on the effectiveness of MDT in wound healing, particularly for diabetic foot ulcers. Hence, MDT can be recommended for use only for research purposes.

Methods

The literature was systematically reviewed. PubMed, ProQuest, and MEDLINE via EBSCO were searched, as were websites for HTA agencies and relevant societies. Articles retrieved were cross-referenced according to topic. All of the studies were observational, cross-sectional, and case series.

Further research/reviews required

More pragmatic trials are warranted to provide further evidence on the effectiveness of using MDT in wound healing, particularly for diabetic foot ulcers.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/086

Title **Thyroid Screening in Pregnant Women**

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Reference Technology Review Report, 026/08.
http://medicaldev.moh.gov.my/uploads/26.thyroid.pdf

Aim

To determine the safety, effectiveness, and cost effectiveness of thyroid screening program in pregnant women.

Conclusions and results

Screening is defined as testing for a disease when there are no signs or symptoms, with the goal to improve health outcomes. Given the potential for serious adverse events associated with maternal thyroid disease and the apparent benefits of treatment, many have recommended routine thyroid function screening in pregnancy. The groups of physicians performing most prenatal care, obstetrician-gynecologists, however, have not advocated routine screening for thyroid disease in pregnancy. Professional associations of endocrinologists have taken varying views, with evidence-based review panels concluding that evidence is insufficient to mandate routine screening, and other expert panels advocating screening. Groups that gathered as part of two multidisciplinary conferences that included endocrinologists, obstetricians, and other experts, concluded that the evidence is insufficient for routine thyroid screening in pregnancy.

Another point of discussion concerns the optimal timing for screening, since changes in thyroid peroxidase (TPO) occur due to immunological adaptations, and serum thyroid stimulating hormone (TSH) decreases in 20% of women at the end of the first trimester. Until larger, properly randomized controlled trials show a beneficial impact of thyroxin treatment on pregnancy outcome, the discussion on the validity of screening will continue.

Recommendations

Universal screening of pregnant women for thyroid disease is not supported by adequate, high-quality evidence. Although current evidence might not confirm the benefits of universal screening for thyroid dysfunction (primarily hypothyroidism), we recommend case finding by measuring TSH in specific groups of patients, including women with: history of hyperthyroid or hypothyroid disease, postpartum thyroiditis (PPT), or thyroid lobectomy; family history of thyroid disease; goiter; thyroid antibodies; symptoms or clinical signs suggestive of thyroid underfunction or overfunction, eg, anemia, elevated cholesterol, and hyponatremia; type 1 diabetes; other autoimmune disorders; infertility; previous therapeutic head or neck irradiation; and history of miscarriage or preterm delivery.

Methods

The literature was systematically reviewed. PubMed, ProQuest, and MEDLINE via EBSCO were searched, as were websites for HTA agencies and relevant societies. Articles retrieved were cross-referenced according to topic. The studies reviewed were systematic reviews, guidelines, and observational studies.

Further research/reviews required

Further clinical research is warranted to provide evidence of the effectiveness of routine screening for thyroid disease in pregnancy.

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INAHTA Briefs

Issue 2009/087

Title **G-VIR® Glove**

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Reference Technology Review Report, 023/08.
http://medicaldev.moh.gov.my/uploads/23.gvir.pdf

Aim

To assess the safety, effectiveness, and cost effectiveness of G-VIR® glove.

Conclusions and results

There is poor evidence that G-VIR® gloves are safe and offer mechanical protection (glove barrier) especially in the surgical setting. No randomized controlled trials demonstrate clinical tolerance and effectiveness of this device. As regards cost implications, this technology is reported to be more expensive than the current practice in high-risk surgeries using double gloves.

Recommendation

This technology is not recommended until more clinical research is obtained.

Methods

The literature search included the following electronic databases: HTA sites, eg, INAHTA, ANZHSN, EuroScan, ARSENIPS; EBM reviews; Cochrane Database of Systematic Reviews; Cochrane Database of Clinical Trial Registers; MEDLINE, Current Contents, Cochrane Controlled Trials Registry; and general databases, eg, Google and Yahoo. The manufacture's website was also searched for further information.

The databases were searched using the following search terms: glove, surgical glove, virus inhibiting, HIV/HCV, protection, blood exposure accident, blood-borne viruses, needle puncture, viral contamination. No limitations were imposed on the search.

Further research/reviews required

Further randomized controlled trials are required to demonstrate the safety and effectiveness of this technology compared to double gloving.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/088

Title **MammaPrint**

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Reference Health Technology Assessment Report, 018/08.
http://medicaldev.moh.gov.my/uploads/18.mammprint.pdf

Aim

To determine the effectiveness and cost effectiveness of MammaPrint as a diagnostic or prognostic assay for breast cancer.

Conclusions and results

MammaPrint may be used as a diagnostic tool. However, evidence is lacking to support the clinical utility of MammaPrint assay for any subset of breast cancer patients. Likewise, no evidence supports the benefit of this test to predict chemotherapy benefit and improvement in clinical outcomes by the gene expression profiling test. Some limitation was listed on microarray assay, eg, instability of gene lists, overoptimistic performance indicators, and inadequate validation. Regarding cost effectiveness, the Agency for Health Care Research and Quality (AHRQ) showed inconclusive economic outcomes for all of the gene profiling tests.

Recommendations

- Two ongoing randomized controlled trials – TAILOR (Trial Assigning Individualized Options for Treatment) and MINDACT (Microarray for Node-negative Disease may Avoid Chemotherapy) – could provide significant answers about the clinical value of the multigene predictors of this microarray technology.
- It is suggested that this technology should not be adopted until the findings of the two clinical trials mentioned above have been published.

Methods

Electronic databases used in the search for relevant articles included: PubMed, MEDLINE, CINAHL, Cochrane database of systematic reviews, HTA Databases, Horizon scanning databases (CADTH, ASERNIP-S, Defra, EuroScan), FDA website, and Google search engine. Additional articles were identified by reviewing the bibliographies of retrieved articles. This review mainly focused on studies published from 2007 up to 2008.

The search strategy used the following terms, either alone or in combination: Mamaprint, MammaPrint AND Breast cancer, microarray AND breast cancer AND prognostic effectiveness OR efficacy, cost effectiveness, and cost analysis.

Further research/reviews required

Further quality evidence is warranted to support the effectiveness and cost effectiveness of MammaPrint as a diagnostic and prognostic tool for patients with breast cancer.

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INAHTA Briefs

Issue 2009/089

Title **Khan Kinetic Treatment™**

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Reference Technology Review Report, 025/2008.
http://medicaldev.moh.gov.my/uploads/25.khan.pdf

Aim

To assess the safety, effectiveness, and cost effectiveness of Khan Kinetic Treatment™.

Conclusions and results

Limited evidence addressed the safety of Khan Kinetic Treatment and the effectiveness of Khan Kinetic Treatment in treating chronic low back pain and chronic neck pain. No evidence was retrievable on the cost effectiveness of Khan Kinetic Treatment.

Recommendations

Based on the review, routine use of Khan Kinetic Treatment in treating pain from spinal abnormalities is not recommended until further evidence can be obtained from good-quality clinical research.

Methods

Databases searched included: PubMed, Ovid full text, EBM Reviews-Cochrane database of systematic reviews, EBM Reviews-Cochrane Central Register for Controlled Trials, HTA databases, Food and Drug Administration (FDA), and Google. Additional articles were identified by reviewing the bibliographies of retrieved articles. All relevant literature was critically appraised, and evidence was graded according to the US/Canadian Preventive Services Task Force.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/090

Title **Tea Tree Oil as Topical Antiseptic**

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Reference Technology Review Report, 019/2008.
http://medicaldev.moh.gov.my/uploads/19.tea.pdf

Aim

To assess the safety, effectiveness, and cost effectiveness of tea tree oil as topical antiseptic.

Conclusions and results

Poor-level evidence indicated that tea tree oil could cause systemic and dermatological toxicity and gynecomastia in prepubertal boys. No evidence was retrievable regarding approval of tea tree oil by the US Food and Drug Administration (FDA).

Evidence was insufficient to show the effectiveness of tea tree oil as topical antiseptic. No evidence was retrievable on the cost effectiveness of tea tree oil as topical antiseptic.

Recommendations

Based on the review, tea tree oil is not recommended for routine use as a topical antiseptic in hospitals until further evidence can be obtained from good-quality clinical research.

Methods

Databases searched included: PubMed, Ovid Full Text, Cochrane database of systematic reviews, Cochrane Central Register for Controlled Trials, HTA databases, US Food and Drug Administration (FDA) website, and Google. Additional articles were identified by reviewing the bibliographies of retrieved articles and from documents submitted by a company. Relevant articles were appraised and evidence was graded according to the US/Canadian Preventive Services Task Force.

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INAHTA Briefs

Issue 2009/091

Title **Cytotron**

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Reference Technology Review Report, 022/08.
http://medicaldev.moh.gov.my/uploads/22.Cytotron.pdf

Aim

To assess the effectiveness, safety, and cost effectiveness of the Cytotron or Rotational Field Quantum Magnetic Resonance (RFQMR) device.

Conclusions and results

No evidence was retrieved from the main scientific databases as regards the effectiveness of Cytotron and RFQMR, and only one study was obtained from the website of the device itself. In the nonrandomized, noncontrolled clinical trial, RFQMR was found to be significantly effective in treating osteoarthritis of the knee joint. The noted improvement persisted when evaluated after one month. Caution is warranted when applying the findings from the study to local scenarios. Evidence was insufficient to support the effectiveness of Cytotron, and no evidence was retrieved on its safety, cost effectiveness, or use in cancer treatment.

Recommendations

Cytotron is not recommended for treating chronic conditions such as cancer and degenerative diseases (eg, osteoarthritis) until more scientific evidence is available to support its effectiveness, safety, and cost effectiveness.

Methods

Electronic databases used to search the literature included: PubMed/MEDLINE, Cochrane, INAHTA, Horizon Scanning, other relevant websites, eg, the US FDA website, the Agency for Healthcare Research and Quality, and general search engines. The search strategy used the following terms, alone or in combination: Cytotron, Rotational Field Quantum Magnetic Resonance, RFQMR. No limitations were applied in the search.

Further research/reviews required

Further research is warranted to obtained evidence on the effectiveness, safety, and cost effectiveness of the Cytotron or Rotational Field Quantum Magnetic Resonance device.

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INAHTA Briefs

Issue 2009/092

Title **SureTouch**

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Reference Technology Review Report, 013/08.
http://medicaldev.moh.gov.my/uploads/13.suretouch.pdf

Aim

To assess the effectiveness, safety, and cost effectiveness of SureTouch or palpation/tactile imaging.

Conclusions and results

Very limited quality evidence was available to support the effectiveness and cost effectiveness of palpation/tactile imaging (TI), and none was available regarding its safety. Four cross-sectional studies were retrieved on the technology used by SureTouch, but none on SureTouch per se. The retrievable evidence showed the technology to have reasonable sensitivity, specificity, and positive predictive value (PPV). It could also characterize and differentiate between benign and malignant breast cancer and improve communication among healthcare providers in managing such conditions. The TI modality also showed potential in providing cost-effective breast cancer screening and diagnosis.

Recommendations

Further scientific evidence is required to support the effectiveness, safety, and cost effectiveness of SureTouch and similar technologies. However, it can be recommended as a research tool in the screening of breast cancer.

Methods

The literature search included the following electronic databases: PubMed/MEDLINE, Cochrane, INAHTA, Horizon Scanning, other relevant websites (eg, US FDA website), and general search engines. The search strategy used the following terms, alone or in combination: SureTouch, breast neoplasms [Mesh], cancer, screen, tactile imaging, stress imaging, mechanical imaging, imaging, three-dimensional [Mesh], elasticity imaging techniques [Mesh], visual mapping system, digital sensing device, pre-mammogram instrument, palpation image, digital breast exam, real-time palpation imaging, screening. No limitations were imposed on the search.

Further research/reviews required

Further evidence is needed on the effectiveness, safety, and cost effectiveness of SureTouch or palpation/tactile imaging.

Written by Yusof MAM and Bakri R, MaHTAS, Malaysia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/093

Title **Natural-Health/Pure Swietenia Mahogany Seed**

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Reference Technology Review Report, 024/08.
http://medicaldev.moh.gov.my/uploads/24.mahagony.pdf

Aim

To assess the effectiveness, safety, and cost effectiveness of Natural-Health/Pure Swietenia Mahogany Seed.

Conclusions and results

Evidence was insufficient to support the effectiveness of Natural-Health, Naturo, or Swietenia Mahogany. No evidence was retrieved on its safety and cost effectiveness. An animal study on Swietenia Mahogany obtained from the general database showed that mahogany seed extract had a potentially positive effect on healing gastric ulcers. Swietenia Mahogany falls under dietary supplements and does not need to be registered with FDA nor obtain FDA approval before being produced or sold.

Recommendations

Natural-Health/Pure Swietenia Mahogany Seed is not recommended until further evidence supports its effectiveness, safety, and cost effectiveness in treating any medical problem for which it is intended.

Methods

The literature search included the following electronic databases: PubMed/MEDLINE, Cochrane, INAHTA, other relevant websites (eg, US FDA website), and general search engines. The search strategy used the following terms, alone or in combination: Natural-Health, Naturo, Swietenia Mahogany. No limitations were imposed on the search.

Further research/reviews required

Further evidence is needed on the effectiveness, safety, and cost effectiveness of Natural-Health/Pure Swietenia Mahogany Seed.

Written by Yusof MAM and Bakri R, MaHTAS, Malaysia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/094

Title **Vitamin C, EDTA, and Ultraviolet in Cancer Treatment**

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Reference Technology Review Report, 027/09.
http://medicaldev.moh.gov.my/uploads/27.vit_c.pdf

Aim

To assess the effectiveness, safety, and cost effectiveness of vitamin C, ethylenediaminetetraacetic acid (EDTA), and ultraviolet in treating cancer.

Conclusions and results

Evidence was insufficient to support the effectiveness and safety of vitamin C in treating cancer, and we found no evidence on its cost effectiveness. Our findings were based on 5 studies (1 health technology assessment, 1 large randomized, controlled clinical trial, and 3 small nonrandomized, noncontrolled clinical trials). The possibility to infer findings to vitamin C specifically is limited because the studies used multicomponent interventions. They showed no significant decrease in risk of all-cause mortality, or changes in response rate and overall survival for (combined) vitamin C as a treatment for advanced cancer. In terms of safety, vitamin C was well-tolerated in high doses (oral and intravenous). No evidence was retrieved on the effectiveness, safety, and cost effectiveness of EDTA and ultraviolet in treating cancer.

Recommendations

Vitamin C, EDTA, and ultraviolet are not recommended in cancer treatment until further scientific evidence is available to support their effectiveness, safety, and cost effectiveness.

Methods

We searched electronic databases for scientific literature: PubMed/MEDLINE, Cochrane, INAHTA, and general search engines. The search strategy used the following terms, either alone or in combination: neoplasms [MeSH] AND therapeutics [MeSH]), cancer OR neoplasms; cancer treatment; ascorbic acid [MeSH]; vitamin C; edetic acid [MeSH]; ethylenediaminetetraacetic acid OR EDTA; ultraviolet therapy [Mesh]; ultraviolet treatment. In the PubMed/MEDLINE database, the following limitations applied: humans, clinical trial, meta-analysis, randomized controlled trial, review, and English.

Further research/reviews required

Further evidence is needed on the effectiveness, safety, and cost effectiveness of vitamin C, ethylenediaminetetraacetic acid (EDTA), and ultraviolet in treating cancer.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/095

Title **Intensive Training/Habilitation of Children with Congenital and Acquired Brain Damage**

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Reference Report no. 27-2008. ISBN 978-82-8121-225-1.
www.kunnskapssenteret.no/Publikasjoner/4401.cms

Aim

To determine what the research shows regarding the effectiveness of intensive training/rehabilitation in children with brain damage.

Conclusions and results

We summarized results from 7 systematic reviews and 20 separate studies. According to the summary, Constraint Induced (Movement) Therapy (CIMT/CI) may be better than usual treatment at improving upper-limb function in children with spastic unilateral cerebral palsy (CP). There is uncertainty related to this result. Early intervention in infants at risk for brain damage, or with acquired brain damage, may also improve motor and cognitive development better than usual treatment. The quality of the evidence ranged from moderate to low according to GRADE. Since heterogeneity, sparse data, and methodological flaws characterize the rest of the included reviews and studies, our evidence does not show whether other intensive training interventions are better than usual training. Meta-analysis was not possible due to heterogeneity in population, interventions, and outcome measurements.

We did not find evidence (that met our inclusion criteria) on programs such as Advanced Bio-Mechanical Rehabilitation, Doman, Family Hope, and the Kozijavkin method. Only evidence of CIMT/CI and early intervention showed possible promising effects.

Methods

We systematically searched for systematic reviews, randomized controlled trials, and controlled before-and-after studies in the Cochrane Database of Systemic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE Cochrane), Health Technology Assessment Database (HTA), MEDLINE, EMBASE, Pedro, Cochrane Central, CINAHL, ERIC, PsycINFO, and Swemed. Two people independently selected studies that fulfilled the inclusion criteria.

We critically appraised relevant articles that met our inclusion criteria (below) for quality of method, and described the included reviews and studies in text and tables. As the participants, interventions, and outcome measures were too heterogeneous to assimilate in a meta-analysis, we summarized the results descriptively.

Inclusion criteria for the report were:

Population: Children and young people aged 0 through 18 years with acquired and congenital brain damage.

Intervention: Systematic and focused training and habilitation with a minimum range of 3 times/week up to several times/day for 1 or more periods. Focused interventions that contribute to the child's development of movements' functions and social, mental, and communication skills.

Child-related outcome: Quality of life, language/communication, ability to care for themselves, ability to move around, social, cognitive, and, executive functioning, motor abilities, ADL, and general health.

Family-related outcomes: Quality of life, sense of coherence, parent competence, satisfaction with services, compliance, parents' physical and mental health, economy, stress, and optimism.

Further research/reviews required

Fully achieving the aim requires further and rigorous research.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/096

Interventions to Improve Easy Access of Hormonal Contraceptives to Women – Aged 20 to 24 Years

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Reference Report no. 12-2008. 978-82-8121-204-6.
www.nokc.no/Publikasjoner/2470.cms

Aim

To assess interventions intended to improve easy access to hormonal contraceptives among women aged 20 to 24 years.

Conclusion and results

We summarized the results from one Cochrane review only. The methodological quality of the review was high, but the quality of the documentation varied according to GRADE. This review found that advanced provision of emergency contraception to young women did not decrease pregnancy rates, nor did it have a negative impact on sexually and reproductive health behaviors exceeding that found in the control group (who received information only about emergency contraception).

We identified only one systematic review. This Cochrane review answered the last question that we addressed. Even though we conducted a comprehensive search for literature in relevant databases we did not identify additional relevant studies or reviews.

Methods

We searched for relevant systematic reviews, randomized controlled trials, and controlled trials in international databases, and we appraised and synthesized studies that met our inclusion criteria.

Further research/reviews required

Further controlled trials are needed to answer the questions addressed.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/097

Title **Knee Arthroscopy, Development of Criteria for Appropriateness**

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Reference ISBN 978-8496990-23-4.
www.juntadeandalucia.es/salud/servicios/contenidos/aetsa/pdf/Artroscopia_final.pdf

Aim

To develop standards on the appropriateness of knee arthroscopy in patients with acute, chronic problems, joint-related diseases, or in the core of knee systemic diseases.

Conclusions and results

The following objectives were pursued in developing the appropriateness standards:

- To assess the efficacy of knee arthroscopy in patients with acute, chronic problems, joint-related diseases, or in the core of knee systemic diseases.
- To select relevant clinical variables when indicating and performing knee arthroscopy.
- To extract clinical conditions that had been excluded from the clinical trials and have appropriateness agreement in the experts' panel.

The first round of voting, following the scoring definitions proposed by RAND, resulted in: 229 indications (29.8%) were considered appropriate, 387 (50.4%) uncertain, and 152 (19.8%) inappropriate. The observed disagreement score was moderate: 122 (15.9%) indications were scored as disagreement, 174 (22.7%) as agreement, and 472 (61.4%) as indeterminate.

In the second round of voting: 393 (51.2%) indications were considered appropriate, 196 (25.5%) uncertain, and 179 (23.3%) inappropriate. The disagreement score was visibly lower than in the first round: 0 (0%) indications were scored as disagreement, 348 (45.3%) as indeterminate, and 420 (54.7%) as agreement.

Standards on the appropriateness of knee arthroscopy, which may be applied to patients with different knee pathologies, were realized. The standards can used to form clinical practice guidelines (CPG) to improve appropriate use, decrease variability, and improve healthcare quality. They can be used retrospectively (by matching the standards with clinical records) to determine the percent of procedures performed for appropriate reasons, or not. This can help avoid procedures for inappropriate indications and promote those for appropriate reasons. Also, the appropriateness standards can help in decision-making and considering patients' preferences.

Methods

The RAND/UCLA method, which combines scientific evidence with the best opinions of experts, was followed. For each clinical indication, the expert gives his/her opinion on the appropriateness of a procedure in a quantitative way. An indication is considered to be appropriate when the benefits to patients sufficiently outweigh the possible risks or negative consequences. An indication is classified as inappropriate when the risks outweigh the benefits.

A bibliographic review was conducted, and a checklist of 768 indications was composed. A panel (11 orthopedic and traumatology surgeons with different specialization in arthroscopic surgery) scored the appropriateness grade for every indication from 1 (very inappropriate) to 9 (very appropriate). The indications were scored twice: anonymously in the round one, and during a meeting in round two. Based on the median of the panels' scores and their agreement score, each indication was classified as appropriate, uncertain, or inappropriate for knee arthroscopy.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/098

Title **Perfusion MR Imaging in Differentiating Brain Gliomas; Meta-Analysis and Economic Assessment**

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Reference ISBN 978-84-96990-25-8. www.juntadeandalucia.es/salud/servicios/contenidos/aetsa/pdf/AETSA_2006-12_RMPerfusion.pdf

Aim

To estimate the following parameters for perfusion MR imaging (pMRi): sensitivity, specificity, positive probability rate, and negative probability ratio. To estimate cost-effectiveness ratios for perfusion MR imaging.

Conclusions and results

We retrieved 15 studies that compared the results from pMRi with those of histology (reference test). Main threats to internal validity in most studies included small sample sizes and the lack of knowledge about the time elapsed between testing, the experience of pathologists and radiologists, and handling of difficult-to-assess results. We found no important threats to external validity.

Results concerning the estimated parameters were:

- Sensitivity: 0.958.
- Specificity: 0.806.
- Positive probability ratio: 3.923.
- Negative probability ratio: 0.086.

Sensitivity analysis did not change the results. Cost-effectiveness analysis of the strategies, using life-years as effectiveness, yielded an average cost per patient that was 147.36 higher with pMRi. The incremental cost-effectiveness ratio (ICER) of pMRi compared to biopsy is 788.22 per life year.

PMRi can provide good results in differentiating the malignancy grade of brain gliomas. Further, and better, research is needed to provide scientific evidence of the role that pMRi should play in differentiating the malignancy grade of brain gliomas. Using the incidence estimated for the Spanish population (3.5 per 100 000 pop.) and the sensitivity and specificity parameters of the test, the use of pMRi would mean diagnosing 51 patients with a grade lower than what they actually have. However, the use of biopsy would yield an additional 14 cases of complications and 20 cases of death.

The average cost per patient of pMRi was 147.36 higher than in biopsy, albeit effectiveness measured in life years was also higher with pMRi (0.19 years). Cost-effectiveness analysis yielded 776 as a result of cost per life-year ratio (ICER) for pMRi compared to biopsy. Likewise, the results are sensitive due to probability of death caused by biopsy. The reason lies in the fact that when the biopsy is lower than 0.005, then pMRi becomes a dominant alternative.

The use of pMRi would entail an additional annual cost of approximately 444 000 euros.

Until better scientific evidence is obtained, pMRi can serve as an additional test in cases where previous diagnostic testing has not clarified the grade of glioma malignancy.

Methods

We systematically reviewed the literature, searching reference databases, agencies on health technology assessment, scientific societies, scientific journals, and ongoing research registries. Studies were selected based on the inclusion criteria, scoring their quality by QUADAS and statistically treating the data extracted by means of quantitative meta-analysis.

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INAHTA Briefs

Issue 2009/099

Economic Assessment of Mitral Valve Insufficiency Treatment

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Reference ISBN 978-84-96990-24-1. www.juntadeandalucia.es/salud/servicios/contenidos/aetsa/pdf/AETSA_2006-31_Insuf_valv_mitral.pdf

Aim

To compare the cost-effectiveness ratios of surgical strategies for mitral valve insufficiency from the health system perspective.

Conclusions and results

The chargeable costs for surgeries were 27 020 and 34 297 euros (EUR) for repair and replacement, respectively. Life expectancy was 14.486 years for repair and 11.766 years for replacement. The cost-effectiveness analysis of surgeries used to treat mitral valve insufficiency showed that the dominant alternative was intervention through repair, since it costs less and is more effective than replacement.

Methods

A Markov model was used to analyze cost-effectiveness. The health conditions considered were life and death, and life expectancy was used as the effectiveness measure in the cost-effectiveness analysis. The costs associated with surgeries and effectiveness were extracted from the literature.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/100

Title **Diagnostic Accuracy of Infrared Tympanic, Oral, Axillary and Temporal Thermometry, Compared with Rectal Readings when Identifying Fever in Adult Hospitalized Patients**

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Reference Report no. 19 – 2009. ISBN 978-82-8121-284-8.
www.kunnskapssenteret.no/Publikasjoner/6875.cms

Aim

To summarize documentation on the diagnostic accuracy of infrared tympanic, oral, axillary, and temporal thermometry compared to rectal readings.

Conclusions and results

Correct and observer-independent use of infrared tympanic thermometry can be challenging in a clinical setting. Comparing temperature measurements of different body sites might also be problematic because the measurements at different sites are all estimates for what we wish to know, the core temperature. Although this review considered rectal measurement to be the reference standard, we acknowledge that this is imperfect in many ways.

Our review shows that few studies have assessed the accordance between infrared tympanic and rectal thermometry in detecting and excluding fever. We found 8 small studies that compared different types of infrared tympanic thermometers to rectal measurement. These studies generally showed that infrared tympanic thermometry had low sensitivity, but high specificity in detecting and excluding rectal fever compared with rectal measurements. Since these results were based on few patients with elevated temperature, the sensitivity values are uncertain, as expressed by wide confidence intervals. Different cut-off values for defining fever in these studies also contributed to uncertainty about sensitivity and specificity.

We found no documentation on the diagnostic accuracy of temporal thermometry, and very few studies that compared oral and axillary thermometry with rectal thermometry.

Methods

We performed systematic literature searches in several health-related databases (per October 1, 2008). We included clinical, prospective, cross-sectional studies and used rectal thermometry (mercury or digital) as the reference test. Only studies conducted in emergency wards, general hospital wards, or nursing homes were included.

Further research/reviews required

Given the widespread use of infrared tympanic thermometer, further documentation is needed concerning the diagnostic accuracy and repeatability of newer models used in clinical settings.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/101

Title **Dual Diagnoses – Severe Mental Illness and Substance Use Disorder. Part 2 – Effect of Psychosocial Interventions**

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Reference Report no. 25 – 2008. ISBN 978-82-8121-222-0. ISSN 1890-1298.
www.kunnskapssenteret.no/Publikasjoner/4201.cms?threepage=1

Aim

To summarize the effects of psychosocial interventions in people with dual diagnoses (concurrent severe mental illness and substance use disorder).

Conclusions and results

The psychosocial interventions in question were: integrated treatment, case management, assertive community treatment, cognitive behavioral therapy (CBT), motivational interviewing, family therapy, social skills training, self-help groups, housing care, and vocational rehabilitation. Reported outcomes were substance use, mental state, functioning, and quality of life. The report summarized the effects of the interventions compared to other psychosocial interventions or usual treatment.

We included two systematic reviews, neither of which reported compelling evidence to demonstrate the superiority of one type of psychosocial intervention over another. However, there was some indication of motivational interviewing having a positive effect on alcohol consumption. There were also indications of motivational interviewing combined with cognitive behavioral therapy having a positive effect on social functioning and quality of life. It was not possible to draw conclusions on the effects of the other psychosocial interventions.

Methods

The results in this report are based on systematic reviews (overview of overviews). We searched the following databases in January 2008: Cochrane Database of Systematic Reviews, MEDLINE, EMBASE, PsycINFO, Database of Abstracts of Reviews of Effect (DARE), Health Technology Assessment Database (HTA), and SveMed.

Further research/reviews required

Further research is needed to enhance knowledge in this field. Both of the included systematic reviews pointed to the lack of reliable research.

Written by Kirkehei I, NOKC, Norway

ISSN 1654-501X

INAHTA Briefs

Issue 2009/102

Title **Hadrontherapy in the Treatment of Cancer**

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Reference ISBN 978-84-393-8073-3.
www.gencat.cat/salut/depsan/units/aatrm/pdf/hadronterapia_07-aatrm.pdf

Aim

To review published reviews of hadron (proton and light ion) therapy indications and its clinical efficacy.

Conclusions and results

Of the 370 publications identified, 12 were included (9 general reviews on cancer and 3 reviews on a specific cancer). Most of the studies included in the reviews analyzed the efficacy of proton therapy rather than ion therapy, and most of these studies were retrospective case series.

Clinical results suggested that the best dose distribution characterizing proton therapy could be translated into clinical benefits for uveal melanoma, skull base chordomas, and chondrosarcomas.

Better results than conventional radiotherapy have been also suggested in several prospective case series and a nonrandomized clinical trial of patients with adenoid cystic carcinoma treated with ion radiotherapy.

Firm conclusions about the efficacy of hadron therapy cannot be drawn because of significant methodological gaps in the evidence. The clinical performance of hadron therapy should be appropriately assessed. In the meantime, available data suggest than in some low-frequency tumors the benefits of hadron therapy could be significant.

Methods

We conducted a systematic review of review reports. Most of the important databases were systematically searched. Reviews on clinical results of hadron therapy for oncological patients were included.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/103

Title **Amotosalen (Intercept®) for the Inactivation of Pathogens for Transfusion Therapy**

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Reference 2009 June. www.gencat.cat/salut/depsan/units/aatrm/pdf/in_amotosalen_intercept_aatrm_2009ca.pdf

Aim

To analyze scientific evidence related to the efficacy, effectiveness, and safety of amotosalen plus ultraviolet light for the inactivation of pathogens in plasma and platelets for transfusion therapy.

Conclusions and results

Three randomized clinical trials (RCT) were selected for platelets, two RCTs and a quasiexperimental study for plasma, and three hemosurveillance studies. Generally, the quality of methodology in the clinical trials of amotosalen was considered good. The RCTs showed no statistically significant differences with respect to post-transfusion platelet recovery on transfusion of similar amounts of platelets in the intervention and control groups. Moreover, it was demonstrated that treatment with amotosalen plus ultraviolet light did not alter platelet hemostatic capacity. Regarding plasma, studies on patients with acquired coagulopathy, congenital coagulopathy, or thrombotic thrombocytopenia purpura did not show statistically significant differences between the intervention and control groups. Treatment-related adverse effects, serious adverse effects, and the deaths observed during treatment were also similar in both groups.

In Spain, plasma inactivated with methylene blood is used in approximately 61% of autonomous communities, whereas fresh frozen plasma subjected to quarantine is used in the rest of autonomous communities. Only the Red Cross Hospital in Madrid uses amotosalen in plasma. Regarding platelets, no pathogen inactivation technique is used in 77% of autonomous communities and the remaining 33% use amotosalen as a pathogen inactivation technique. The use of platelets inactivated with amotosalen would represent an estimated cost increase of 3 359 808.8 euros for 2009 as compared to 2008.

The systematic review showed that amotosalen is effective and safe for pathogen inactivation in plasma and platelets for use in transfusion. In addition, the results from active hemosurveillance subsequent to its commercialization showed good patient (adult and pediatric) tolerance in 14 493 transfusions of platelet concentrations treated with amotosalen.

Methods

Scientific evidence available up to April 2009 was systematically reviewed using the main biomedical databases. Randomized clinical trials were selected. Two reviewers assessed the quality of the methodology, the classification of the evidence, and the degree of recommendation of the studies based on the Scottish Intercollegiate Guidelines Network (SIGN) criteria, and then they synthesized the scientific evidence. To ascertain the current situation of pathogen inactivation in plasma and platelets in Spain, one transfusion center in each autonomous community was contacted to request information. Finally, the impact on the budget of the hypothetical use of amotosalen in platelets was analyzed.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/104

Title **Effectiveness of Two Therapeutic Options in the Treatment of Peripheral Vascular Disease: Sympathectomy and Spinal Cord Stimulation**

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Reference Report no. 6/2008. ISBN 978-84-691-7792-1. www.juntadeandalucia.es/salud/servicios/contenidos/aetsa/pdf/AETSA_2008_6_Simpatectomia.pdf

Aim

To check scientific evidence on the effectiveness of lumbar sympathectomy and spinal cord stimulation in treating peripheral vascular disease of the lower extremities.

Conclusions and results

We found 103 references, including 8 articles on lumbar sympathectomy and 1 on medullar stimulation. Their quality was generally low.

In comparing lumbar sympathectomy and usual treatments we found no differences in mortality, amputations, and seriousness of on-off backing down in II Fontaine stage patients. Patients at more advanced stages of the disease showed greater clinical improvement with lumbar sympathectomy, but the low quality of the studies calls for caution in applying these results. In comparing sympathectomy to E1 prostaglandin, again we found no differences. Comparing surgical and chemical sympathectomy, the chemical alternative showed better results in terms of mortality and hospital stay.

Medullar stimulation showed better results in treated patients compared to patients receiving conventional care (RR 0.74, IC 0.57-0.94). More patients reached Fontaine stage II; the effect size was 33% in terms 10 > of differences of proportions. The most frequent complications were re-interventions (12%), initial problems of implantation (8%), and infections (3%).

Evidence on efficacy of lumbar sympathectomy, based on clinical trials and observational studies of low quality, shows no differences between the two techniques and usual care in stage-II patients. Sympathectomy shows some advantages in patients at stages III and IV. Chemical sympathectomy yielded better results than the surgical option in terms of mortality and amputations, but the results are not statistically significant. Compared to conventional treatment, electrical medullar stimulation reduces the risk of amputations, improves the clinical state of patients, and relieves pain.

Methods

In systematically reviewing the literature (1996-2007), we focused our initial search strategy on systematic reviews and found 1 on spinal cord electrical stimulation that included references from 2005. We updated this review, adding references from the past 2 years.

The final systematic search was run by inserting MeSH terms, sympathectomy and spinal cord stimulation, in the following databases: MEDLINE, EMBASE, Cochrane Library, INAHTA, CRD, and other resources on Internet, eg, ECRI and Biomed Central.

Inclusion criteria: Adult patients with chronic non-revascularizable ischemia of lower extremities.

Outcomes: Recovery or preservation of extremities, clinical improvement, treatment of ulcers, complications, use of analgesics, hospital stay, mortality, and quality of life. Quality was assessed with CASPe criteria for clinical trials and an ad hoc questionnaire for observational studies.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/105

Title **Outcomes of Transanal Endoscopic Surgery in Patients With Rectal Tumors**

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Reference Report no. 19/2006. ISBN 978-84-96990-06-07. www.juntadeandalucia.es/salud/servicios/contenidos/aetsa/pdf/AETSA_2006-19_CirugTransanal1.pdf

Aim

To compare the benefits and complications of transanal endoscopic microsurgery (TEM) with radical surgery and other local resection procedures in patients with early-stage rectal adenoma and cancer.

Conclusions and results

Two of the original 3 papers with a control group were retrieved from the previous, good-quality systematic review. These two included a clinical trial and a cohort study, both of poor quality. A new search identified 74 articles from which we selected four: 1 medium quality, controlled clinical trial and 3 cohort studies with limitations in internal validity. In most of the new papers comparing TEM versus local surgical techniques (3 studies), the only endpoints considered were postoperative complications and incomplete tumor resection. Both of these events were less frequently reported in TEM patients. We found 3 new studies that compared TEM and radical surgical techniques and added these to the 2 papers from the previous review. The 5 studies show that most endpoints have better outcomes in TEM patients, both as regards technical endpoints and survival. The studies, however, reveal discrepancies in recurrence rates. All results should be interpreted with caution since the studies present major flaws in internal validity. In particular, 87% of patients undergoing radical surgery had rectal cancer, compared to only 50% of the TEM patients. Also, no adjustments were made for possible confounding factors in the comparative analysis of the groups. Assessment of functional outcomes with the different techniques was only vaguely addressed.

The quality of evidence on the efficacy of TEM in comparison to other surgical options does not currently enable recommendations to be issued for more widespread use of the technique.

Methods

The literature was systematically reviewed to update a previous review of articles published up to August 2002.

The search strategy was validated and updated to July 2006, running searches on MEDLINE, PreMEDLINE, and EMBASE. The Cochrane Library, INAHTA, and the Internet were also searched.

Inclusion criteria for the articles were as follows: study design (RCTs and controlled observational studies), population characteristics (patients over 18 years of age with rectal tumors – early-stage adenomas and carcinomas), procedures for comparison (TEM vs radical surgery and other local resection procedures), and outcomes (at least one of the following: duration of surgery, blood loss, analgesia use, hospital stay, rate of conversion to radical surgery, complications, mortality, recurrence, survival, anus-rectal dysfunction, and presence of residual tumor). Studies were critically appraised by using the CASPe scale for systematic reviews and clinical trials, together with a list of criteria devised ad hoc for cohort studies. A qualitative summary of the results is provided.

Written by Silvia Vallejo Godoy and Soledad Márquez Calderón, AETSA, Spain

ISSN 1654-501X

INAHTA Briefs

Issue 2009/106

Title **The Effectiveness of Interventions to Increase the Delivery of Effective Smoking Cessation Treatments in Primary Care Settings – the ABCs**

Agency **HSAC, Health Services Assessment Collaboration**
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Reference HSAC Report 2009; 2(9). Brinson, D and Ali, W. ISBN 978-0-9864551-1-7 (online), ISBN 978-0-9864551-2-4 (print). ISSN 1178-5748 (online), ISSN 1178-573X (print)

Aim

To summarize the evidence on the effectiveness of interventions to increase the likelihood of healthcare professionals initiating elements of the ABC approach for smoking cessation in primary care settings.

Conclusions and results

The ABC approach refers to interventions that increase the documentation of smoking status (Ask), provide brief advice to stop smoking (Brief advice), and offer/provide or make referrals to smoking cessation treatments or services (Cessation support), as compared to usual care.

The evidence base identified in this review provides good evidence on the effectiveness of a range of interventions aimed at increasing the likelihood of healthcare professionals initiating elements of the ABC approach in primary care settings (the review does not consider patient-level outcomes, ie, quit rates). The inherent assumption is that if people receive brief advice and support to quit, some will do so. Healthcare professionals were studied as individuals, in groups, or within an entire clinic or practice. Effective interventions included, training, multicomponent interventions, reminders, financial incentives, and audit and feedback. Sharing the responsibility for office-based smoking cessation activities among all staff appears to be a promising strategy.

Methods

A systematic method of literature searching and selection was employed in preparing this review. Our literature search used the following bibliographic databases: MEDLINE and EMBASE and, where applicable, the Cochrane Database of Systematic Reviews (CDSR), the Database of Abstracts of Reviews of Effects (DARE), and other sources. Searches were limited to English language material published from 1990 onward. The searches were completed on November 24, 2008. We identified 464 citations, and after consideration of titles and abstracts using the study selection criteria, 130 full papers were retrieved and scrutinized in detail for possible inclusion in the review. As a result, 42 publications (including 5 review articles) were eligible for inclusion and were critically appraised.

Further research/reviews required

Further studies using well-operationalized baseline and outcome variables are needed to evaluate which combinations of intervention components are more or less effective, and what relative contributions individual components might make to programs implemented in New Zealand primary care settings.

Written by David Brinson, HSAC, New Zealand

ISSN 1654-501X

INAHTA Briefs

Issue 2009/107

Title **Treatment of Infantile Colic**

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Reference Report no. 14–2009. ISBN 978-82-8121-276-3.
www.kunnskapssenteret.no/Publikasjoner/6526.cms

Aim

To determine the effects of treatments for infantile colic.

Conclusions and results

We summarized the results from 4 systematic reviews and found that the following interventions might somewhat reduce the duration of crying:

- Advise parents to reduce stimulation of the child
- Cows' milk free formula to child

Use of sucrose may have an ameliorating effect on infant colic. The included overviews convey substantial uncertainty about the effects of the other evaluated options.

Our review shows four promising interventions that might reduce the duration of infant crying, eg, reducing stimulation of the child and use of sucrose and cows' milk free formula to child. These results must be interpreted with caution due to substantial methodological concerns regarding the individual studies included in the reviews.

Methods

We systematically searched for literature in relevant international databases, included articles that met our inclusion criteria, and critically appraised and summarized the results.

Further research/reviews required

Further, rigorous research is necessary to determine the effects of treatments for infantile colic.

Written by Hilde T Myrhaug, NOKC, Norway

ISSN 1654-501X

INAHTA Briefs

Issue 2009/108

Title **Interventions for Promoting Development in Children Born Preterm**

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Reference Report no. 07 - 2006. ISBN 82-8121-089-3. ISSN 1890-1298. Reinar LM, Kornør H, Langengen IW, Markestad T. www.kunnskapssenteret.no/Publikasjoner/1029.cms

Aim

To determine the effects of: early interventions and other treatments for children born preterm; interventions to prevent impairments; and interventions aimed at parents of preterm children.

Conclusions and results

We included 6 systematic reviews. *Developmental* care in special care bay units might improve nutrition in the short term for children born preterm. Children receiving developmental care (ie, NIDCAP – Newborn Individualized Care and Assessment Program) had less need for respiratory help and had a slightly shorter hospital stay. These children also showed better neurodevelopment results at 12 and 24 months of age. Other results showed that children at risk of developing impairments might have positive effects from interventions related to their age. Specific and general development programs had positive effects on physical development. Preterm children or children with low birth weight gained from early intervention for physical development. *The Kangaroo method* was safe and had some positive effects on nutrition in children born preterm. Due to the lack of reliable research, no conclusions can be drawn on the effects of massage in preterm children.

Methods

The results presented in this report are based on systematic reviews (overview of overviews). We searched the following databases in September 2005: Cochrane Library (Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effect (DARE), Health Technology Assessment Database (HTA), EMBASE, MEDLINE, CINAHL, PsycINFO, and Eric.

Further research/reviews required

All included systematic reviews pointed to the lack of relevant and reliable research in this area.

Written by Reinar, Liv M, NOKC, Norway

ISSN 1654-501X

INAHTA Briefs

Issue 2009/109

Title **Percutaneous Heart Valve Implantation in Congenital and Degenerative Valve Disease. A Rapid Health Technology Assessment**

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Reference Report no. 95 (C), 2008

Aim

To summarize evidence supporting the use of percutaneous heart valves in (1) degenerative aortic valve and (2) congenital pulmonary outflow tract disease, as compared to conservative medical therapy or traditional surgical valve replacement.

Conclusions and results

(1) The position of percutaneous aortic valve (PAV) insertion within the management spectrum of aortic valve stenosis is unknown. Results from randomized controlled trials (RCT) are not available, and clinical data can only be deduced from observational studies. Issues on safety and clinical effectiveness involving the use of PAV remain unanswered. The ongoing US-based PARTNER-IDE RCT is expected to clarify if inoperable patients are better off with PAV than with medical treatment, and if patients at high risk for surgery have a lower risk with PAV than with conventional aortic valve replacement.

(2) Conservative (ie, medical) treatment is not an option in patients with a degenerated pulmonary homograft conduit, although optimal timing for correction is unknown. The feasibility and safety of percutaneous pulmonary valve (PPV) insertion is excellent, at least in the hands of one operator. Short-term hemodynamic and clinical performance is good. Long-term durability of the valve is not known. Long-term effectiveness in postponing future surgery is unknown. Unfortunately, no RCTs are planned to resolve these questions.

Recommendations

(1) Reimbursement of PAV cannot be defended because of patient safety concerns and a poorly defined target population. The decision whether to reimburse PAV technology is to be reconsidered when the results of the ongoing PARTNER IDE RCT become available. If this RCT provides evidence on safety and effectiveness of the PAV, its acceptability (cost effectiveness) and affordability (budget impact) need to be assessed.

(2) For PPV, conditional reimbursement is proposed because of uncertainties about clinical effectiveness. Because of the skills needed to perform this procedure, and the limited number of eligible patients, a maximum concentration of this service (ie, restricted to 1 center) is desirable. With conditional reimbursement, every case should be well documented in a registry. An annual re-evaluation should be done to assess procedure-related mortality and long-term effectiveness of the device.

Methods

Standard HTA report, eventually resulting in the finding that current evidence is based on published and unpublished case series only.

Further research/reviews required

(1) For PAV: await the results of the ongoing PARTNER-IDE RCT.

(2) For PPV: an RCT devoted to long-term effectiveness would require a follow-up of many decades and is therefore unrealistic. Existing and new case series should be closely followed.

Written by Hans Van Brabandt, KCE, Belgium

ISSN 1654-501X

INAHTA Briefs

Issue 2009/110

Title **Effect of Smoking Habits on Treatment Outcome**

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Reference Report no. 29 – 2008. ISBN 978-82-8121-228-2.
www.kunnskapssenteret.no/binary?download=true&id=8887

Aim

To evaluate smoking status against the outcome following scaling and root planing (SRP), or surgical flap procedures in patients diagnosed with periodontitis.

Conclusions and results

Established periodontitis can be treated by the dentist and usually includes scaling and root planing, surgical flap procedures, gingivectomy, antibiotics, or combinations of these procedures. Compared to non-smokers, smokers probably show a poorer prognosis following periodontal treatment. Treatment efficacy among ex-smokers and never-smokers seems to be comparable, but the conclusions are impaired by methodical weaknesses in the studies.

We identified 38 relevant research papers. Tooth loss among patients undergoing periodontal therapy was reported in one of the studies and showed a statistically insignificant trend toward increased risk of tooth loss in the smoker group (Odds Ratio 2.27; 95% Confidence Interval 0.86 to 5.94).

The mean difference (MD) effect estimate and 95% confidence interval (CI) indicated that non-smokers may show better effects from periodontal therapy than smokers do in terms of pocket depths (MD 0.33; 95% CI 0.22 to 0.43 mm) and clinical attachment levels (MD 0.30; 95% CI 0.19 to 0.41 mm). The greatest difference in treatment efficacy between smokers and non-smokers was evident when pretherapeutic pocket depths were large (> 7 mm) Pocket depth: (MD 0.87; 95% CI 0.49 to 1.24 mm). Attachment level: (MD 0.75; 95% CI 0.33 to 1.18 mm).

Methods

A systematic search for relevant literature included: MEDLINE, EMBASE, SveMed, and Cochrane Library. We used predefined inclusion and exclusion criteria to establish the relevance of the identified literature. Results from relevant research articles were summarized in tables and described in the text, and in meta-analysis where appropriate.

Further research/reviews required

Randomization to smoking habits is not possible, and large, high-quality observational studies using standardized treatment and measurement procedures and dose-response correlation analysis could increase the level of evidence.

Written by Kjetil G Brurberg, NOKC, Norway

ISSN 1654-501X

INAHTA Briefs

Issue 2009/111

Title **Treatment of Infants Suspected with KISS (Kinematic Imbalance Due to Suboccipital Strain)**

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Reference Report no. 17 – 2009. ISBN 978-82-8121-279-4

Aim

To assess the effects of treatment techniques for infants with suspected kinematic imbalance due to suboccipital strain (KISS).

Conclusions and results

Several academic disciplines (eg, manual therapist, chiropractors, and osteopaths) offer treatment for infants with suspected KISS. Treatment options include spinal manipulation of the upper neck joints and exercises for relaxation and mobilization.

We identified one randomized controlled trial showing that osteopathy can potentially reduce the degree of postural asymmetry in infants, but the study did not reveal any changes in vegetative parameters following treatment. It must be emphasized that these conclusions are based solely on one small study, suggesting that the strength of the evidence is too low to draw reliable conclusions about treatment effects.

We found no evidence suggesting that manual therapeutic, osteopathic, or chiropractic treatment strategies in infants are associated with risks for injuries or harmful side effects, but the level of evidence is very low. Hence, it is impossible to draw conclusions about treatment effects and potential adverse effects.

Methods

Several databases, including The Cochrane Library, MEDLINE, EMBASE, PEDro, and AMED, were systematically searched for trials evaluating the effectiveness of manipulation or mobilization techniques in infants suspected of having KISS. Databases were also searched for evidence on adverse effects.

Further research/reviews required

Randomized controlled trials on short- and long-term treatment effects are needed with respect on asymmetry and vegetative outcomes (eg, excitability, excessive crying, and eating and sleeping disorders). Large observational studies may add valuable information about adverse effects.

Written by Kjetil G Brurberg, NOKC, Norway

ISSN 1654-501X

INAHTA Briefs

Issue 2009/112

Title **Exercise Testing for the Prediction of Cardiac Events in Patients with Diabetes**

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Reference May 2009 (English). ISBN 978-1-897443-56-9 (print), ISSN 978-1-897443-57-6.
www.ihe.ca/documents/Exercise_Testing_Diabetes.pdf

Aim

To evaluate the safety and prognostic value of exercise testing in predicting cardiac events in patients with diabetes, chronic obstructive pulmonary disease (COPD), or arthritis compared to physician judgment based on medical history and physical examination alone.

Conclusions and results

No eligible systematic reviews or primary studies evaluated exercise testing in patients with COPD or arthritis. Five prognostic studies examined the association between prognostic variables derived from exercise electrocardiogram (ECG) or cardiopulmonary exercise testing and the number of cardiac events in patients with diabetes over a 3- to 16-year period. Although most patients in these studies did not have cardiovascular disease, the patient groups were heterogeneous in terms of co-morbidities and the type, duration, and presence of secondary complications of diabetes.

None of the 5 studies reported any adverse events during or immediately after exercise testing. The prognostic value of variables measured during an exercise ECG (4 studies) and a cardiopulmonary exercise test (1 study) were examined in relation to cardiovascular mortality and nonfatal cardiac events. None of the studies considered physician judgment as a prognostic variable. All studies included body mass index, blood pressure, and resting heart rate as covariates.

The studies demonstrated that ECG ST-segment depression, a low Duke Treadmill Score, delayed heart rate recovery, impaired chronotropic response, reduced metabolic rate, and low peak oxygen uptake were independent predictors of cardiovascular mortality and non-fatal cardiac events. However, the prognostic value of these variables might be overestimated. No conclusions could be drawn on the prognostic value of exercise testing in patients with COPD or arthritis.

Recommendations

Exercise is key in clinical management of diabetes, but patients with diabetes often have asymptomatic myocardial ischemia. Hence, sedentary patients with diabetes may be at risk of future cardiac events if their exercise program is more vigorous than brisk walking. Exercise testing might provide information useful in predicting the risk of cardiac events during or immediately after exercise in patients with diabetes who plan to enter a structured, community-based exercise program. However, evidence is lacking as regards the incremental prognostic value of exercise testing compared to physician judgment.

Methods

All relevant primary studies and systematic reviews of prospective cohort studies published from 1997 to 2009 were identified by systematically searching *The Cochrane Library*; the Centre for Reviews and Dissemination databases (NHS EED, HTA, DARE), MEDLINE, EMBASE, the Web of Science, PEDro, SPORTDiscus, and websites of health technology assessment agencies, research registers, evidence-based resources, and practice guideline clearinghouses. Reference lists of retrieved articles were also searched. No language restrictions were applied.

Two reviewers, using a 10-item checklist, independently assessed methodological quality of the studies. Scoring disagreements were resolved by consensus. Data were synthesized qualitatively.

Further research/reviews required

A cohort study is needed to determine whether exercise testing provides additional information about the risk of exercise-related cardiac events in patients with chronic diseases compared to physician judgment based on medical history and physical examination alone.

Written by Bing Guo and Christa Harstall, IHE, Canada

ISSN 1654-501X

INAHTA Briefs

Issue 2009/113

Title **Age-Related Macular Degeneration: The Role of Current Treatment Strategies**

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Reference ISBN 978-84-393-8075-7.
www.gencat.cat/salut/depsan/units/aatrm/pdf/degeneracion_macular_edad-aatrm09.pdf

Aim

To analyze the available scientific evidence regarding the effectiveness and safety of photodynamic therapy, pegaptanib, and ranibizumab in treating neovascular type age-related macular degeneration (AMD).

Conclusions and results

One systematic review of photodynamic therapy, two randomized controlled trials of pegaptanib (VISION study) and three of ranibizumab (MARINA, ANCHOR, FOCUS), which met the inclusion criteria, were selected. All were of high quality, except for the VISION study, which was rated as having moderate quality.

Patients treated with these drugs *lost less vision* compared to their corresponding control group at 12 months ($p < 0.05$). The benefit was 11% with photodynamic therapy and 15% with 0.3 mg pegaptanib. For the 0.5 mg ranibizumab dose, between 22% and 32% of the patients benefited from ranibizumab or ranibizumab plus photodynamic therapy, compared to placebo or placebo plus photodynamic therapy. The benefit of ranibizumab was maintained at 24 months, and 37% of the patients did not suffer a loss of *less than 15 letters* compared to placebo. Moreover, patients treated with pegaptanib and ranibizumab *improved visual acuity* compared to the control group (4% with 0.3 mg pegaptanib and 18%-35% with 0.5 mg ranibizumab; $p < 0.05$). Adverse effects were generally transient and rated from mild to moderate. The meta-analysis could not be performed due to differences observed between the studies.

To prevent visual loss in patients with neovascular AMD, ranibizumab is effective and safe compared to placebo for up to 2 years of treatment (*Degree A of recommendation*) and compared to photodynamic therapy up to 1 year (*Degree B)*. Also, pegaptanib may be effective and safe compared to placebo during 1 year of treatment (*Degree B*). Photodynamic therapy is effective and safe in patients with predominantly classic neovascular AMD compared to placebo up to 2 years (*Degree A*).

Methods

Scientific evidence up to December 2007 was reviewed via the main biomedical data databases. Randomized clinical trials and systematic reviews were selected. Using the criteria of the Scottish Intercollegiate Guidelines Network, two reviewers assessed internal validity and the degree of recommendation of the studies. The scientific evidence was synthesized.

Further research/reviews required

Additional studies are required to assess the impact of treatment by means of health-related quality of life tools and in terms of the treatment's efficiency.

Written by Oliva G and Navarro L, CAHTA, Spain

ISSN 1654-501X

INAHTA Briefs

Issue 2009/114

Title **Prenatal Screening and Treatment Strategies to Prevent Group B Streptococcal and Other Bacterial Infections in Early Infancy: Cost Effectiveness and Expected Value of Information Analyses**

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Reference Volume 11.29. ISSN 1366-5278. www.ncchta.org/project/1473.asp

Aim

To determine the cost effectiveness of prenatal strategies for preventing group B streptococcus (GBS) and other serious bacterial infections in early infancy and to establish the expected value of further information.

Conclusions and results

Current best practice (treat only high-risk women) and universal testing by culture or polymerase chain reaction (PCR) were not cost-effective options. Immediate extension of current best practice to treat all preterm and high-risk term women (11% treated) would result in substantial net benefits. Currently, addition of culture testing for low-risk term women, while treating all preterm and high-risk term women, would be the cost-effective option (21% treated). If available in the future, vaccination combined with treating all preterm and high-risk term women with no testing for low-risk women, would probably be marginally more cost effective and would limit antibiotic exposure to 11% of women. However, the effectiveness of vaccination is uncertain and is based on expert opinion of vaccine efficacy. The value of information is highest (67 million pounds sterling [GBP]) if vaccination is included as an option.

Recommendations

Our results suggest that immediate extension of current practice to treat all preterm and high-risk term deliveries would be beneficial. Thereafter, it is not clear whether the optimal choice would be culture-based testing for low-risk women, or vaccination plus treatment of all preterm and high-risk term women. Vaccination is unlikely to be available for the next 5 years and could not be implemented without phase III trials. Research into vaccine efficacy, before deciding whether to adopt culture-based screening for low-risk women, or vaccination for all without screening, may be beneficial.

Methods

See Executive Summary link at www.ncchta.org/project/1473.asp.

Further research/reviews required

The expected value of information analyses indicated that spending on further research could be worthwhile and would provide maximum returns of up to GBP 27 million or GBP 67 million. Further research aimed at the realization of a GBS vaccine should be prioritized. Cost effectiveness of vaccine compared with other interventions should be re-evaluated after phase III trials. Policy makers should consider adoption of treatment for preterm and high-risk term women, and research into vaccine efficacy, before deciding whether to adopt culture-based screening for low-risk women, or vaccination for all without screening. Studies comparing culture with PCR testing or no intervention in the low-risk term groups (7, 11 and 12) might also be informative, but would need to be extremely large.

Written by Professor Ruth Gilbert, University College London, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/115

Title **A Systematic Review and Economic Model of the Clinical Effectiveness and Cost Effectiveness of Interventions for Preventing Relapse in People with Bipolar Disorder**

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Reference Volume 11.39. ISSN 1366-5278. www.hta.ac.uk/project/1504.asp

Aim

To determine the clinical and cost effectiveness of pharmacological and psychosocial interventions used to prevent relapse in people with bipolar disorders.

Conclusions and results

Bipolar, or manic-depressive, disorder is a frequent, severe, mostly recurrent mood disorder associated with high morbidity and mortality. Pharmacological and psychosocial interventions have been used to prevent relapses in people with bipolar disorders.

Our review of clinical effectiveness included 45 trials. All but one study tested the intervention or comparator in adults. Twenty-eight studies included participants diagnosed as bipolar I and II or not specified, 14 studies included only bipolar I participants, and 3 studies included only bipolar II participants. Trials were available of lithium, valproate, lamotrigine, carbamazepine, olanzapine, imipramine, quetiapine, amitriptyline, perphenazine, and flupenthixol, and psychosocial methods (cognitive behavior therapy [CBT], psychoeducation, family intervention, crisis management, and integrated group therapy).

Standard meta-analysis produced the following results, but not all findings are supported by equally strong evidence. Placebo-controlled trials show evidence of the efficacy of lithium, valproate, lamotrigine, and olanzapine as maintenance therapy for preventing relapse in bipolar disorder. To prevent manic relapses, olanzapine and lithium are efficacious. To prevent depressive symptoms, valproate, lamotrigine, and imipramine are efficacious. No trials show evidence for the efficacy of combination therapy, despite its widespread use. The review revealed that psychosocial therapies have not been investigated thoroughly. Some evidence shows that CBT, group therapy, and family therapy might be beneficial as adjuncts to pharmacological maintenance treatments. Insufficient information regarding adverse effects and dropout rates were available to enable any meaningful assessment of the relative tolerability of the treatments reviewed. Similarly, no assessment could be made of the relative effects of treatment on suicide rate and mortality. Many comparisons between treatments have not been investigated in trials. To further investigate the relative efficacy of the treatments, the data were further analyzed using methods for making indirect comparisons.

Recommendations

See Executive Summary link at www.hta.ac.uk/project/1504.asp.

Methods

See Executive Summary link at www.hta.ac.uk/project/1504.asp.

Further research/reviews required

See Executive Summary link at www.hta.ac.uk/project/1504.asp.

Written by Dr Nerys Woolacott, University of York, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/116

Title **An Assessment of The Impact of NHS Health Technology Assessment Program**

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Reference Volume 11.53. ISSN 1366-5278. www.ncchta.org/project/1440.asp

Aim

To determine: 1) how the impact of the NHS HTA program should be measured and the strengths and weaknesses of the models available; 2) the impact of the first 10 years of the NHS HTA program (1993-2003) and factors associated with HTA research that have made an impact.

Conclusions and results

The literature review showed the payback framework to be the best method for assessing the impact of research programs. The HTA program was shown to have had considerable impact in terms of knowledge generation and perceived impact on policy and to some extent on practice. Each project generated almost 3 peer-reviewed publications and numerous presentations. 85% of principal investigators considered their project had, or would have, an effect on policy and 64% that it had changed behavior, or would do so. This high impact may have resulted partly from the HTA program's objectives, in that topics tend to be of relevance to the NHS and have policy customers. The required use of scientific methods, notably systematic reviews and trials, coupled with strict peer reviewing, may have helped projects publish in high-quality, peer-reviewed journals. Factors associated with impact include: existence of policy customer (eg, NICE) and the track record of the research team.

Recommendations

This study concluded that the HTA program has had considerable impact in commissioning high-quality scientific research on topics that matter to the NHS. Recommendations were made on how the HTA program could improve, and on how the payback framework might be developed.

Methods

The literature review included assessments of research programs, investigating the strengths and weaknesses of the main approaches, identifying models of research impact, and providing recommendations for future work. To evaluate the impact of the first 10 years we used a multiple methods approach (Hanney et al, 2003b), which triangulated NCCHTA documentation, a survey of lead researchers, and a sample of detailed case studies using interviews and documentary analysis.

Further research/reviews required

Further research was recommended on case studies, a rolling *impact* program, and on improved methods for *scoring* impact.

Written by Dr Steve Hanney, University of Brunel, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/117

Title **A Systematic Review and Economic Model of Switching From Non-Glycopeptide to Glycopeptide Antibiotic Prophylaxis for Surgery**

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Reference Volume 12.01. ISSN 1366-5278. www.ncchta.org/execsumm/summ1201.shtml

Aim

To determine whether there is a level of methicillin-resistant Staphylococcus aureus (MRSA) prevalence at which a switch from nonglycopeptide to glycopeptide antibiotic prophylaxis is indicated in surgical environments with a high risk of MRSA infection.

Conclusions and results

Systematic reviews: The effectiveness review included 16 randomized controlled trials (RCTs), with a further 3 studies included for adverse events only. There was no evidence that glycopeptides were more effective than nonglycopeptides in preventing surgical site infections (SSIs). Most of the trials did not report either the incidence of MRSA infections during the trial or the MRSA prevalence of the surgical unit. The cost-effectiveness review included 5 economic evaluations of glycopeptide prophylaxis. One study incorporated health-related quality of life and undertook a cost-utility analysis. None of the studies was undertaken in the UK and none explicitly modeled antibiotic resistance.

Supplementary reviews: The supplementary reviews provided few insights into how to assess cost-effectiveness in the context of resistance. No studies modeled cost-effectiveness alongside epidemiological models of resistance. In addition, there was little information regarding the impact of surgical infections on post-discharge costs and patient quality of life.

Recommendations

See Executive Summary link at www.ncchta.org/execsumm/summ1201.shtml.

Methods

We addressed this issue by undertaking: i) A systematic review of the effectiveness of glycopeptide compared with nonglycopeptide prophylaxis; ii) A systematic review of economic evaluations of the cost effectiveness of glycopeptide prophylaxis compared to appropriate comparators; iii) A series of supplementary reviews to support the economic modeling; iv) A modeling approach to estimate the cost effectiveness of glycopeptide prophylaxis compared to appropriate comparators, using orthopedic surgery as an example.

Further research/reviews required

Future research needs to address the complexities of decision making relating to infection control in general and MRSA prevention in particular. Focusing on MRSA alone is too limited, and the prophylactic use of glycopeptides is only one aspect of infection control. Research including evidence synthesis and decision modeling comparing a full range of interventions for infection control, which extends to other infections not just MRSA, is needed. A long-term research program to predict the pattern of drug resistance and its implications for future costs and health is needed. Development of a full model or algorithm that clinicians could use to guide prophylaxis would require collaboration by experts. In practice it would be difficult to use such a model by defining a MRSA threshold for a particular hospital, and emphasis should be given to basing decisions on an individual patient's level of risk.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/118

Title **Does Befriending by Trained Lay Workers Improve Psychological Well-Being and Quality of Life for Carers of People with Dementia, and at What Cost? A Randomized Controlled Trial**

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Reference Volume 12.04. ISSN 1366-5278. www.ncchta.org/execsumm/summ1204.shtml

Aim

1) To determine whether social support intervention (usual care plus access to an employed befriending facilitator) is effective compared to usual care alone; and 2) To document direct and indirect costs in the intervention and control groups and establish incremental cost effectiveness.

Conclusions and results

Of 316 people expressing interest in participating, 236 (75%) were randomized into the trials (116 intervention; 120 controls). At the main endpoint (15 months postrandomization) 202 carers (96 interventions; 106 controls) were still involved in the trial (14% attrition). There was no evidence of effectiveness or cost effectiveness from the primary analyses on the intention-to-treat population. The mean incremental cost per incremental QALY gained was in excess of 100 000 pounds sterling (GBP), with only a 42.2% probability of being below GBP 30 000 per QALY gained. Analyses on secondary outcomes were similarly negative, and there was no evidence of cost effectiveness in the alternative scenarios considered, except where care-recipient QALYs were included. In this case, the mean incremental cost per incremental QALY gained was GBP 26 848, with a 51.4% probability of being below GBP 30 000 per QALY gained. Only 60 carers (52%) took up the offer of being matched with a trained, lay befriender. Of these, only 37 (32%) were befriended for 6 months or more. A subgroup analysis of controls versus those befriended for 6+ months found a reduction in HADS-depression scores that approached statistical significance. The target duration for befriending relationships was 6 months or longer.

Recommendations

Access to a befriender facilitator is neither an effective nor a cost-effective intervention in supporting carers of people with dementia, although there is a suggestion of cost-effectiveness for the care-dyad (carer and care recipient).

Methods

For further details see www.ncchta.org/execsumm/summ1204.shtml.

Further research/reviews required

Additional research is required to establish: characteristics of carers most likely to take up befriending; befriender-carer characteristics of successful matches; interplay between statutory and voluntary support services and support from families; carer wellbeing in the context of receipt of befriending, and placement of care recipients in long-term residential/nursing care.

Future cost-effectiveness evaluations of carer support should include outcomes for both the carer and care recipient. Further work is required on economic methods for carer intervention research.

Written by Dr Georgina Charlesworth, UCL, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/119

Title **A Multi-Centre Retrospective Cohort Study Comparing the Efficacy, Safety, and Cost Effectiveness of Hysterectomy and Uterine Artery Embolization for the Treatment of Symptomatic Uterine Fibroids. The HOPEFUL Study**

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Reference Volume 12.05. ISSN 1366-5278. www.ncchta.org/execsumm/summ1205.shtml

Aim

To examine the medium-term effects of hysterectomy and uterine artery embolization (UAE) in treating symptomatic uterine fibroids.

Conclusions and results

Hysterectomy is the standard treatment for symptomatic uterine fibroids. During the mid 1990s a minimally invasive, uterus-conserving treatment was described, i.e. uterine artery embolization (UAE). Evidence from a few, small, randomized controlled trials (RCTs) comparing the two treatments suggested UAE is a safe, effective treatment up to 12 months. Long-term safety and efficacy remain unknown.

Data were available for 1108 women (649 UAE and 459 hysterectomy). The cohorts presented a different baseline profile for many confounders, including educational level (UAE higher), ethnicity (UAE more ethnically diverse), and parity (more UAE women nulliparous). After adjusting for confounders, clustering by center, and missing values, fewer complications were experienced by women in the UAE cohort compared to the hysterectomy cohort (odds ratio 0.48, 95%CI: 0.26, 0.89). When only severe/major complications were considered, this odds ratio was reduced to 0.25 (95%CI: 0.13, 0.48). Anticipated general side effects of UAE occurred in 32.7% of the UAE cohort, of which 8.9% also experienced complications. Obesity and medical comorbidity predisposed women to complications, while prophylactic antibiotics appeared to protect against both complications and the anticipated side effects of UAE. More women in the hysterectomy cohort reported relief from fibroid symptoms (89% versus 80%, $p<0.0001$) and feeling better (81% versus 74%, $p<0.0001$), but paradoxically only 70% (compared to 86%, $p=0.007$) would recommend their treatment to a friend.

Recommendations

See Executive Summary link at www.ncchta.org/execsumm/summ1205.shtml.

Methods

See Executive Summary link at www.ncchta.org/execsumm/summ1205.shtml.

Further research/reviews required

This study confirms the medium-term safety of UAE and generates hypotheses of vital importance for women with symptomatic fibroids. Further research is required on the following questions:

- Which subgroups of women will be benefit most from UAE? And which types of fibroids respond to UAE?
- Which UAE techniques are optimal with regard to treatment success and cost effectiveness?
- Which treatments for fibroids including UAE and myomectomy offer the most successful option for future fertility? (Particularly for infertile patients undergoing in vitro fertilization.)
- What is the role of prophylactic antibiotic use prior to UAE?
- How does hormone replacement therapy after UAE affect recurrence of fibroid symptoms?

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/120

Title **Methods of Prediction and Prevention of Pre-Eclampsia: Systematic Reviews of Accuracy and Effectiveness Literature with Economic Modeling**

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Reference Volume 12.06. ISSN 1366-5278. www.ncchta.org/execsumm/summ1206.shtml

Aim

To identify combinations of test and treatments that would predict and prevent pre-eclampsia.

Conclusions and results

This health technology assessment addressed the aim in 3 ways: i) a series of systematic reviews of test accuracy in predicting pre-eclampsia; ii) a series of systematic reviews of effectiveness of interventions with potential to reduce cases of pre-eclampsia; iii) health economic evaluation, including an economic model, of the combined effect of tests and treatments and their cost effectiveness.

Main findings of test accuracy reviews: The quality of studies and test accuracy was generally poor in the 27 tests reviewed. Some tests achieved high specificity, but at the expense of compromised sensitivity. Only a few tests reached specificity above 90%. These were body mass index >34, alphafoetoprotein, fibronectin, kallikrein, and uterine artery Doppler (bilateral notching). Only kallikrein had a sensitivity of over 80%. A few tests not commonly found in routine practice, eg, kallikreinuria, seemed to offer the promise of high sensitivity, without compromising specificity, but this would require further investigation.

Main findings of effectiveness reviews: This report presents 16 systematic reviews of interventions, of which 15 provide estimates of effectiveness in pre-eclampsia.

Recommendations

In the authors' opinion, none of the tests evaluated are sufficiently accurate to recommend for routine use in clinical practice. Calcium and antiplatelet agents, primarily low-dose aspirin, are the interventions shown to prevent pre-eclampsia. The most cost-effective approach to reducing pre-eclampsia is likely to be an effective, affordable, and safe intervention applied to all mothers without prior testing to assess levels of risk. However, we believe it is premature on cost-effectiveness grounds to suggest the implementation of a *treat all* intervention strategy, eg, advice to rest or pharmacological interventions such as low-dose aspirin or calcium supplementation.

Methods

See Executive Summary link at www.ncchta.org/execsumm/summ1206.shtml.

Further research/reviews required

Rigorous evaluation is needed of tests with modest cost whose initial assessments suggest that they may have high levels of both sensitivity and specificity. Similarly, high-quality, adequately powered randomized controlled trials need to investigate whether interventions such as advice to rest are effective in reducing pre-eclampsia. An economic model should be developed. It should consider not just pre-eclampsia, but other related outcomes, particularly those relevant to the infant, eg, perinatal death, preterm birth, and small for gestational age. Such a modeling project should provide for primary data collection on the safety of interventions and their associated costs.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/121

Title **Payment to Healthcare Professionals for Patient Recruitment to Trials: Systematic Review and Qualitative Study**

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Reference Volume 12.10. ISSN 1366-5278. www.ncchta.org/execsumm/summ1210.shtml

Aim

To: i) synthesize evidence on the effectiveness of offering monetary incentives to healthcare professionals to recruit patients to clinical trials; ii) overview the ethical issues as debated in the published literature; and iii) identify UK guidelines on financial incentives to healthcare professionals to recruit patients to trials.

Conclusions and results

The primary research aimed to: i) identify attitudes, beliefs, and behavior of healthcare professionals and consumers in relation to financial incentives for recruitment to trials; ii) explore how financial incentives are viewed in relation to other barriers and facilitators to healthcare professionals recruiting patients to clinical trials; and iii) overview UK practices regarding payment of financial incentives to healthcare professionals for recruiting patients to trials.

Three cross-sectional surveys met the inclusion criteria of the review. These considered recruitment rates and the attitudes and characteristics of clinicians in relation to some financial incentive or reimbursement. One primary care study reported that successful patient recruitment is determined more by motivation driven by the research group than by financial incentives, the research topic, or research experience.

Recommendations

Evidence on the effectiveness of payment to healthcare professionals for patient recruitment to trials is very limited in quality and quantity, and it is inconclusive.

The ethical stance outlined in Good Clinical Practice in research, despite lacking scientific support, was widely endorsed. This precludes payment to patients and allows reasonable payment to clinicians, subject to disclosure of any possible conflicts of interest.

Methods

See Executive Summary link at www.ncchta.org/execsumm/summ1210.shtml.

Further research/reviews required

The authors recommend research on: i) improved reporting on organizational aspects of trials known to affect recruitment, eg, on type and extent of payments; ii) retrospective analysis of factors associated with different levels of recruitment to RCTs, eg, payment of expenses to patients; iii) prospective comparative research on trial recruitment, eg, between commercial and publicly funded trials in NHS research networks and between the roles of investigators and collaborators; iv) qualitative research on participants' experiences of being involved in different kinds of trials and the appropriateness of guidelines on payment for participation; and v) consideration, by funders of clinical trails, of proposals to include trial experiments of payment methods, comparing different levels of disclosure and payment.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/122

Title **A Systematic Review of the Effectiveness of Strategies for Reducing the Fracture Risk in Children with Juvenile Idiopathic Arthritis with Additional Data on Long-Term Risk of Fracture and Cost of Disease Management**

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Reference Volume 12.03. ISSN 1366-5278. www.ncchta.org/execsumm/summ1203.shtml

Aim

1) To review outcome measures in children with juvenile idiopathic arthritis (JIA) and low bone mineral density and/or fragility fractures. 2) To review evidence for effectiveness and safety of bisphosphonates and calcium and/or vitamin D in these children. 3) To assess long-term bone health in adults with JIA. 4) To review the costs of treating children with JIA and low bone mineral density and/or fragility fractures. 5) To evaluate the cost of treating JIA.

Conclusions and results

Review of outcomes: 22 studies evaluated dual energy x-ray absorptionometry (DXA), 2 evaluated quantitative computerized tomography (QCT), and 7 evaluated quantitative ultrasound (QUS). DXA was sensitive to differences between different subtypes of disease, disease severity, and factors such as treatment with corticosteroids, but results in children must be interpreted with care due to technical issues. QCT provides a true volumetric density, but scanning equipment is harder to access and doses of radiation are relatively high. QUS is a promising technique, but data on children are limited. Two studies described the use of either patient-based outcomes or fractures as outcome measures. Twenty-four studies examined biochemical markers of bone turnover, but results were not consistent.

Systematic review of effectiveness: 16 studies assessing bisphosphonates were identified (1 randomized controlled trial, 3 controlled cohort studies, 11 case series, 1 case report). At baseline, children with JIA had bone mineral density below the expected values. In all studies, treatment increased bone mineral density compared with baseline.

Recommendations

DXA is currently the most practical outcome measure, but results in children must be interpreted with care. Limited evidence shows that bisphosphonates are effective in managing children with JIA, but many questions remain unanswered about their use, eg, optimum dose and frequency of administration and length of treatment.

Methods

See Executive Summary link at www.ncchta.org/execsumm/summ1203.shtml.

Further research/reviews required

The ongoing arc-funded randomized controlled trial of bisphosphonates and 1 alphahydroxycholecalciferol in children with JIA should address some research issues that have been identified, eg, the effectiveness and safety of risedronate in corticosteroid-treated children. Other questions include the choice of bisphosphonate and optimal dose and route of administration, effectiveness and safety in noncorticosteroid-treated children and long-term effectiveness and safety.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/123

Title **The Clinical Effectiveness and Cost Effectiveness of Central Venous Catheters Treated with Anti-Infective Agents in Preventing Bloodstream Infections: A Systematic Review and Economic Evaluation**

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Reference Volume 12.12. ISSN 1366-5278. www.ncchta.org/execsumm/summ1212.shtml

Aim

To assess the clinical and cost effectiveness of central venous catheters (CVCs) treated with anti-infective agents (AI-CVCs) in preventing catheter-related bloodstream infections (CRBSIs).

Conclusions and results

Thirty-two trials met the clinical inclusion criteria, including 7 different AI-CVCs. Generally, the trials were of a poor quality in terms of reported methodology, microbiological relevance, and control of confounding variables. Pooled results suggest a statistically significant advantage for AI-CVCs compared to standard CVCs in reducing CRBSI (OR 0.45 [95% CI: 0.34 to 0.60], fixed effects).

Recommendations

The use of AI-CVCs reduces the rates of CRBSI for durations of between 5 and 12 days and >20 days when CVCs are inserted in the femoral or jugular veins. Published evidence suggests that AI-CVCs are cost effective for high-risk patients compared to standard CVCs. Our simple decision model estimated the incremental cost-effectiveness ratios (ICERs) for a range of assumptions and demonstrated that all reasonable scenarios show AI-CVCs to be dominant, ie, in terms of cost effectiveness (they are cheaper and more effective). Overall, AI-CVCs are clinically effective and relatively inexpensive, and their integration into standard care can be justified. However, the use of these anti-infective catheters without the appropriate use of other practical care initiatives will have only a limited effect on preventing CRBSIs.

Methods

See Executive Summary link www.ncchta.org/execsumm/summ1212.shtml

Further research/reviews required

To take account of all relevant clinical parameters (including mortality) related to the effectiveness of AI-CVCs, a single clinical trial would need to include an estimated 10 000 patients in each study arm. It is highly unlikely that such a trial would ever be funded. Comparative trials are required to determine which, if any, of the treated catheters is the most effective. This review has demonstrated that AI-CVCs can be effective in reducing the number of CRBSIs compared with standard CVCs. Results of the included studies also indicate that rates of CRBSI can be minimized when standard CVCs are used. Hence, recommendations for pragmatic research related to the effectiveness of 'bundles' of care that may be effective in reducing rates of CRBSI are warranted. Such research would require local audits of CRBSI rates and assessment of current care practices in order to evaluate the clinical and cost effectiveness of implementing a package of care to reduce CRBSI rates.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/124

Title **Stepped Treatment of Older Adults on Laxatives. The STOOL Trial**

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Reference Volume 12.13. ISSN 1366-5278. www.ncchta.org/execsumm/summ1213.shtml

Aim

1. To investigate the clinical and cost effectiveness of bulk-forming, stimulant, and osmotic laxatives.
2. To investigate the clinical and cost effectiveness of adding a second type of laxative agent in treating patients whose constipation is not resolved by a single agent.
3. To define the meaning of constipation in older people from the perspective of primary care professionals and older patients.
4. To investigate the use of treatments by older people for constipation.
5. To investigate the adherence by older people to prescribed treatments for constipation.

Conclusions and results

There are no findings from the trial about the clinical or cost effectiveness of different management strategies in treating constipation. General-practitioner participants provided patient-centered definitions that focused on the idea of a change from the norm, as defined by the individual and 'textbook' definitions that focused on reduced frequency associated with a range of unpleasant and other clinical symptoms. Nurses' definitions of constipation included both a patient-centered perspective and the description of particular symptoms associated with constipation. Older participants defined constipation in terms of frequency of bowel movements and changes in normal bowel routine. Older participants reported that constipation is: 1) linked to specific diseases, medical conditions, or health problems; 2) caused by the consumption of specific medications or surgical procedures; 3) caused by diet or eating habits; 4) is part of the aging process; 5) due to not going to the toilet when one has the urge to defecate; 6) hereditary; 7) caused by stress or worry; and 8) caused by environmental exposure.

Recommendations

1. Constipation means different things to different people.
2. There is little shared understanding between patients and professionals about 'normal' bowel function.
3. There is little consensus in general practice of the optimum management strategies for chronic constipation, and there is continuing uncertainty about the most effective strategies to employ.
4. Chronic constipation is seen as less important than other prevalent conditions, eg, diabetes, in general practice because it was not an agreed management target. Hence, practitioners had little interest in constipation as a research topic.

Methods

See Executive Summary link at www.ncchta.org/execsumm/summ1213.shtml.

Further research/reviews required

Studies are required: 1) to investigate different methods of recruitment within the constraints of current ethical guidelines on 'opting in'; 2) to identify barriers and facilitators to recruitment to complex trials in general; and 3) to investigate the effectiveness or cost effectiveness of different laxatives and treatment strategies in managing chronic constipation using patient preference trials and natural cohort observational studies.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/125

Title **Topical or Oral Ibuprofen for Chronic Knee Pain in Older People. The TOIB Study**

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Reference Volume 12.22. ISSN 1366-5278. www.ncchta.org/execsumm/summ1222.shtml

Aim

To determine whether general practitioners (GPs) should advise their older patients with chronic knee pain to use topical or oral nonsteroidal antiinflammatory drugs (NSAIDs).

Conclusions and results

Global WOMAC scores were equivalent when comparing the oral and topical groups at all follow-up assessments in both the randomized controlled trial (RCT) and the patient preference study (PPS). No differences were found in any of the secondary outcomes. However, the RCT suggested that those in the topical groups were more likely to have more severe overall pain and disability as measured by the chronic pain grade and to report changing treatment because of inadequate pain relief. This equivalence in outcome may be because topical or oral NSAIDs are equally effective, or that they are equally ineffective. No differences were found in the rate of major adverse effects. Some differences appeared in the number of minor adverse effects. In the RCT: 17% of those in the oral group and 10% of those in the topical group had a defined respiratory adverse effect (95% CI for difference -17%, -2.0). Also a difference appeared in mean creatinine, suggesting an adverse effect from oral NSAIDs on renal function. The mean difference in change of serum creatinine was: -3.7mMol/L (-6.5, -0.9) more in the oral group than the topical group; and 11% of those in the oral group reported changing treatment because of adverse effects compared with 1% in the PPS (P=0.02). None of these differences were observed in the PPS.

Recommendations

Advice to use either oral or topical preparations has an equivalent effect on knee pain, but oral NSAIDs appear to produce more minor adverse effects than topical NSAIDs. Generally, these data support advice to use topical NSAIDs in preference to oral NSAIDs for older people with knee pain. However, for patients who prefer oral NSAID preparations rather than a topical NSAID, particularly those with more widespread or severe pain, the oral route is a reasonable treatment option as long as patients are aware of the risks of potentially serious adverse effects from oral medication.

Methods

See Executive Summary link at www.ncchta.org/execsumm/summ1222.shtml.

Further research/reviews required

These results suggest several future studies that would further inform strategies to reduce NSAID-related adverse events and to further delineate the role of topical NSAIDs. These include:

1) developing and testing strategies to change prescribing behavior and ensure that older patients are aware of the potential risks and benefits of using NSAIDs; 2) observational studies to estimate rates of different predefined minor adverse effects associated with the use of oral NSAIDs in older people; and 3) long-term studies of topical NSAIDs in those for whom oral NSAIDs are not appropriate, eg, the very elderly.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/126

Title **The Clinical Effectiveness and Cost Effectiveness of Screening Programs for Amblyopia and Stabismus in Children up to the Ages of 4-5 Years: A Systematic Review and Economic Evaluation**

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Reference Volume 12.25. ISSN 1366-5278. www.ncchta.org/execsumm/summ1225.shtml

Aim

To estimate the cost effectiveness of screening for amblyopia and strabismus in children up to the ages of 4 to 5 years by developing a decision-analytic model that incorporates defined criteria to inform the suitability of screening for a condition.

Conclusions and results

Due to the likelihood of uncertainty in key areas of the model, an objective of the study was to identify major areas of uncertainty and inform future research priorities in this disease area. The reference cases results showed that screening programs that included autorefraction dominated screening programs without autorefraction. Analyses based on the cost per case of amblyopia prevented showed screening at either 3 or 4 years prevented cases at a low absolute cost (2000 – 4000 pounds sterling [GBP]). However, when these results were extrapolated to estimate the cost per quality-adjusted life-year (QALY) gained, the reference case analysis found that no form of screening is likely to be cost effective at currently accepted values of a QALY. Considerable uncertainty surrounds the natural history parameters. Wide ranging sensitivity analyses found that the results were robust to most parameter changes. The only parameter that radically affected the results was the utility effect of vision loss in one eye. No direct evidence of a utility effect was identified, and the reference case assumed no effect. When a small effect is assumed (reduction in utility of 2 percentage points), the incremental cost per QALY gained becomes extremely attractive for both screening at 3 years and at 4 years. The expected value of perfect information was shown to be large when the unilateral vision loss utility parameter was allowed to vary, but not when it was kept constant at zero.

Recommendations

The cost-effectiveness results from the amblyopia screening and lifetime models show that the cost effectiveness of screening for amblyopia is dependent on the long-term utility effects of unilateral vision loss. Evidence is limited on any such effect, but our subjective interpretation of the literature is that the utility effects are likely to be minimal.

Methods

See Executive Summary link at www.ncchta.org/execsumm/summ1225.shtml.

Further research/reviews required

A prospective study of the utility effects of unilateral vision loss is the main research recommendation.

Written by Mrs Carolyn Czoski-Murray, University of Sheffield, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/127

Title **A Preliminary Model-Based Assessment of the Cost Utility of a Screening Program for Early Age-Related Macular Degeneration**

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Reference Volume 12.27. ISSN 1366-5278. www.ncchta.org/project/1387.asp

Aim

To estimate the cost effectiveness of screening for age-related macular degeneration (AMD) by developing a decision analytic model.

Conclusions and results

Due to the likelihood of uncertainty in key areas of the model, an objective of the study was to identify major areas of uncertainty and inform future research priorities in this disease area.

At a cost per screen of 3 pounds sterling (GBP), the mean results show that the most effective strategy (annual screening from age 50 years) produces an additional 0.0057 quality-adjusted life-years (QALYs) per person (discounted at 3.5%) compared to no screening, at an additional cost of GBP 73 per person. Arranging the screening programs in increasing order of effectiveness, the mean results show that annual screening from age 60 years has the highest acceptable incremental cost per QALY of GBP 17 399. The probabilistic results reveal significant levels of uncertainty such that the 95% credible interval for annual screening from age 60 years ranges from this option dominating the previous option to an incremental cost per QALY of GBP 722 485. Plotting a cost-effectiveness acceptability frontier shows that while annual screening from age 60 years has the highest net benefits at a value of QALY of GBP 30 000, the associated probability of this option being the most cost effective is only around 20%. The sensitivity analyses around potential future treatment options indicate that screening may become more cost effective with the new treatments, though even greater levels of uncertainty surround these estimates.

Recommendations

The extent of the uncertainty around the mean result, the additional resources, and possible reorganization of services required to implement screening indicate that it may be preferable to reduce the level of uncertainty before implementing a *de novo* screening program for AMD.

Methods

Systematic literature reviews were undertaken of the epidemiology and natural history of the different forms of AMD, the effectiveness of alternative AMD treatment options and screening tests, and health-related quality of life and patient utilities relating to AMD. The review of the effectiveness of interventions for AMD was restricted to high-quality reviews and horizon scanning to identify potential interventions. The data derived from the review informed the structure and implementation of the decision analytic model, which was also informed by an iterative process of discussions with expert ophthalmologists.

Further research/reviews required

Of prime importance is the need to assess how routine data may be used to describe clinical presentation rates of age-related maculopathy (ARM). Other potential studies include a pilot study of the effectiveness of screening and opticians' referral patterns for AMD, and a costing study of blindness as a continuum of association with deterioration in vision.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/128

Title **Absorbent Products for Urinary/Fecal Incontinence: A Comparative Evaluation of Key Product Designs**

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Reference Volume 12.29. ISSN 1366-5278. www.ncchta.org/project/1303.asp

Aim

1) To compare the performance and cost effectiveness of the key absorbent product groups to provide a more solid basis for guiding selection and purchase. 2) To carry out the first stage in developing a quality-of-life instrument to measure the impact of absorbent product use on users' lives.

Conclusions and results

The UK health service, nursing homes, and public spend around 94 million pounds sterling (GBP) per year on incontinence pads (absorbent products) to contain urine and/or feces, but the research base for making informed choices between different product designs is weak. The work involved three clinical trials focusing on the three biggest market sectors. Each trial had a crossover design in which each participant tested all products within their group in random order.

Results presented are for statistically and clinically significant findings. *Trial 1:* Disposable inserts were better for leakage, other variables (including skin health, but not discreetness), and overall than the other three designs. However, some women preferred menstrual pads (6/85) or washable pants (13/85), both of which are cheaper to use. Washable inserts were worse both overall and for leakage than the other three designs (72/85 found them unacceptable). *Trials 2a and 2b:* Findings from the community (Trial 2a) and nursing home (Trial 2b) trials were broadly similar. The leakage performance for the disposable inserts was worse than the other designs for day and night, and pull-ups were preferred over inserts for daytime use. The new T-shape diaper was not better overall than the disposable diaper. There were differences in performance and preference findings for men and women, and men had more severe urinary incontinence than women – mean daytime urine mass 375g for (community-dwelling) men and 215g for women, difference 148g (CI:79.8, 217.7). Pull-ups (most expensive) were better overall for women during the day and also for community-dwelling women during the night.

Recommendations

See Executive Summary link at www.ncchta.org/project/1303.asp.

Methods

See Executive Summary link at www.ncchta.org/project/1303.asp.

Further research/reviews required

1) Translational research: to pilot the feasibility of providing choice and combinations of designs to users. 2) Development of more effective washables for women with light incontinence and more effective and appealing (particularly to women) washables for moderate-heavy incontinence. 3) Development of specifically male disposable products for moderate-heavy incontinence. 4) Further development of a tool to measure quality of life for users of absorbent products. 5) Clinical trial of designs for community-dwelling, carer-dependent men and women with moderate-heavy incontinence.

Written by Dr Mandy Fader, University of Southampton, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/129

Title **A Systematic Review of Repetitive Functional Task Practice with Modeling of Resource Use, Costs and Effectiveness**

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Reference Volume 12.30. ISSN 1366-5278. www.ncchta.org/project/1488.asp

Aim

1) To determine if repetitive functional task practice (RFTP) after stroke improves global or limb-specific function or activities of daily living (ADL).
2) To determine if treatment effects are dependent on the amount of practice, or the type or timing of the intervention.
3) To provide estimates of the cost effectiveness of RFTP.

Conclusions and results

Description of studies: Thirty-one studies (1078 participants) were identified. The efficacy of RFTP was considered overall and separately for repetitive task training (RTT), constraint-induced movement therapy (CIMT), and treadmill (TM) training. We found no published trials of either CIMT or TM in the UK, and only 3 RTT trials were UK-based. *RTT:* We found 14 trials: 13 parallel-group randomized controlled trials (RCTs) and one quasi-randomized trial. Four trials had 25 participants or less; six had between 26 and 49 participants; and four had 50 participants or more. *CIMT:* We found 11 trials, all of which were parallel-group RCTs. Ten trials had 25 participants or less, one had 50 participants or more. *TM:* We found six trials: five parallel-group RCTs, and one cross-over trial. Two trials had 25 participants or less, one had between 26 and 49 participants, and three had 50 participants or more.

Study quality: The overall quality of the included trials provided a degree of confidence in the results for RTT and TM training. The results for CIMT must be considered in the light of small sample size. Economic modeling suggested that RFTP was cost effective. Given a threshold for cost effectiveness of 20 000 pounds sterling (GBP) per QALY gained, RFTP is cost effective so long as the net cost per patient is less than GBP 1963.

Recommendations

The evidence suggests that some form of RFTP can be effective in improving lower limb function at any time after stroke, but the duration of intervention effect is unclear. Despite evidence of statistically significant effect for arm function, the evidence is insufficient to draw firm conclusions on upper limb interventions. If task-specific training is used, adverse effects should be monitored. While the effectiveness of RFTP is relatively modest, this sort of intervention appears to be cost effective.

Methods

See Executive Summary link at www.ncchta.org/project/1488.asp.

Further research/reviews required

Further research should: 1) address practical ways to deliver RFTP interventions; 2) evaluate constraint-induced movement therapy for upper limb and hand function; 3) be directed toward evaluating suitable methods to maintain functional gain; 4) include a baseline ADL measure; 5) be powered to detect whether RFTP interventions are cost effective; 6) include indirect costs; and 7) use quality of life as an outcome measure to facilitate economic analysis.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/130

Title **The Effectiveness and Cost Effectiveness of Minimal Access Surgery Amongst People with Gastro-Esophageal Reflux Disease - A UK Collaborative Study. The REFLUX Trial**

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Reference Volume 12.31. ISSN 1366-5278. www.ncchta.org/project/1134.asp

Aim

To determine the clinical effectiveness, cost effectiveness, and safety of a policy of relatively early laparoscopic surgery versus medical management in people with gastroesophageal reflux disease (GORD) judged suitable for both.

Conclusions and results

The two randomized groups were well balanced at entry. Participants had been taking GORD medication for a median of 32 months; their mean age was 46 years, and 66% were men. Of 178 randomized to surgery, 111 (62%) actually had fundoplication. A mix of clinical and personal reasons (some related to long waiting times) were given for those not having surgery. A total or partial wrap procedure was performed, depending on surgeon preference. Complications were uncommon, and none was life threatening. By equivalent to 12 months after surgery, 38% in the randomized surgical group (14% among those who had surgery) were taking reflux medication compared to 90% in the randomized medical group. Substantial differences (a third to a half SD) favored the randomized surgical group across the health status measures, the size depending on assumptions about the proportion that actually had fundoplication. These differences were the same or somewhat smaller than differences observed at 3 months. The lower the reflux score at trial entry, the larger the benefit observed after surgery. A parallel group who wished to have surgery had the lowest reflux scores at baseline. These scores improved substantially after surgery, and by 12 months were better than in a fourth group who chose to continue medical management. The estimated within-trial cost per QALY was 19 000 pounds sterling (GBP) to GBP 23 000; modeling a range of longer-term scenarios indicated likely cost-effectiveness at a threshold of GBP 20 000 per QALY, but with wide uncertainty.

Recommendations

Among patients requiring long-term medication to control symptoms of GORD, surgical management significantly increases general and reflux-specific, health-related quality of life measures at least up to 12 months after surgery. Complications of surgery were rare. A surgical policy is, however, more costly. At a threshold of GBP 20 000 per QALY, it may well be cost effective, especially when putative longer-term benefits are taken into account, but this is uncertain. Hence, judgments are required about cost effectiveness. The more troublesome the symptoms, the greater the potential benefit from surgery.

Methods

See Executive Summary link at www.ncchta.org/project/1134.asp.

Further research/reviews required

Uncertainty about cost effectiveness would be greatly reduced by more reliable information about relative longer-term costs and benefits of surgical and medical policies in managing GORD. This could be through extended follow-up of the REFLUX trial cohorts (which is being undertaken) or by follow-up of other cohorts of fundoplication patients.

Written by Professor Adrian Grant, University of Aberdeen, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/131

Title **Performance of Screening Tests for Child Physical Abuse in Accident and Emergency Departments**

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Reference Volume 12.33. ISSN 1366-5278. www.ncchta.org/project/1413.asp

Aim

To determine the performance of screening tests for physical abuse in injured children attending accident and emergency (A&E) departments in the United Kingdom.

Conclusions and results

We examined 7383 articles, retrieved 448 papers, and included 66 studies in the reviews, including 11 unpublished studies. The quality of studies was poor.

We found consistent evidence that physical abuse is common, and affects about 1 in 11 children in the UK each year. Based on weak evidence we estimated that physical abuse accounts for only 1 in 100 injury attendances at A&E (equivalent to about 0.2 physically abused children attending A&E per 100 children in the community/year). These figures suggest that just fewer than 1 in 50 physical abuse episodes present to A&E. We found clear evidence that physically abused children attending A&E are missed, but performance of the clinical screening assessment was poorly quantified. No test was highly predictive of physical abuse. We found no clear evidence that repeated A&E attendance or type of injury were predictive of physical abuse.

Recommendations

Few physically abused children present to A&E, and some abused and injured children may not receive the medical care they need. Improving the clinical screening assessment or adding a community liaison nurse is likely to be more useful than protocols, except where the pediatric expertise of assessors is minimal. Without more experienced assessors, improvements in detection will be at a cost of increased referrals and could overwhelm capacity.

Methods

See Executive Summary link at www.ncchta.org/project/1413.asp.

Further research/reviews required

1) Well-designed, large-scale studies should evaluate the effectiveness of assessments currently used in A&E to identify abused children and initiate appropriate interventions. In particular, the role and effectiveness of the community liaison nurse warrants further research.

2) Studies need to evaluate the feasibility, acceptability, and effectiveness of new tests, eg, direct questioning of school-age children about injuries, assessment of bruising on the head and face, timing of attendance at A&E, information from the cumulative record of healthcare use, and information from agencies outside health.

3) Monitoring is needed of the incidence of abuse identified by professionals working with children and how this changes over time. National data on reasons for child protection registration should be extended to referrals to social services and analyzed alongside studies of abuse identified by professionals to determine how much is referred.

Written by Professor Ruth Gilbert, UCL, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/132

Title **Systematic Review and Economic Modeling of Effectiveness and Cost Utility of Surgical Treatments for Men with Benign Prostatic Enlargement**

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Reference Volume 12.35. ISSN 1366-5278. www.ncchta.org/project/1468.asp

Aim

To assess the relative clinical effectiveness and cost utility of established and emerging interventional treatments for men suffering symptoms or complications due to benign prostatic enlargement (BPE).

Conclusions and results

Specific objectives: 1) determine the clinical effectiveness of alternative procedures; 2) determine the magnitude of risk of their short- and long-term side effects; 3) rank the clinical effectiveness and risk profile of new interventional procedures against transurethral resection of prostate (TURP), currently considered the standard of care; 4) estimate the cost utility of the alternate procedures; 5) assess the effects of skill and learning on cost effectiveness; 6) identify clinical indications and contraindications for specific procedures; 7) assess the speed of development in the field; and 8) identify areas requiring further research.

TURP was found to provide a consistently high level of improvement of symptoms, maintained in the long term. Improvement in quality of life and peak urine flow rate were also observed. Minimally invasive procedures (eg, TUMT and TUNA) result in less symptom improvement and less increase in flow rate. Ablative procedures (eg, TUVP and HoLEP) give similar symptom and quality-of-life improvement to TURP. Holmium laser enucleation of prostate (HoLEP) resulted in greater improvement in flow rate.

Recommendations

See Executive Summary link at www.ncchta.org/project/1468.asp.

Methods

The research was based on four interrelated components: 1) development of care pathways for the chosen treatment options for men presenting with symptoms or complications resulting from benign prostatic enlargement; 2) systematic review of the literature of the effects of the alternative procedures; 3) systematic review of economic evaluations to inform point 4 below; 4) construction of Markov model and cost-utility analysis of the treatment options.

See Executive Summary link at www.ncchta.org/project/1468.asp.

Further research/reviews required

Research should concentrate on the design of rigorous, high-quality RCTs, using standardized definitions of outcome with improved reporting, including reasons for re-operation. In the context of the NHS and the patient, it is likely that choices based on strategies of management are more important than choices based on individual interventions. Areas for further research include: 1) for men who might currently be managed medically, a systematic review including modeling to determine how many years of medical treatment are necessary to offset the cost of treatment with a minimally invasive or ablative intervention in the first instance; and 2) better research into the true costs of the different interventions as a critical driver of economic evaluations.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/133

Title **Controlling Hypertension and Hypotension Immediately Post-Stroke (CHHIPS) – A Randomized Controlled Trial**

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Reference Volume 13.09. ISSN 1366-5278. www.ncchta.org/project/1351.asp

Aim

To determine whether manipulation of blood pressure (BP) – by 1) reducing raised levels with labetalol or lisinopril within 36 hours of cerebral hemorrhage or infarction (depressor limb) or 2) increasing low BP levels with phenylephrine within 12 hours of cerebral infarction (pressor limb) – alters death and dependency at two weeks or long-term mortality. Secondarily, to determine the safety of such therapy in terms of early neurological deterioration, the efficacy of sublingual lisinopril and intravenous labetalol compared to matching placebo, and the cost effectiveness of such treatment.

Conclusions and results

We found no significant difference in death or dependency at 2 weeks between those receiving active depressor treatment with lisinopril or labetalol compared to those receiving placebo. However, fewer people than projected were recruited to the trail. Active treatment was not associated with an increase in early neurological deterioration, despite significantly greater reductions in BP at 24 hours and 2 weeks with active therapy compared to placebo. Active treatment was generally well tolerated, and no major safety problems were identified. Treatment discontinuation rates were similar in active and placebo groups. Survival analysis showed lower mortality at 3 months in the active treatment group than in the placebo group (p=0.05). The pressor arm was closed early due to recruitment problems. Hence, conclusions regarding acute post-stroke pressor therapy cannot be drawn from this study.

Recommendations

Oral and sublingual lisinopril and oral and intravenous labetalol are effective BP lowering agents in acute cerebral infarction and hemorrhage and do not increase the likelihood of early neurological deterioration. The study was underpowered to detect a difference in disability or death at 2 weeks, the primary outcome measure.

Methods

See Executive Summary link at www.ncchta.org/project/1351.asp.

Further research/reviews required

Further work is needed to confirm these results and assess if the effectiveness of labetalol differs from lisinopril in terms of reducing death or dependency after acute stroke, and whether earlier lowering of BP post-stroke (than was achieved in CHHIPS) would be of greater benefit. We remain uncertain as to the best management of BP in acute stroke. The CHHIPS Pilot Trial would indicate that labetalol or lisinopril can safely reduce BP after acute stroke, and this may translate into decreased mortality at 3 months. These findings need to be acted on by formulating the definitive trial of BP lowering in acute stroke. The role for increasing BP in acute stroke remains unresolved, but the CHHIPS Pilot Trial entry criteria indicate that this therapy would apply to a very small number of people.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/134

Title **Treatment of Severe Ankle Sprain: A Pragmatic Randomized Controlled Trial Comparing the Clinical Effectiveness and Cost Effectiveness of Three Types of Mechanical Ankle Support with Tubular Bandage. The CAST Trial**

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Reference Volume 13.13. ISSN 1366-5278. www.ncchta.org/project/1309.asp

Aim

To estimate the clinical effectiveness of 3 methods of ankle support (below-knee cast, Aircast® ankle brace, and Bledsoe® boot) compared to tubular compression bandage (Tubigrip®) in terms of recovery of function (primary outcome), recovery of normal occupation, (secondary outcome), and avoidance of residual symptoms, eg, recurrent instability; and to measure the cost effectiveness of each strategy, including treatment and subsequent healthcare costs.

Conclusions and results

Optimum treatment for severe ankle sprains is unclear. Treatment options include no intervention, physiotherapy, different types of braces and supports, immobilization, and surgical repair of ligaments. Recent systematic reviews highlight a lack of good-quality evidence to aid clinical decision making. Well-conducted and adequately powered randomized controlled trials (RCTs) are needed to determine the effectiveness of different clinical approaches.

After adjusting for age, sex, and baseline score, the below-knee cast offered a small, but statistically significant, benefit at 4 weeks in terms of pain, foot and ankle-related quality of life (QoL), and the physical component score of the SF-12. Neither the Aircast brace nor Bledsoe boot was statistically significantly or clinically different from Tubigrip. At 12 weeks, and in comparison to Tubigrip, the below-knee cast was statistically significantly better in terms of pain, activities of daily living, sports and QoL. Calculation of effect sizes suggests these benefits were small to moderate, depending on the domain of outcome. The Aircast brace was associated with clinically and statistically significant changes in QoL and the mental component score of the SF-12, but not other domains. We found no difference between treatments in the outcomes at 9 months.

Recommendations

See Executive Summary link at www.ncchta.org/project/1309.asp.

Methods

See Executive Summary link at www.ncchta.org/project/1309.asp.

Further research/reviews required

The role of physiotherapy is not known in these injuries. In view of their poor prognosis in relatively active people, it is important to understand an appropriate regime of exercise and physiotherapy during and after the period of functional support. There are no adequately powered studies of less-severe ankle sprains. In the UK, anticoagulants are not routinely used in lower limb injury, whereas this is standard practice in most of mainland Europe. More research is needed to determine the risk-benefit of such strategies. The scoring systems used can all differentiate between statistically significant changes in scores, but studies have not been undertaken to determine clinically significant score differences.

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INAHTA Briefs

Issue 2009/135

Title **Blood Glucose Self-Monitoring in Type 2 Diabetes: A Randomized Controlled Trial**

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Reference Volume 13.15. ISSN 1366-5278. www.ncchta.org/project/1330.asp

Aim

To test whether self-monitoring of blood glucose (SMBG), used with or without instruction in incorporating findings into self-care can improve glycemia control in noninsulin treated diabetes compared with standardized usual care.

Conclusions and results

Four hundred fifty-three patients were randomized with mean (SD) HbA1c 7.5% (1.1). The differences in 12-month HbA1c between the three groups (adjusted for baseline HbA1c) were not statistically significant (P=0.12). The difference in unadjusted mean change in HbA1c from baseline to 12 months between the control and less-intensive self-monitoring groups was -0.14% (95%CI -0.35 to 0.07) and between the control and more-intensive self-monitoring groups was -0.17% (95%CI -0.37 to 0.03). SMBG was found to be significantly more expensive compared to standardized usual care, by 92 pounds sterling (GBP) and GBP 84 for the less-intensive SMBG and the more-intensive SMBG groups respectively. SMBG appears to have an initial negative impact on health status measured with EQ-5D. Cost-utility analysis showed that it is unlikely that either investigated forms of SMBG are cost effective compared to standardized usual care. In-depth interviews identified groups of patients who used SMBG to monitor the impact of different lifestyle choices and used this to motivate adherence to these choices. However, some patients did not find SMBG helpful. Questionnaires about health-related beliefs did not identify an increase in perceived control over diabetes, but did find an increase in perceived seriousness of diabetes in the group carrying out more intensive self-monitoring.

Recommendations

See Executive Summary link at www.ncchta.org/project/1330.asp.

Methods

See Executive Summary link at www.ncchta.org/project/1330.asp.

Further research/reviews required

1) The qualitative element of the trial identifies a group of patients who consider that use of SMBG provides them with motivation to adopt and maintain behaviors that lead to better diabetes control. Further work is required to characterize those who gain most benefit in terms of glycemia control and whether this is related to use of the procedure. 2) Our results suggest that routine use of SMBG may not be appropriate for reasonably well controlled patients, but its role in managing patients with less well controlled diabetes is not clear. A pragmatic strategy of self-management education with HbA1c monitoring and intensifying drug therapy may be appropriate in the first instance. If glycemia control is not then achieved, SMBG may be appropriate – firstly to explore any potential motivating effect, and secondly because insulin treatment is likely to be required. Exploring the utility of this strategy may be appropriate. 3) An increased rate of hypoglycemia is reported among individuals using self-monitoring. Further research needs to establish whether these differences are likely to result from biochemical differences or greater awareness of hypoglycemia as a cause of symptoms.

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INAHTA Briefs

Issue 2009/136

Title **How Far Does Screening Women for Domestic (Partner) Violence in Different Health-Care Settings Meet Criteria for a Screening Program? Systematic Reviews of Nine UK National Screening Committee Criteria**

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Reference Volume 13.16. ISSN 1366-5278. www.ncchta.org/project/1501.asp

Aim

To identify, appraise, and synthesize research relevant to selected UK National Screening Committee (NSC) criteria for a screening program relating to partner violence; and to judge whether the evidence is sufficient to fulfill selected NSC criteria for implementation of screening (in healthcare settings) for partner violence.

Conclusions and results

Research questions: Seven review questions are linked to key NSC criteria. Question I: What is the prevalence of partner violence against women and its health consequences? (NSC criterion 1), Question II: Are screening tools valid and reliable? (NSC criteria 5 & 6), Question III: Is screening for partner violence acceptable to women? (NSC criterion 7), Question IV: Are interventions effective once partner violence is disclosed in a healthcare setting? (NSC criteria 10 & 15), Question V: Can mortality or morbidity be reduced following screening? (NSC criterion 13), Question VI: Is a partner violence screening program acceptable to health professionals and the public? (NSC criterion 14), Question VII: Is screening for partner violence cost effective? (NSC criterion 16).

The evidence is insufficient to implement a screening program for partner violence against women, either in health services generally or in specific clinical settings. Question I: The prevalence in the UK of partner violence against women and the magnitude of health sequelae varies with study design and population. Even the lower estimates for prevalence, morbidity, and mortality show it to be a major public health problem and potentially an appropriate condition for screening and intervention. Question II: Several short screening tools are relatively valid and reliable for use in healthcare settings. The HITS has the best predictive power, concurrent and construct validity and reliability, with a suitable cut-off score.

Recommendations

See Executive Summary link at www.ncchta.org/project/1501.asp.

Methods

See Executive Summary link at www.ncchta.org/project/1501.asp.

Further research/reviews required

1) Trials of system-level interventions to improve the response of health services to survivors of partner violence. These may incorporate routine or selective enquiry and, potentially, could compare differences in outcomes between the two policies. 2) Trials of psychological and advocacy interventions after disclosure of partner violence in healthcare settings measuring quality of life, mental health, and further abuse. 3) Trials to test theoretically explicit interventions to help understand what works (or does not work) for whom, when, and in what contexts. 4) Qualitative studies to explore what women want from interventions after disclosure of partner violence. 5) Longitudinal studies to measure the long-term prognosis for survivors of partner violence after identification in healthcare settings.

Written by Professor Gene Feder, University of Bristol, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/137

Title **The Role of Magnetic Resonance Imaging in the Identification of Suspected Acoustic Neuroma: A Systematic Review of Clinical and Cost Effectiveness and Natural History**

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Reference Volume 13.18. ISSN 1366-5278. www.ncchta.org/project/1514.asp

Aim

To determine: 1) the place of magnetic resonance imaging (MRI) in investigating patients with unilateral hearing loss and or tinnitus for suspected acoustic neuroma (AN); 2) the cost effectiveness of MRI versus other diagnostic strategies in these patients; 3) what is known about the natural history of acoustic neuroma; and 4) to identify published and unpublished literature and extract the relevant evidence to help answer the questions of which tests (including combinations and sequencing) are best to use and also how do acoustic neuromas grow and affect individuals.

Conclusions and results

In current clinical practice, MRI is the first-line investigation for identification of suspected AN in appropriately selected patients. The GdT1W sequence remains the *gold standard* sequence for evaluating cases where the screening sequence is indeterminate and for characterizing any suspected pathology. Non-contrast, high-resolution, 3D T2W or T2*W sequences, enable accurate evaluation of the VIII and VII cranial nerves within the CPA and IAC and evaluation of the cochlear and labyrinth. Given the recent improvement in resolution and reduction in cost of MRI, ABR can no longer be considered appropriate for the primary test used to screen for an acoustic neuroma. While it is relatively inexpensive and offers acceptable sensitivity for medium to larger tumors, its ability to reliably indicate tumors under 1cm is poor. ABR also fails to provide clinically useful results in patients with severe to profound hearing loss (typically a hearing threshold greater than 70 dBHL at 4 kHz).

Recommendations

MRI is the first-line investigation for identification of suspected AN in appropriately selected patients. Non-contrast, high-resolution, 3D T2W or T2*W sequences should be the first-line evaluation followed by GdT1W MRI if necessary. This strategy is a good cost-effective option. The incidence of acoustic neuroma may be increasing. Symptomatology does not predict incidence or growth. Growth rates are variable, and regression can occur. No factors have been identified that predict growth.

Methods

See Executive Summary link at www.ncchta.org/project/1514.asp.

Further research/reviews required

1) Research to provide evidence to further understand the pathophysiological mechanisms by which patients become symptomatic. 2) A consensus method of measuring tumors and evaluating growth, taking into account their three dimensions. 3) Long-term prospective longitudinal studies with agreed criteria to evaluate tumor growth. 4) Establishment of a national tumor registry for acoustic neuroma in the UK.

Written by Dr Heather Margaret Fortnum, University of Nottingham, NETSCC, United Kingdom

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INAHTA Briefs

Issue 2009/138

Title **Dipsticks and Diagnostic Algorithms in Urinary Tract Infection: Development and Validation, Randomized Trial, Economic Analysis, Observational Cohort, and Qualitative Study**

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Reference Volume 13.19. ISSN 1366-5278. www.ncchta.org/project/1205.asp

Aim

1) To estimate independent clinical and dipstick predictors of urinary tract infection (UTI) and develop clinical scores to predict infection. 2) To test the clinical scores in an independent sample. 3) To understand the natural history of UTI and its key determinants. 4) To perform a randomized controlled trial (RCT) comparing management using the clinical and dipstick scores with common alternative management strategies. 5) To estimate resource use in each management strategy and estimate cost effectiveness. 6) To understand women's understanding and concerns in the presentation and management of UTI.

Conclusions and results

Validation testing study: 66% of women had confirmed UTI. A dipstick rule – based on the presence of nitrite, or both leucocytes and blood – was moderately sensitive (75%), but less specific (66%) (positive predictive value [PPV] 81%, negative predictive value [NPV] 57%). The NPV was 76% for all three dipstick results being negative; the PPV 92% for having nitrite *and* either blood or leucocyte esterase. Offensive smell (of urine) was not found to be predictive in this sample; for a clinical score using the remaining three predictive clinical features the NPV was 67% for none of the features, and the PPV 82% for three features.

Observational study: Compared with infections that were sensitive to antibiotics, resistant infections lasted 56% longer (incidence rate ratio [irr] 1.56; 95% confidence interval 1.22 to 1.99, p<0.001), and no antibiotics 62% longer (irr 1.62; 1.13 to 2.31, p=0.008). Symptom duration was shorter if the doctor was perceived to be positive about diagnosis/prognosis, and longer with somatic symptoms, previous cystitis, and severe symptoms.

Randomized trial: Antibiotic use differed between antibiotic management groups (immediate 97%, MSU 81%, dipstick 80%, symptom score 90%, delayed 77%, likelihood ratio test p=0.011), and also in using MSUs at the initial consultation (23%, 89%, 36%, 33%, 15% respectively, p<0.001), but the difference in symptomatic outcomes was small.

Qualitative study: When patients are asked to delay taking antibiotic medication, the sometimes protracted, uncomfortable, and worrying journey from "person to patient" needs to be acknowledged, their expressions of bodily change validated, and the rationale for not taking the antibiotics made clearer.

Recommendations

See Executive Summary link at www.ncchta.org/project/1205.asp.

Methods

The report covers 6 studies, including a validation development study concerning the diagnostic clinical score and diagnostic dipstick score (training study). Patients with suspected UTI had UTI confirmed using the European Urinalysis guidelines standard. Independent clinical and dipstick predictors of diagnosis were estimated, and both a dipstick score and a clinical score were developed.

Further research/reviews required

See Executive Summary link at www.ncchta.org/project/1205.asp.

Written by Professor Paul Little, University of Southampton, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/139

Title **Systematic Review of Respite Care in the Frail Elderly**

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Reference Volume 13.20. ISSN 1366-5278. www.ncchta.org/project/1461.asp

Aim

To systematically review the literature on the effectiveness and cost effectiveness of breaks in care as a means to improve the well being of informal carers of frail and disabled older people living in the community; and to identify (via a synthesis of qualitative studies) carer needs and barriers to uptake of respite services.

Conclusions and results

Quantitative Synthesis: 104 papers were identified for inclusion, 16 of which were appropriate for meta-analysis. 1) Carer burden was reduced at 2 to 6 months follow-up in single-sample studies, but not in RCTs and quasiexperimental studies. 2) Depression was reduced in RCTs in the short term and for home care, but not day care. These effects, however, were not significant in random effects models. The trend was for longer interventions to have more positive effects than shorter. 3) Respite had no effect on anxiety, but had positive effects on morale, anger, and hostility. Quality of life was worse after respite care. 4) Institutionalization rates increased after respite use.

Qualitative Synthesis: 70 papers were identified for inclusion. Uptake of respite care was influenced by: 1) carer attitudes to caring and respite provision; 2) the care-giving relationship; 3) knowledge of and availability of services; 4) acceptability toward and impact of respite care on care recipients; 5) hassles resulting from use of respite care; 6) quality of respite care; and 7) appropriateness and flexibility of service provision.

Respite needs to provide a mental break, not just a physical break. Carers expressed needs for active information about services, support offered early in the care-giving career, access to a variety of services with flexible provision, reliable transport services, continuity of care, good quality care, appropriate environments, care th at provides benefits (socialization and stimulation) for the care recipient (CR), and appropriate activities for the CR's level of abilities and interests.

Recommendations

Some evidence supports respite having a positive effect on carers, but the evidence was limited and weak. Few trials were available, and studies were heterogeneous with poor definition of respite interventions. Flexibility of respite provision and responsiveness to carer needs was highlighted as an important aspect of care. The qualitative review identified a need for information, respite early in the care-giving career, better training of formal carers (particularly in relation to dementia care), continuity of care, better transport services, and good-quality services that provide stimulation to care recipients.

Methods

See Executive Summary link at www.ncchta.org/project/1461.asp.

Further research/reviews required

See Executive Summary link at www.ncchta.org/project/1461.asp.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/140

Title **Neuroleptics in the Treatment of Aggressive Challenging Behavior for People with Intellectual Disabilities: A Randomized Controlled Trial (NACHBID)**

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Reference Volume 13.21. ISSN 1366-5278. www.ncchta.org/project/1322.asp

Aim

To investigate the value of giving antipsychotic drugs to adults with intellectual disability when they show challenging behavior (manifest mainly by anger and aggression).

Conclusions and results

We tested a specific research question involving representatives from both groups of antipsychotic drugs: Do typical and atypical antipsychotic drugs (haloperidol and risperidone) given in flexible dosage reduce aggression in challenging behavior in learning disability to a greater extent than placebo medication in both the short term (4 weeks) and medium term (12-26 weeks)?

Eighty-six patients, predominantly male (62%) (1 with borderline intellectual disability, 30 with mild, 41 with moderate, and 14 with severe intellectual disability) with similar distribution by randomized group, were randomized from 10 centers in England and Wales, and one in Queensland, Australia between November 6, 2002 and August 24, 2006. Twenty-two clinicians recruited patients, with three recruiting 40 patients between them. Since this was a much lower rate of recruitment than planned, we extended the recruitment period from 24 to 45 months. There were no dropouts from assessment in the first 4 weeks, 29% at 12 weeks, and 43% at 26 weeks (with all patients and clinicians having the option to discontinue the study after 12 weeks). The mean daily dosage for risperidone was 1.07mg rising to 1.78mg, and haloperidol 2.54 mg rising to 2.94mg. Aggression declined dramatically with all three treatments after 1 week, but this was maintained to a greater extent with placebo. After 4 weeks placebo showed the greatest reduction (79%, vs 57% for combined drugs) (P=0.06). None of the other secondary measures showed any drug-placebo differences.

Recommendations

This trial provides no evidence that either risperidone or haloperidol given in conventionally low doses offer any advantages over placebo in short- and medium-term treatment of aggressive, challenging behavior in intellectual disability, and over 4 weeks placebo was somewhat more effective in reducing aggression. Placebo treatment is also cheaper than the other two treatments over a 6-month period in terms of total costs. It is concluded that placebo is the most cost-effective of the three treatments for aggressive challenging behavior.

Methods

See Executive Summary link at www.ncchta.org/project/1322.asp.

Further research/reviews required

The current use of antipsychotic drugs in treating aggressive challenging behavior in intellectual disability requires review. The findings suggest that much of this prescribing may be unnecessary, and other forms of treatment, probably of a psychological nature, should be tested in randomized studies.

Written by Professor Peter Tyrer, Imperial College London, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/141

Title **Randomized Controlled Trial to Determine the Clinical and Cost Effectiveness of Selective Serotonin Reuptake Inhibitors Plus Supportive Care, Versus Supportive Care Alone, for Mild to Moderate Depression with Somatic Symptoms in Primary Care. The THREAD (Threshold for Antidepressant Response) Study**

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Reference Volume 13.22. ISSN 1366-5278. www.ncchta.org/project/1356.asp

Aim

To determine whether treatment with a selective serotonin reuptake inhibitor (SSRI) antidepressant is effective and cost effective for mild to moderate depression in primary care. Secondary aims were: to explore whether treatment is more effective for moderate depression than for mild; and explore patient factors that might predict outcome, and/or predict a beneficial response to antidepressants.

Conclusions and results

More than 90% of patients in each arm received supportive care from the general practitioners (GPs), with a mean number of consultations of around 4 during the 12-week treatment period. SSRI antidepressants were received by 87% of patients in the SSRI plus supportive care arm, and also by 20% of patients in the supportive care alone arm. Longitudinal analyses demonstrated statistically significant differences in favor of the SSRI plus supportive care arm in terms of lower Hamilton Depression Rating Scale (HDRS) scores, higher scores on the SF-36 mental health subscale, and higher scores on the MISS, but not in terms of lower Beck Depression Inventory (BDI) scores. Significant mean differences in HDRS score adjusted for baseline were found at both follow-up points when analyzed separately, but were relatively small: 2.3 points at 12 weeks and 1.7 points at 26 weeks. The number needed to treat (NNT) for remission (to HDRS < 8) was 6 (95% CI 4 to 26) at 12 weeks and 6 (3 to 31) at 26 weeks, and the NNTs for significant improvement (HDRS fall of >=50%) were 7 (4 to 83) and 5 (3 to 13) respectively. Costs were slightly higher in the SSRI plus supportive care arm, but not significantly different.

Recommendations

See Executive Summary link at www.ncchta.org/project/1356.asp.

Methods

See Executive Summary link at www.ncchta.org/project/1356.asp.

Further research/reviews required

More studies of drug and nondrug treatments for mild depression in primary care are needed, as the evidence base for the treatment of mild depression is still relatively small. More research is needed on the natural history of mild to moderate depression and predictors of chronicity because, although many patients recover within weeks without treatment, a significant number do not improve over 6 months of follow-up. More research is needed to identify the most effective elements of supportive care. More research is needed into the differences between the HDRS, BDI, and other measures of depression, to explore whether they measure different aspects of depression and differ in sensitivity to change in relation to drug, psychological, and other treatments. Better measures of outcome for depression studies need to be developed, including patient-derived measures.

Written by Mrs Judy Chatwin, University of Southampton, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/142

Title **Diagnostic Strategies Using DNA Testing for Hereditary Hemochromatosis in At-Risk Populations: A Systematic Review and Economic Evaluation**

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Reference Volume 13.23. ISSN 1366-5278. www.ncchta.org/project/1502.asp

Aim

To evaluate the use of DNA tests for detecting hereditary hemochromatosis (HHC) in subgroups of patients suspected of having the disorder and in family members of those diagnosed with hemochromatosis.

Conclusions and results

Objectives: 1) determine the clinical validity of DNA tests to diagnose HHC; 2) summarize the evidence on the clinical utility of diagnostic strategies using DNA tests to detect cases for treating or monitoring in terms of clinical effectiveness and cost effectiveness; 3) compare the costs and consequences by decision analysis modeling of diagnostic algorithms for HHC and family testing strategies with and without DNA testing in terms of cost per case detected: 4) review the psychosocial literature and compare the psychosocial benefits and harms of adding DNA testing to diagnostic algorithms; and 5) identify priorities for future primary research.

We found 11 studies that could be used to estimate the clinical validity of genotyping for the C282Y mutation in diagnosing genetic hemochromatosis. Study quality varied, and different definitions had been used for the clinical phenotype. Clinical sensitivity of C282Y homozygosity for hereditary hemochromatosis ranged from 28.4% to 100% in the 11 studies; when considering only the most relevant studies, sensitivity ranged from 91.3% to 92.4%. Clinical specificity ranged from 98.8% to 100%. No clinical effectiveness studies met the inclusion criteria for the review. Two cost-effectiveness studies conducted in North America were identified, both of reasonable quality, but their generalizability to the UK is unclear.

Recommendations

Results suggest that using a diagnostic strategy that incorporates DNA testing saves costs in identifying cases and testing offspring of hemochromatosis patients. The results for siblings suggest that DNA testing is not cost saving, although cost effectiveness might be shown if the benefit of reassurance were to be incorporated in modeling. The preferred strategy is DNA testing in conjunction with testing iron parameters when clinical indications clearly raise suspicion of being at risk for hemochromatosis due to biochemical criteria or familial risk.

Methods

See Executive Summary link at www.ncchta.org/project/1502.asp.

Further research/reviews required

Epidemiological research (using national databases) is required on the environmental and other genetic factors that affect the penetrance of the genetic mutation, to identify those people homozygous for the mutation who are likely to develop iron overload.

Written by Ms Jackie Bryant, SHTAC, University of Southampton, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/143

Title **Development of a Decision Support Tool for Primary Care Management of Patients with Abnormal Liver Function Tests Without Clinically Apparent Liver Disease: A Record-Linkage Population Cohort Study and Decision Analysis (ALFIE)**

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Reference Volume 13.25. ISSN 1366-5278. www.ncchta.org/project/1460.asp

Aim

To determine the natural history of abnormalities in liver function tests (LFTs) before overt liver disease presents in the population, derive predictive algorithms for liver disease, and analyze cost-utility to lead to decision aids that would identify those requiring further investigation, or none, with the potential for early diagnosis or reducing National Health Service (NHS) costs.

Conclusions and results

From 1989 to 2003 in primary care, 95 977 patients had 364 194 incident-initial LFTs without obvious liver disease. This cohort had a median follow-up of 3.7 years. Of these 21.7% had at least one abnormal LFT and 1.3% (1213) developed liver disease. Elevated transaminases were strongly associated with diagnosed liver disease, hazard ratio (HR)=4.20 (3.54, 4.98) for mild levels and HR=11.99 (9.26, 15.52) for severe levels vs normal. For gamma-glutamyltransferase (GGT) these hazards were 2.46 (2.12, 2.86) and 13.21 (10.60, 16.46) respectively. Low albumin was strongly associated with all-cause mortality, 2.65 (95% CI 2.47, 2.85) for mild levels and 4.99 (95% CI 4.26, 5.84) for severe levels. Predictive algorithms were developed for three time periods; 0 to 3 months, 3 months to 1 year, and over 1 year, for liver disease diagnosis, liver mortality, and all-cause mortality using the Weibull regression model. All LFTs and several interaction terms were predictive of liver disease, and high probability of liver disease was associated with being female, methadone use, alcohol dependency, history of cancer, and deprivation. The shorter-term models had overall c-statistics of 0.85 and 0.72 for outcome of liver disease at 3 months and 1 year respectively, and 0.88 and 0.82 for all-cause mortality at 3 months and 1 year respectively. Calibration was also good for models predicting liver disease.

Recommendations

From this large population-based, data-linked database we developed several predictive algorithms, which displayed good discriminative performance and calibration. Further work will seek to develop these into user-friendly decision aids. Cost-utility analyses indicated that identifying high-risk patients for immediate referral to secondary care would be cost effective, while in low-risk patients re-testing in primary care was more cost effective.

Methods

See Executive Summary link at www.ncchta.org/project/1460.asp.

Further research/reviews required

The derived predictive algorithms could be further developed into user-friendly computerized decision aids. These could be evaluated in cluster-randomized trials to assess their value in aiding decisions in primary care. This will facilitate optimal decision-making, both for the benefit of the patient and the NHS.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/144

Title **Paracetamol and Ibuprofen for the Treatment of Fever in Children: The PITCH Randomized Controlled Trial**

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Reference Volume 13.27. ISSN 1366-5278. www.ncchta.org/project/1412.asp

Aim

To assess the relative clinical and cost effectiveness of paracetamol and/or ibuprofen in treating fever in children.

Conclusions and results

Paracetamol and ibuprofen are increasingly used together for fever, despite a lack of evidence regarding their clinical or cost effectiveness.

For additional time without fever in the first 4 hours, using both medicines was superior to paracetamol (adjusted difference 55 minutes, 95% CI 33 to 77; p<0.001) and may have been as good as ibuprofen (16 minutes, 95% CI -6 to 39; p=0.2). Both medicines together cleared the fever 23 minutes (2 to 45; p=0.015) faster than paracetamol, but no faster than ibuprofen (-3 minutes, -24 to 18; p=0.8). For additional time without fever in the first 24 hours, both medicines were superior to paracetamol (4.4 hours, 2.4 to 6.3; p<0.001) and ibuprofen (2.5 hours, 0.6 to 4.5; p=0.008). No benefits for discomfort or the other fever-associated symptoms were found, although power was low for these outcomes. An exploratory analysis showed that children with higher discomfort levels had higher mean temperatures. No difference in adverse effects was observed between treatment groups. In 24 hours, 8% and 11% of children respectively received more than the recommended maximum number of doses of paracetamol and ibuprofen.

Recommendations

Doctors, nurses, and parents wishing to use medicines to treat young children unwell with fever should be advised to use ibuprofen first, and that to maximize the time without fever over 24 hours, two medicines are superior to either one. Pragmatically, we speculate that if a child remains unwell after a first dose of ibuprofen, subsequent use of both medicines will be more effective than either monotherapy. However, if two medicines are used, we recommend that all dose times are carefully recorded to avoid accidental overdosing. The economic analysis shows that the use of both medicines should not be discouraged on the basis of cost to either parents or the National Health Service.

Methods

See Executive Summary link at www.ncchta.org/project/1412.asp.

Further research/reviews required

For *dose-by-weight* regimens to be used safely in the community, studies should investigate the dose implications of differences between estimates of children's weights measured by parents using domestic scales and those measured by professionals using pediatric scales. Furthermore, adequately powered research is needed to investigate the relative effectiveness of two versus one medicine for discomfort and other fever-associated symptoms. An adequately powered study is also needed to improve the precision of the cost-effectiveness estimates.

Written by Dr Alastair D Hay, University of Bristol, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/145

Title **Decision-Making Tool (DMT) for Patients with Non Valvular Atrial Fibrillation**

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Reference Report no. 2006/28. ISBN 978-84-96990-14-2. www.juntadeandalucia.es/salud/servicios/contenidos/aetsa/pdf/AETSA_2006-28_HATD_Fibrilacion.pdf

Aim

To use a decision-making tool (DMT) on treatments to prevent stroke in nonvalvular atrial fibrillation (NVAF) patients; to know the effectiveness and safety of the most common treatments to prevent stroke in NVAF patients; to use a patient decision aid (PtDA) and an instruction manual for professionals (IMPr); and to validate the DMT.

Conclusions and results

1. Systematic review on effectiveness and safety of antithrombotic treatments for atrial fibrillation. The studies reported greater protection of oral anticoagulant (OAC) than platelet drugs or no treatment against stroke even at different risk stages (RRR: 68%; IC 95%: 50%-79% [% of OAC at adjusted doses vs. no treatment]), aspirin vs no treatment: 21% (0%-38%) and OAC at adjusted doses vs aspirin 52% (37%-63%)]. However, globally, the risk of severe hemorrhage was higher with warfarin/acenocumarol than with aspirin (3.30% and 1.83%, respectively), albeit a study reported that the risk could increase in elderly patients (13.08% in those aged 80 or more; 4.7% in those aged <80) and in the early stages of the treatment (58% of hemorrhages in the first 90 days).
2. Contents: information for the patient and for professionals. Graphic design: drawings, graphics, pictures of people featuring the range of situations, and descriptive icons; the numerical expressions were outlined always from the same denominator (100) and in absolute risks.
3. Validate DMT. Results from the pivotal study showed differences in appraising the DMT depending on the patient's sociocultural level (see full report).

NVAF patients treated with anticoagulant or antiplatelet drugs have a lower risk of stroke than those who are not. Patients treated with acenocumarol or warfarin have a lower risk of stroke than those treated with acetylsalicylic acid. The risks of severe hemorrhage are higher in patients treated with anticoagulants than with platelet drugs and increase in relation to age, but the risk of stroke is lower with anticoagulants. DMT is formed by PtDA and IMPr.

Methods

1. Systematic review on the effectiveness and safety of antithrombotic treatments for atrial fibrillation: Followed a Cochrane Collaboration protocol.
2. Contents and the graphic design: Addressed the theoretical proposals on risk reporting. An AETSA Group classified the contents into: Contents for the patient and contents for the professional staff. A specialized company outlined the graphic design. The final outcome was subject to the group's appraisal.
3. Validate DMT. Cognitive surveys to professionals and patients and a survey on aspects of form, legibility, and utility. Escuela Andaluza de Salud Pública (EASP) professionals suggested proposals to improve DMT by means of a group technique. Part of the AETSA group discussed survey results and proposals. Changes were to be included in a new version of DMT.

Written by Teresa Hermosilla Gago, Silvia Vidal Serrano, Mª Luz Buzón Barrera, AETSA, Spain

ISSN 1654-501X

INAHTA Briefs

Issue 2009/146

Title **Efficacy of Laparoscopy in Hepatobiliary Pathology**

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Reference Report no. 2/2008. ISBN 978-84-691-4040-6. www.juntadeandalucia.es/salud/servicios/contenidos/aetsa/pdf/2008_2_Laparoscopia_def.pdf

Aim

To elaborate a critical synthesis of the evidence available on the efficacy of laparoscopic surgery in treating hepatobiliary diseases (including liver resection caused by several indications).

Conclusions

The main nosological entities studied are: cholecystolithiasis, choledocholithiasis, and liver cystic and tumor lesions. Different technical variants are assessed concurrently for every entity.

The report addresses the following questions:

1. What is the efficacy of laparoscopic cholecystectomy?
2. What is the efficacy of laparoscopic treatment of lithiasis of the main bile duct?
3. What is the efficacy of laparoscopic treatment of cystic dilatation of bile duct?
4. What is the efficacy of laparoscopic treatment of liver cysts?
5. What is the efficacy of laparoscopic treatment of liver tumors?
6. What is the efficacy of liver resection through laparoscopic tract?

Evidence on the efficacy of laparoscopic surgery in hepatobiliary pathology, with the exception of laparoscopic cholecystectomy, is scarce and of low methodological quality. This obstructs forming any kind of recommendation except for the need to conduct good quality head-to-head studies to clarify the present uncertainty.

Methods

Cochrane Library Plus 2006, number 1, MEDLINE, and EMBASE, TRIP Database, International Agencies for Health Technology Assessment, Agency for Health Technology Assessment of Instituto de Salud Carlos III, OSTEBA and AATRM. Cohort, case control, transversal studies, and case series that had been published between 1988 and 2006. English or Spanish.

We described systematic reviews, clinical practice guidelines, and clinical trials following the standardized criteria of data extraction and internal validity assessment as proposed by the *Scottish Intercollegiate Guidelines Network*. Where it was necessary to assess cohort and design studies of a lesser level of evidence, the information was summarized using the procedure mentioned above for the other designs, assessing their methodological quality in a similar fashion.

Once the evidence had been analyzed, a summary of the articles was drafted to update every topic section. We classified every type of study and assessed the evidence. To establish the degree of evidence in every type of study, we used a proposal from the Centre for Evidence-based Medicine at Oxford.

We classified the overall quality of the evidence for each intervention as high, moderate, or low. In assessing the overall quality of every endpoint we took into account: the design of the studies, internal validity, assessment of whether the evidence is direct or indirect, the consistency and accuracy of results, and other factors such as possible publication bias.

Written by Carlos Manterola Delgado, Pablo Alonso Coello, Montserrat Tort Donada, Flora Martínez Pecino, AETSA, Spain

ISSN 1654-501X

INAHTA Briefs

Issue 2009/147

Title **Efficacy of Biventricular Pacemakers for Heart Failure**

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Reference Report no. 1/2008. ISBN 978-84-691-4039-0. www.juntadeandalucia.es/salud/servicios/contenidos/aetsa/pdf/2008_1nf_Marcapasos_biventriculares.pdf

Aim

To overview and critically synthesize the best evidence available on the efficacy of biventricular pacemakers or cardiac resynchronization therapy (CRT) in treating chronic heart failure.

Conclusions and results

CRT in addition to traditional treatment reduces mortality for any cause in patients with symptomatic heart failure. The benefit is extensive for patients in functional class NYHA II to IV (New York Heart Association) and evident in the first 3 months of treatment (High quality [HQ]). The benefit is due mainly to reducing mortality from progression of heart failure (HQ). The association of CRT with an implantable defibrillator does not alter the benefit (HQ). Controversy surrounds sudden death since scientific studies report effects opposite to this variable (HQ).

CRT reduces hospitalization from progression of heart failure, yielding higher benefit to patients in functional class NYHA III/IV (Moderate quality).

Regarding parameters in heart failure patients, CRT is associated with an increased distance covered at 6 minutes (Moderate quality [MQ]) and growth in the peak of oxygen uptake (MQ). At 3 months CRT improves the quality of life of heart failure patients when added to traditional treatment. The benefit is higher in CRT patients, but without implantable defibrillator (HQ). CRT is beneficial if complemented with traditional treatment and reduces symptoms in patients with heart failure (HQ). The evidence available and magnitude of benefit are insufficient to confirm a possible clinical relevance of the outcomes.

CRT increases ejection fraction of left ventricle (HQ) and improves other echocardiographic parameters (MQ). CRT reduces duration of QRS interval (MQ).

CRT is safe and well tolerated. Mortality rate is low: after implantation, up to discharge from hospital (lower than 1%), and after discharge from hospital (about 1%).

One in 10 biventricular pacemakers cannot be implanted successfully (HQ). Most severe complications arise from introducing the cable in the left ventricle and include: anomalous position of the cable, perforation of coronary core, and cardiac perforation (HQ).

Methods

We used relevant databases to search the scientific literature (English, Spanish) for studies and summarized the recommendations referring to the review topic. (See full report for details.) Then, each study was classified. To establish the levels of evidence for every type of study, we used the proposal of the CEBM of Oxford. The quality of the evidence for every intervention was classified as high, moderate, or low, and assessed regarding study design, internal validity, direct or indirect evidence, consistency, accuracy of results, etc.

Written by David Rigau Comas, Ivan Solà Arnau, Pablo Alonso Coello, and Flora Martínez Pecino, AETSA, Spain

ISSN 1654-501X

INAHTA Briefs

Issue 2009/148

Title: Diagnostic Performance of Clinical Prediction Models for Pulmonary Embolism

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Reference Report no. 3/2008. ISBN 978-84-691-4638-3. www.juntadeandalucia.es/salud/servicios/contenidos/aetsa/pdf/2008_3_Embolismo_PulM.pdf

Aim

To assess the diagnostic performance of scores or clinical models used to determine pre-test probability in diagnosing pulmonary embolism (PE). To describe other outcomes from the scores or models that differ from the diagnostic performance (DP).

Conclusions and results

The search resulted in 428 references, and 11 original observational studies with no control group were finally included in the review. Most assessed more than one score. The accuracy of the scores as opposed to empiricism was studied in 3 good-quality works. The studies did not find any relevant difference in DP of the 2 options when estimating pre-test probability of PE. When comparing the accuracy of scores, the results varied widely.

The 2-category Wells score was more specific than sensitive in 2 good-quality studies; sensitivity varied in both, from 60% to 62%. Nine studies assessed the 3-category Wells score. Two studies assessed it in groups of patients with low frequency of PE, providing different results on sensitivity (S) and specificity (Sp) (92% of S and moderate Sp in one study, and 54% of S in the other), although both studies coincided in high negative predictive value of the score (>96%). In patients with moderate and high frequency of PE, the studies matched in presenting the 3-category Wells score as more sensitive than specific: S was over 90% in patients with moderate frequency (MF) of PE (two studies), and it ranged from 66% to 91% (5 studies) in patients with high frequency (HF) of PE. The Geneva score, assessed in 5 studies, was more sensitive than specific. Its results matched those of Wells scores favorably in the only study that had applied the score prospectively. Both results achieved S >70%. The DP of Wells algorithm, Charlotte rules, and Rodger and Pisa models were each assessed in one study only. Only the Pisa model proved, in a statistically significant way, a superior DP than Wells and Geneva scores (94% of the area under the ROC curve for this model vs 54% for the Geneva score and 75% for Wells score). Despite being a good-quality study, problems related to external validity jeopardize its applicability. These studies reported no results on clinical effectiveness in applying the scores.

Methods

MEDLINE, ECRI, Cochrane Library, CRD, INAHTA, NGC, and EMBASE. Inclusion criteria: adults with suspected PE, intervention (any tool structured to estimate pre-test probability of PE), gold standard (usual and supplementary tests to diagnose PE and/or 3 months clinical follow-up), results (DP and/or clinical outcomes from applying the scores) and design (CT and observational studies with or without control group). We used the QUADAS tool to critically assess the original studies. The data were summarized qualitatively.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/149

Title **Efficacy and Effectiveness of Screening for Abdominal Aortic Aneurysm in a High-Risk Population. Cost-Effectiveness Analysis. Applicability in the National Health Care Service**

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Reference Report no. INF 2007/01. www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60056&uri=/Docs/Avalia-t/INF2007_01%20CRIBADO%20Aneurisma%20AORTA.pdf&hifr=1000&seccion=0

Aim

To evaluate mass screening for abdominal aortic aneurysm (AAA) in risk groups and its applicability in the National Health Service (NHS).

Conclusions and results

Conclusions: Ample, high-quality, scientific evidence is available. Studies show that AAA screening in men aged 65 to 75 years decreases AAA-associated mortality and follow-up of AAA of 3 to 5 cm. As the follow-up time increases there is a decrease in the number of men to screen and an increase in the number of life-years gained. Open surgery has lower mortality when it is scheduled, but not when it is emergent. Mass screening for AAA by abdominal ultrasound is recommended in men aged 65 to 75 years.

Results: One systematic review, 1 meta-analysis, and 7 retrospective articles that met the selection criteria. The review and meta-analysis analyzed 36 studies, the most important being: Wester (Australia) with 41 000 men aged 65 to 79 years; Chichester (UK) with 6433 men and 9342 women aged 60 to 80 years; Viborg (Denmark) with 12 639 men aged 64 to 73 years; and MASS (UK) with 67 800 men aged 65 to 74 years. All of the studies used ultrasound as the screening method, defining aneurysm as a dilation with a diameter ≥3 cm. The other 7 articles not included in the review or the meta-analysis also used ultrasound screening and defined AAA the same as the previous authors. The current meta-analysis, which includes the later studies, does not modify the conclusions from the previous systematic review and meta-analysis undertaken by the Task Force. The economic evaluation search yielded 222 abstracts, of which 24 were read in full text. Only 13 met the selection criteria, most of which were European (10/13). The most recent studies present the results in AVAG or AVAC, but the studies published before 2000 give results only in terms of costs. The applicability in the NHS was assessed using a theoretical simulation of a program for AAA screening in the Galician Autonomous Community (Spain), where the results advise a screening program since 40 to 42 lives could be saved annually.

Recommendations

Screening is recommended in risk groups, eg, smoking women, men and women older than 50 years with a history of AAA in the first-degree family. It is recommend to follow patients when the AAA is ≥3 cm and to treat with open surgery or EVAR if AAA is 5 to 5.5 cm, grows >1 cm/year, and/or when the patient presents symptoms.

Methods

Scientific literature from 1976 to April 2006 was systematically reviewed in two phases. First search: 1976 to 2005, specific and not exhaustive. Second search: 2005 to April 2006, exhaustive and not very specific. Selection criteria: study design (systematic revisions, clinical meta-analysis, clinical trials, and cohort), outcome measures assessed (reduction of mortality by AAA, long-term survival, quality of life). Literature up to July 2006 was searched for economic studies. Selection criteria: complete economic evaluation in adult populations screened by abdominal ultrasound. There were no language restrictions.

The following databases were searched: MEDLINE, EMBASE, HTA, DARE, NHS EED, Cochrane Collaboration, NIH, CenterWacht, CCT, NCI, Medical Research Council, NTIS, IME (Índice Médico Español-Spanish Medical Index), and NRR. For economic literature: MEDLINE, HTA, DARE, NHS EED, Cochrane Library Extra, IME, and IBECS (Índice Bibliográfico en Ciencias de la Salud).

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/150

Title **Identification, Prioritization, and Assessment of Obsolete Health Technologies. A Methodological Guide**

Agency **AVALIA-T, Axencia de Avaliación de Tecnoloxías Sanitarias de Galicia**
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www.sergas.es/MostrarContidos_N2_T01.aspx?IdPaxina=60570

Aim

To propose a methodology to identify, prioritize, and assess obsolete health technologies.

Conclusions and results

To assess any obsolete health technology, a standardized process that enables *identification, prioritization,* and *assessment* must be established. It is essential to determine the impact to be expected *a priori* from defining any given technology as obsolete, since the greater the impact, the more the health system will benefit from its assessment and subsequent exclusion.

Identification: five potential detection sources, classified as active or proactive, were established. Active sources include: 1) direct consultation of medical literature; 2) consultation of new and emerging technology databases; 3) consultation of systematic reviews; and 4) consultation with secretariats tasked with updating National Health System, hospital, or regional service portfolios. Proactively, networks of health professionals would submit reports on potentially obsolete technologies to HTA agencies or units. After identification of potentially obsolete technologies, assessment agencies would use a standardized procedure to confirm that the technology could be classified as potentially obsolete. It could then be prioritized, or assessed if it had already been prioritized.

Prioritization: to prioritize potentially obsolete technologies for assessment, a prioritization tool (PriTec tool) and a Web application were created. The tool has three domains (population/end-users; risk/benefit; and costs, organization, and other implications) and 10 criteria. The domains are weighted on the scale. Clinicians, managers, and end-users participated in the weighting and in selecting the criteria. Using these results, a Web application in Spanish and English was made available free of charge (via the avalia-t website). It enables up to 50 potentially obsolete health technologies to be compared and prioritized for assessment purposes.

Assessment: to assess a potentially obsolete technology, an assessment-document structure was proposed to compare benefits (efficacy, safety, efficiency, cost, etc) of the potentially obsolete versus the proposed alternative technology. The technology assessment section is based on a systematic review and should meet the requirements of being straightforward, methodical, and reproducible.

Methods

We searched for scientific literature up to April 2009 in specialized databases, eg, HTA, DARE, NHS EED, and Cochrane Plus Library; and in general databases, eg, MEDLINE, EMBASE, IME (Índice Médico Español-Spanish Medical Index), and IBECS (Índice Bibliográfico en Ciencias de la Salud).

We also reviewed several databases and Internet search engines with special emphasis on the websites of national HTA agencies and government bodies, particularly in the area of health services research. We selected records in which any type of obsolete technology was assessed or which contained opinions, ideas, advantages, or limitations concerning any aspect linked to obsolete health technologies. Since we used no inclusion or exclusion criteria, records were selected on the consensus of two authors. In addition to the systematic review, a specific methodology was developed for each of the 3 sections of the guide.

Further research/reviews required

None.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/151

Title **Post-Introduction Observation of Health Technologies. A Methodological Guideline**

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www.sergas.es/MostrarContidos_N2_T01.aspx?IdPaxina=60570

Aim

To establish a structured methodological framework to observe new technologies after their introduction into clinical practice.

Conclusions and results

The specific goals are: 1) to develop a prioritization tool; 2) to identify the most appropriate data-collection instruments for post-introduction observation and their advantages and limitations; and 3) to establish outcome indicators for assessing the different aspects of post-introduction observation.

Post-introduction observation of new technologies is a strategy to complement the procedures implemented to regulate the incorporation and introduction of new technologies. This methodological guideline is the first document published on the topic and could serve as a reference for any national or international body in planning and/or implementing post-introduction observation activities. It provides specific procedures and strategies to plan, implement, and evaluate the utilization of new technologies. The guideline consists of 3 sections. The first section provides the final list of selected prioritization criteria (n=14) and describes the tool developed for prioritizing health technologies susceptible to post-introduction observation. The second section describes and assesses 4 instruments that could be used for data collection, along with an outline of the advantages, drawbacks, and considerations to remember when using them for post-introduction observation purposes. The third section of the guideline lays down the basic requirements for implementing a post-introduction observation system. It also presents 14 specific outcome indicators for assessing the various aspects of post-introduction observation of new technologies.

Recommendations

Apply and adapt post-introduction observation methodology to different contexts.

Methods

The information sources for this guideline are based on systematic reviews and the consensus of experts. The group of experts is comprised of professionals from the various Spanish health technology assessment (HTA) agencies/units. A group of panelists representative of medical managers/administrators, clinicians, and end-users of health services from the different autonomous regions carried out the final selection and weighting of prioritization criteria.

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INAHTA Briefs

Issue 2009/152

Title **Albumin Dialysis and Molecular Adsorbent Recirculating System (MARS®) in the Treatment of Liver Failure**

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Reference Report no. CT 2008/02. www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60058&uri=/Docs/Avalia-t/CT2008_02MARS.pdf&hifr=1200&seccion=0

Aim

To assess the medical efficacy and safety of extracorporeal albumin dialysis using the MARS® system in treating acute liver failure (ALF) and acute-on-chronic liver failure (AoCLF); and to estimate the cost of this technology versus standard medical treatment.

Conclusions and results

Eight randomized clinical trials (RCTs), 1 meta-analysis, and 2 cost-effectiveness studies were selected. The presence of heterogeneity and small sample size were observed in many of the studies included, which hindered proper evaluation of the technique. The MARS® system reduces mortality nonsignificantly, both in patients with acute and those with acute-on-chronic liver failure. Its principal indication would be in patients with severe liver failure, while the organ regenerates or is transplanted. Its use should, in all cases, be limited usually to sessions of 6 to 8 hours daily. This technique can be considered safe and well-tolerated by patients, with adverse effects similar to those that appear in the control group. In addition, it brings about favorable hemodynamic changes in patients, reduces the grade of hepatic encephalopathy and that of plasma concentration of bilirubin and creatinine, though these levels tend to rise when treatment is halted. Bearing in mind that each patient received 3 to 5 sessions, the cost of the technique ranged from 6300 euros (EUR) to EUR 10 500 per patient. The MARS® system yielded a savings of approximately EUR 4000 to EUR 6000 per surviving patient, with the cost per quality-adjusted life-year (QALY) gained being EUR 47 171.

Recommendations

Despite the abundant literature on the use of the MARS® system in liver failure, few quality studies have been done, with many of these displaying methodological limitations. Accordingly, uncertainty continues to surround the efficacy of this technique in treating ALF and AoCLF, and practice guidelines fully supported by scientific evidence cannot as yet be established. If the technique is introduced in the health system, it should be in a restricted way and in selected centers and patients.

Methods

A systematic review was conducted of the scientific literature published from January 1995 to August 2008. From among the papers yielded by the bibliographic search, only those were selected that met a series of selection criteria (study design, patient characteristics, and outcome variables). Data were then extracted and the evidence summarized.

Written by Gerardo Atienza, AVALIA-T, Spain

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INAHTA Briefs

Issue 2009/153

Title **Holmium Laser Enucleation of Benign Prostatic Hyperplasia**

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Aim

To assess the efficacy and safety of holmium laser enucleation of the prostate (HoLEP) versus transurethral resection in treating benign prostatic hyperplasia.

Conclusions and results

Benign prostatic hyperplasia (BPH) is characterized by an increase in glandular size and is one of the most frequent benign tumors in males aged >50 years. Surgical treatment is targeted at improving obstructive urinary symptoms and patients' quality of life, with transurethral resection of the prostate (TURP) constituting the gold standard. Other alternatives developed in recent years include holmium laser technique, which uses energies of 60W to 100W to enable complete enucleation of the prostate.

No significant differences were observed between holmium laser enucleation of the prostate and TURP in maximum urinary flow (Qmax), at either 6 or 12 months of follow-up. Likewise, a subsequent study reported no differences at 3 years of follow-up. Postmictional volume of residual urine (PVR) was lower in the HoLEP group, though this was not clinically relevant, and no differences were observed in urinary symptoms as measured by the International Prostate Symptom Score/American Urological Association (IPSS/AUA) scales. Compared to TURP, HoLEP resulted in less urinary catheterization time and shorter hospital stays and blood loss, albeit at the cost of a longer intervention time. There were no differences vis-à-vis TURP in the appearance of adverse effects, and intervention rates proved similar.

While scientific information shows that HoLEP is at least as effective as TURP, the studies have methodological limitations, which prevent firm conclusions from being drawn. HoLEP reduces patients' obstructive symptoms and, as compared to TURP, yields similar Qmax and better PVR results. No differences were observed between the techniques in sexual function, quality of life, or IPSS/AUA scale assessments. HoLEP is associated with longer intervention time, though with a lower degree of blood loss, hospital stay, and urinary catheterization time than TURP. No differences were observed between techniques in terms of adverse effects and reintervention rates.

Recommendations

Although holmium laser technique cannot be conclusively recommended as treatment for BPH on the basis of current evidence, this technique could be an alternative to TURP in future. Surgical teams need to be adequately trained, and selection criteria need to be established to identify patients eligible for treatment. Should the health system use holmium lasers, follow-up protocols and a register should be created to enable the effectiveness and safety of this technique to be assessed.

Methods

The scientific literature was systematically reviewed, including qualitative and quantitative synthesis (meta-analysis). A first bibliographic search of the Cochrane Library Plus, DARE, HTA, MEDLINE, and EMBASE databases retrieved all published systematic reviews, meta-analyses, and clinical practice guidelines. After these had been evaluated, a quality meta-analysis was selected and updated by conducting a second bibliographic search of general databases (MEDLINE, EMBASE) and repositories of published or ongoing RCTs (Clinical Trials Registry, Cochrane Central Register of Controlled Trials, Current controlled trials, and National Institute of Health Research), to locate randomized controlled clinical trials that compared HoLEP to TURP.

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INAHTA Briefs

Issue 2009/154

Title **Renal Replacement Therapy in Advanced Chronic Kidney Disease. Review of the Starting Criteria in Dialysis Programs and Assessment of the Efficacy and Effectiveness of an Early Start**

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Aim

To analyze, based on residual kidney function, the influence of time of initiation of dialysis on morbidity and mortality in chronic renal failure sufferers during the first years of dialysis; and to assess the influence of initiation of dialysis on patients' quality of life.

Conclusions and results

Early initiation appears to have worse results in hemodialysis than in peritoneal dialysis, with gender and the presence or absence of diabetes being the variables that most influence outcomes. Patients' initial health status and predialysis care are shown to be more relevant than time of initiation of dialysis, highlighting the importance of a programmed initiation of renal replacement therapy (RRT).

A bibliographic search retrieved 1463 studies. Of these, 10 met the selection criteria and were included. No randomized clinical trial (RCT) was retrieved. Studies included had a cohort design. As a patient classification criterion, most studies used a kidney function value of 7 to 10 ml/min, 2 studies used a lower value (5 ml/min), and 2 studies compared different kidney function ranges (<5, 5-10 and >10). Whereas studies that used the highest cutoff points (GFR>10) along with studies that compared different kidney function ranges (<5, 5-10, >10) favored delaying initiation of treatment, studies that used lower values (7-8) coincided in supporting early initiation of therapy. The percentage of patients who initiated unprogrammed treatment rose as high as 57%, which influenced outcomes (mortality, nutritional status, and hospital admission or stay). Only 1 study assessed the influence of date of initiation of dialysis treatment on patients' quality of life. During the first 6 months of treatment, an improvement in quality of life was observed in both groups (ie, early- and late-initiation), with the early-initiation group recording better scores, though these differences disappeared after 1 year. Of a possible 10 points, study quality registered a median score of 5.9 and a mean score of 5.5.

Recommendations

Studies of good methodological quality need to ascertain in which population subgroups early initiation of treatment would be beneficial, and studies need to rigorously assess the quality of life of patients who initiate RRT early.

Methods

We systematically reviewed the scientific literature published until February 2009, targeting: (a) specialized systematic-review databases, eg, HTA (Health Technology Assessment), DARE (Database of Abstracts of Reviews of Effectiveness), NHS EED (National Health Service Economic Evaluation Database), and Cochrane Library Plus; and, (b) general databases, such as MEDLINE, EMBASE and ISI Web of Knowledge (Institute for Scientific Information). The databases of the US National Institutes of Health (Clinicaltrials.gov), the UK National Health Service (National Research Register), and other international registries, eg, CCT (Current Control Trials) and CenterWatch, were also consulted. Two independent reviewers examined and selected the papers separately in accordance with pre-established inclusion and exclusion criteria. This information was summarized in evidence tables. Both researchers assessed study quality by using a specially adapted scale.

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INAHTA Briefs

Issue 2009/155

Title **Lead Extraction of Pacemaker or Implantable Cardiac Defibrillator Leads Using Laser Excimer**

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Aim

To assess the efficacy/effectiveness and safety of using excimer laser to remove pacemaker and automatic implantable defibrillator leads.

Conclusions and results

Using excimer laser to remove pacemaker or implantable cardiac defibrillator leads is considered effective and safe, with a low incidence of failure and complications. It enables leads to be removed in situations where other techniques fail or are contraindicated. In view of the learning curve involved, prior training is required at centers experienced in the technique before the procedure can be implemented and performed.

The bibliographic search retrieved 109 studies, 16 of which met the inclusion criteria. One clinical trial was located, with the remainder corresponding to case-series studies. The technique's efficacy – construed as complete removal of the lead – exceeded 90% according to most studies. Regarding complications, the results of the studies showed that using an excimer laser to remove leads entailed a low complication rate, not exceeding 4% for the most relevant complications.

Methods

A review of the scientific literature was conducted in October 2008 stipulating no time limit and covering the principal databases, which included:

- specialized systematic-review databases, eg, HTA (Health Technology Assessment), DARE (Database of Abstracts of Reviews of Effectiveness), NHS EED (National Health Service Economic Evaluation Database), and Cochrane Library Plus; and,
- general databases, eg, MEDLINE, EMBASE, and ISI Web of Knowledge (WoK).

Papers were reviewed and selected on the basis of pre-established selection criteria. The ensuing information was then summarized in evidence tables.

Written by Cantero Muñoz P and Ruano Raviña A, AVALIA-T, Spain

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INAHTA Briefs

Issue 2009/156

Title **Extracorporeal Liver Support of Liver Failure by Means of Prometheus® System**

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Aim

To assess the medical efficacy and safety of extracorporeal albumin dialysis using the Prometheus® system to treat liver failure.

Conclusions and results

Six case series and 5 randomized clinical trials were selected. No cost-effectiveness studies on this technology were identified. Many of the included studies had methodological limitations, which hindered rigorous recommendations about the effectiveness of this technique in treating liver failure. Data were insufficient to assess the impact of the Prometheus® system on survival. In general, no serious adverse effects were described, with the exception of thrombocytopenia, minor bleeding, and circuit leakages. The Prometheus® system led to a drop in mean arterial pressure, probably due to the distribution of the patients' own albumin within the secondary circuit. This system has the capacity to purify both albumin-bound and water-soluble substances, since clearances are significantly higher compared to treatment with MARS®. We observed significant decreases in the levels of bilirubin, bile acids, ammonium, creatinine, and urea without a significant improvement in the grade of hepatic encephalopathy.

Recommendations

Uncertainty continues to surround the effectiveness of the Prometheus® system in treating acute and acute-on-chronic liver failure. This technology must be considered an experimental treatment modality until more data are available about the different aspects of liver failure.

Methods

We reviewed the scientific literature published from January 1999 to March 2009, searching the following databases: MEDLINE, EMBASE, Health Technology Assessment (HTA), Database of Abstracts of Reviews of Effectiveness (DARE), National Health Service Economic Evaluation Database (NHSEED), Cochrane Library Plus, Clinical Trials Registry, and Health Services Research Projects in Progress (HSPROJ). From among the papers identified in the bibliographic search, we selected only those that met a series of selection criteria. The data were then extracted and the evidence summarized.

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INAHTA Briefs

Issue 2009/157

Title **Clinical Impact of Capsule Endoscopy in Obscure Gastrointestinal Bleeding. Systematic Review**

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www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60056&uri=http://www.sergas.es/Docs/Avalia-t/InfCapEndos.pdf&hifr=900&seccion=0&seccion=0

Aim

To analyze the current state of knowledge for assessing the diagnostic effectiveness and impact of capsule endoscopy on management and clinical outcomes of patients with obscure gastrointestinal bleeding. To analyze the clinical utility of capsule endoscopy if used as a first-line investigation tool, and to identify the subgroup of patients that could most benefit from capsule evaluation.

Conclusions and results

Capsule endoscopy (CE) shows a significantly greater diagnostic yield than other conventional procedures in diagnosing small bowel disease. The results suggest that CE might be superior to double balloon enteroscopy, but these studies obtained quality punctuations lower than 50%. Detection rates appear to be higher in patients with visible bleeding and in patients with more severe disease and longer symptomatology. The diagnostic yields seem to depend on the criteria used to classify subjects and present higher values when insignificant or suspicious lesions are included as positive results than when only relevant lesions are considered.

The real effectiveness of CE is unclear. The results on sensitivity, specificity, and positive and negative predictive values are heterogeneous (sensibility, specificity, positive predictive value and negative predictive values ranged from 69%-100%, 48%-100%, 62%-100% and 78%-100%, respectively) and are based mainly on arbitrary classifications. The impact of CE on patient management and clinical outcomes is unknown. The results are heterogeneous and discrepant in some cases. The relevance of some of the lesions diagnosed has been questioned. Given the information available, it is not clear if CE should be used as a first-line diagnostic tool.

Recommendations

Consensus is needed on what constitutes a relevant and non-relevant lesion. It is difficult to assess the method and compare results since there are no clear and homogeneous criteria across studies.

Methods

The following databases were searched in the systematic review: MEDLINE (PubMed), EMBASE (Silver Platter), ISI Current Contents and ISI WEB OF Knowledge, Cochrane Library Plus, NHS Centre for Reviews and Dissemination, IBECS (*Índice Bibliográfico Español en Ciencias de la Salud*) and IME (*Índice Médico Español*) from Dec 2005 to Nov 2006, and updated weekly until May 2007. The search included grey literature and a manual search of reference lists. Two independent investigators reviewed and selected the articles using predefined selection criteria. The information was synthesized in evidence tables and the quality of the original studies assessed, using two scales to evaluate: a) quality of original studies that assess effectiveness of CE versus other diagnostic methods and b) quality of studies that assess the impact of CE on patient management and clinical outcomes.

Further research/reviews required

Further randomized clinical trials are needed to determine the role of CE in the diagnostic algorithm and assess the value of CE versus other diagnostic techniques in terms of changes in clinical management and resolution of bleeding.

Written by Varela Lema L, Puñal Riobóo J, and Ruano Raviña A, AVALIA-T, Spain

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INAHTA Briefs

Issue 2009/158

Title **Efficacy and Safety of Intragastric Balloon in Obese and Overweight Patients. Systematic Review and Case-Registry**

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Aim

To evaluate the effectiveness and safety of the intragastric balloon in overweight and obese patients. Also, to design a systematic data-capture process and to perform a retrospective case-registry of intragastric balloon (Galician hospitals, 2004-2006).

Conclusions and results

Systematic review. Seven studies were included: 1 clinical trial, 1 cohort study, 1 case-control study, and 4 case-series studies. All showed a decrease in weight (7%-18%) and comorbidities. But the weight reduction did not remain after removing the balloon. Technical complications were few, but minor adverse events were common. *Case-registry*. 69 balloons were implanted in 68 patients (48 F and 20 M) with an average age of 42.1 years (18-68). Mean baseline weight and body mass index (BMI) were 128.6 kg (90.5-196) and 47.4 kg/m2 (34.6-68.5), respectively. A 13% weight reduction was achieved with the intragastric balloon; and BMI decreased 5.3 kg/m2. Both results were statistically significant. Weight was regained after removing the device. Technical complications were few, but minor adverse events were common. There were more major adverse events than expected.

Intragastric balloon (IB) appears to allow weight loss in obese patients, but this loss is not maintained. It should not be the first therapeutic option in obese or overweight patients. (Low-calorie diet, physical activity, and modified eating habits are first.) IB must be combined with other interventions (low-calorie diet, etc). Candidates for surgery could benefit from rapid weight loss from IB since the surgical risk diminishes. No studies compare IB to other weight-loss strategies. Since IB is not absolutely safe, patients must be informed and monitored to avoid or minimize complications. The specific indications for IB are important to define.

Recommendations

Patients should be carefully selected based on degree of obesity and comorbidities (BMI≥40 kg/m2 or BMI≥35 kg/m2 with obesity-related pathology) and on contraindications (eg, hiatal hernia, severe esophagitis). Interventions complementing the procedure should be protocolized (eg, diet, bariatric surgery). Patients should be informed about benefits and risks of IB. To minimize complications, the balloon should not be kept in more than 6 months. Active follow-up is proposed to minimize complications and guarantee withdrawal of the balloon. Centers that offer this method must have well-coordinated multidisciplinary teams for treating obesity. The teams must include endoscopy specialists experienced in the procedure, surgeons experienced in obesity surgery, endocrinologists, dieticians, and staff for psychological support.

Methods

Clinical review: We searched relevant databases to update a previous systematic review (December 2005) with a new review of health literature up to November 2006.

Case-registry: 69 IBs at 2 Galician hospitals were retrospectively analyzed. We designed an on-line database and collected data, eg, on patients' previous conditions, balloon implants, and follow-up.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/159

Title **Efficacy of 123i-ioflupane (DaTSCAN©) on the Diagnosis of Parkinsonism Syndromes. Systematic Review and Case Registry**

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www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60056&uri=http://www.sergas.es/Docs/Avalia-t/InfDatScan.pdf&hifr=900&seccion=0&seccion=0

Aim

To assess the efficacy of DaTSCAN© in diagnosing early Parkinson's disease (PD) and determine the efficacy of 123I-FP in the differential diagnosis of vascular parkinsonism, drug-induced parkinsonism, essential tremor, dementia with Lewy bodies (DLB), and Alzheimer's disease (AD).

Conclusions and results

The scientific evidence available indicates that 123I-FP can be useful to differentiate PD from nondegenerative disorders, eg, vascular and drug-induced parkinsonism, differentiate PD from Alzheimer's disease, and AD from DLB. The case registry showed that ioflupano was more useful in diagnosing patients without response to L-dopa or with postural tremor. 123I-FP could not be indicated correctly in some patients. In this registry, a change in the diagnosis was observed in 33% patients and a change in therapy in 51% at 1-year follow-up.

Recommendations

DaTSCAN© seems to show a greater clinical utility when it is used in patients with suspicious early PD, especially when symptoms have started in the previous 1 to 2 years, but it is not useful in patients with advanced PD and responsiveness to L-DOPA.

Methods

We used the following databases to systematically search the literature: Cochrane Library Plus, NHS Centre for Reviews and Dissemination that included the HTA (Health Technology Assessment), DARE (Database of Reviews of Effectiveness) and NHS EED (Economic Evaluation Database), MEDLINE (PubMed), EMBASE (Silver Platter), ISI Web of Knowledge, Tripdatabase, and Clinicaltrials.gov. Nine articles were included in the systematic review (5 cohort studies and 6 cross-over clinical trials). A case registry was performed in collaboration with 4 Galician hospitals. We used statistical software (SPSS 12.0) to analyze the information.

Further research/reviews required

High-quality studies are necessary to assess the diagnostic efficacy of DaTSCAN© to differentiate between movement disorders.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/160

Title **Autologous Chondrocyte Implant (ACI). A Systematic Review**

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www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60518&uri=/Docs/Avalia-t/InfImpCondroc.pdf&hifr=1000&seccion=0

Aim

To assess the efficacy, safety, and costs of autologous chondrocyte implants (ACI) and matrix-induced ACI (MACI) in treating knee and ankle chondral lesions.

Conclusions and results

ACI has yet to be proven more effective than other procedures for knee osteochondral lesions. In the short term (2-3 years), ACI and MACI patients' knee conditions improve. ACI is a safe procedure. Nevertheless, the new variant (MACI) could be safer since it presents fewer hypertrophy-related adverse events.

Two independent investigators used previously established criteria in selecting 24 articles (3 clinical trials, 2 cohort studies, 15 case series studies, 3 systematic reviews, and 1 economic evaluation). Two clinical trials compare ACI with its variant MACI, and the third trial compares ACI with mosaicplasty. One cohort study evaluates ACI against debridement, while the other assesses different ways of implementing ACI. One study was related to the ankle joint, and another one was an economic evaluation, although a systematic review also includes an economic model.

Recommendations

The effectiveness of ACI and MACI has yet to be proven through randomized clinical trials addressing both knee and ankle joints. Patients with associated joint diseases need to have undergone correction of those in conjunction with ACI.

Methods

MEDLINE, EMBASE, ISI WoK, HTA, DARE, NHS EED, Cochrane Library, and other databases were used in a systematic review of the literature. Two independent researchers selected and reviewed the papers according to previously established selection criteria, and the information was synthesized in evidence tables.

Written by Alberto Ruano-Ravina, AVALIA-T, Spain

ISSN 1654-501X

INAHTA Briefs

Issue 2009/161

Title **Clinical Effectiveness of Newborn Screening for Inborn Errors of Metabolism Using Tandem Mass Spectrometry. Systematic Review**

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www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60056&uri=http://www.sergas.es/Docs/Avalia-t/InfTandem.pdf&hifr=900&seccion=0&seccion=0

Aim

To analyze the state of knowledge on the efficacy/effectiveness of neonatal screening of hereditary metabolic diseases, using tandem mass spectrometry; and to compare the neonatal screening services offered in Spain's various Autonomous Regions (ARs).

Conclusions and results

Of 305 studies retrieved in the second search, 9 were included. Many were lacking in quality, and outcome variables and study populations were heterogeneous. MS/MS sensitivity, specificity, and PPV values varied depending on the inborn errors of metabolism (IEM) (sensitivity 91.7%-100%; specificity 99.3%-99.9%; and PPV 2.0%-53%). While the introduction of screening for phenylketonuria (PKU) and medium chain acyl coenzyme A dehydrogenase (MCAD) deficiency yielded benefits in morbidity-mortality, the evidence was unclear for glutaric acidemia type I and tyrosinemia type I. Current knowledge does not support inclusion of the remaining IEM in neonatal screening programs. In Spain, 21 laboratories serve the neonatal screening programs in the ARs.

- The quality and heterogeneity of existing studies on MS/MS-based detection of IEM render comparison difficult and prevent definitive and categorical conclusions on the different aspects assessed.
- MS/MS has a potential for simultaneous detection of a wide range of IEM. It is a rapid and highly sensitive and specific technology for detecting MCAD deficiency and PKU, with these being the best candidates for inclusion in a MS/MS-expanded screening program. Doubts exist as to glutaric acidemia type I and tyrosinemia type I, and no evidence supports the inclusion of the remaining IEM.

Recommendations

- Any decision to include a given disorder in a neonatal screening program must be based on screening's ability to favorably alter the prognosis following early detection and intervention.
- As a priority, it is necessary to draw a portfolio of services in the context of early detection of IEM, based on systematic assessment of their effectiveness and social efficiency. Different aspects of the screening programs in Spain must be standardized by defining common criteria for outcome variables, quality control indices, specimen storage, and incorporating new disorders into screening.
- It is advisable to establish a case registry to enable active and regular follow-up of patients with confirmed diagnoses of IEM which, for healthcare, teaching, and research purposes, would pool information on incidence, trends, survival, etc linked to neonatal screening of metabolic diseases.

Methods

A systematic literature review covered the main biomedical databases. An initial bibliographic search retrieved 6 systematic reviews, whereof the 2004 *NHS R&D Health Technology Assessment Programme* best suited our objectives and was updated accordingly. In the second search, we selected papers using inclusion and exclusion criteria on study design, patient characteristics, and outcome variables analyzed. Data sources included MEDLINE, EMBASE, Cochrane Library Plus, NHS Centre for Reviews and Dissemination, Health Technology Assessment (HTA), and DARE.

Further research/reviews required

Further studies must ascertain the sensitivity and specificity of tandem mass spectrometry in detecting other IEM by assessing the long-term effectiveness of diagnostic strategies and conventional treatment, and the potential impact of early diagnosis using MS/MS.

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ISSN 1654-501X

INAHTA Briefs

Issue 2009/162

Title **Early Detection of Mucopolysaccharidosis and Oligosaccharidosis by Population Screening in the Newborn Period. Systematic Review**

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www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60056&uri=http://www.sergas.es/Docs/Avalia-t/InfMucopolisac.pdf&hifr=900&seccion=0&seccion=0

Aim

To systematically review the efficacy and effectiveness of neonatal mucopolysaccharidosis (MPS) and oligosaccharidosis screening, using tandem mass spectrometry or other analytical techniques.

Conclusions and results

Conclusion: The lack of quality studies that analyze the different aspects of neonatal mucopolysaccharidosis and oligosaccharidosis screening means that their inclusion in neonatal screening programs of congenital errors of metabolism cannot be recommended. Selective performance of diagnostic tests for MPS and oligosaccharidosis would, however, appear wise among patients judged to be at risk, specifically, those who present with metabolic disorders or scant weight gain at birth or in the first weeks of life. To enable active and regular follow-up in such cases, it is advisable to establish a case registry, which for healthcare, teaching, and research purposes would pool information on incidence, trends, survival, and other aspects linked to neonatal screening of these diseases.

Results: Of the papers retrieved in the bibliographic search, 35 were selected (4 clinical trials, 24 case series, 7 single cases). Diagnosis (10 papers) was performed by enzymatic activity assay of deficient blood enzyme (Delfia, tandem mass spectrometry, multiplex or fluorescence) or detection of urinary glycosaminoglycans (dimethyme thylene blue, Alcian blue or bidimensional electrophoresis). Treatment (25 papers) consisted of: enzyme replacement therapy with laronidase (MPS I), rhASB (MPS VI) and idursulfase (MPS II); hematopoietic stem cell transplantation (MPS I, MPS VII, aspartylglucosaminuria, fucosidosis); umbilical cord blood transplantation (MPS I); bone marrow transplantation (eg, MPS I, MPS VI, MPS VII); and peripheral-blood stem cell transplantation.

Recommendations

Epidemiological studies should be conducted to enable us to ascertain the distribution and frequency of these diseases, the validity of diagnoses based on enzymatic determination with tandem mass spectrometry, and the cost effectiveness of the new therapies. We should take advantage of the experience of existing screening teams and routine collection of specimens on paper strips to design and undertake parallel studies (aimed at long-term assessment of results and enabling a definitive conclusion to be arrived at regarding the use of these techniques and implementation of this type of screening in the context of a neonatal program).

Methods

Systematic review of literature from January 1996 to December 2006. Papers were selected using inclusion and exclusion criteria based on study design, patient characteristics, and outcome variables analyzed. Two reviewers, independently, carried out the selection of the studies, critical reading, data extraction, and evaluation of the methodological quality.

Further research/reviews required

The main biomedical databases used were MEDLINE, EMBASE, NHS Centre for Reviews and Dissemination, Health Technology Assessment (HTA), Database of Abstracts of Reviews of Effects (DARE) and Cochrane Library Plus.

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INAHTA Briefs

Issue 2009/163

Title **Intraoperative Radiotherapy in Pancreatic Cancer**

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www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60058&uri=/Docs/Avalia-t/CT2007_01%20RIO%20cancer%20de%20pancreas.pdf&hifr=800&seccion=0

Aim

To assess the efficacy, effectiveness, and safety of intraoperative radiotherapy (IOR) in treating pancreatic cancer; and to estimate the survival of patients with pancreatic neoplasm that have received treatment with IOR.

Conclusions and results

No evidence clearly shows the greater effectiveness of IOR in treating pancreatic cancer versus other treatments in locally advanced and metastatic stages. The quality of life of treated patients is unknown.

Thirteen papers met the pre-established selection criteria. One of the studies was an IOR assessment report, 4 were retrospective cohort studies, and the remaining 8 were case-series studies, 2 of which belonged to the same series. In general, these studies showed that IOR could slightly increase survival among patients with pancreatic cancer in localized stages. However, the results did not conclusively favor IOR for pancreatic cancer in locally advanced and metastatic stages. None of the published studies assessed quality of life.

Methods

The following resources were searched: MEDLINE, EMBASE, ISI Web of Science, Cochrane Library Plus, NHS Centre for Reviews and Dissemination (including the DARE, NHS EED and HTA databases), and Trip Database. Other secondary databases and sources were also searched. The citation lists of all relevant articles were examined to assure complete retrieval of studies.

Two independent researchers selected and reviewed the papers according to previously established selection criteria, and the information was synthesized in evidence tables. Study quality was evaluated by using a scale specifically designed for this report.

Further research/reviews required

Recommended update in 2 years.

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INAHTA Briefs

Issue 2009/164

Title **Intraoperative Radiotherapy in Soft Tissues Sarcomas**

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Reference Report no. CT 2007/02.
www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60058&uri=/Docs/Avalia-t/CT2007_02 RIO sarcomas de partes blandas.pdf&hifr=800&seccion=0

Aim

To assess the efficacy, effectiveness, and quality of life of intraoperative radiotherapy in treating soft tissues sarcomas; and to assess the safety of this treatment.

Conclusions and results

The published evidence does not clearly show better survival from intraoperative radiotherapy compared with other procedures for soft tissue sarcomas. It could lower the risk of local recurrence in highly selected patients. Intraoperative radiotherapy is a relatively safe procedure.

Twelve studies and a systematic review were included. Most of the studies were case series without a comparison group. The studies showed different survival depending on the sarcoma location and its extension. The most frequent adverse effects relate to tissue dehiscence and ischemic processes. Periferic neuropathy can also present in some types of sarcomas. None of the results address quality of life, and the quality of the published studies is poor.

Methods

The following resources were searched: MEDLINE, EMBASE, ISI Web of Science, Cochrane Library Plus, NHS Centre for Reviews and Dissemination (including the DARE, NHS EED, and HTA databases), and Trip Database. Other secondary databases and sources were also searched. The citation lists of all relevant articles were examined to assure complete retrieval of studies.

Two independent researchers selected and reviewed the papers according to previously established selection criteria, and the information was synthesized in evidence tables. Study quality was evaluated using a scale specifically designed for this report.

Further research/reviews required

Recommended update in 2 years.

Written by Alberto Ruano-Ravina and Miguel Conde-Rodríguez, AVALIA-T, Spain

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INAHTA Briefs

Issue 2009/165

Title **Effectiveness and Safety of Real Time Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration**

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www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60058&uri=/Docs/Avalia-t/CT2007_03%20EBUS%20TBNA.pdf&hifr=1000&seccion=0

Aim

To assess the effectiveness of real-time endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in different pathologies compared to other available techniques for lymph node staging; and to assess the safety of real-time EBUS-TBNA in different pathologies.

Conclusions and results

1) EBUS-TBNA appears to be a safe and highly sensitive and specific technique for examining and staging mediastinal and hilar lymph nodes in patients with known or suspected lung malignancy; 2) this technique could decrease the overall number of procedures needed for staging/diagnosing lymph nodes and replace invasive techniques, but negative results always must be confirmed; 3) it is not yet possible to establish the exact place of EBUS-TBNA in the algorithm for suspected lung cancer or mediastinal staging or assess its usefulness for estimating prognoses or guiding the choice of treatment; 4) the evidence is insufficient to determine its use in other pathologies, eg, sarcoidosis or lymphoma.

The 13 original studies showed that sensitivity (Se) for EBUS-TBNA ranged from 85% to 100% and negative predictive value (NPV) from 11% to 97.4%. Specificity (Sp) and positive predictive value (PPV) were 100% in all studies. One study found that the Se, Sp, PPV, and NPV found for EBUS-TBNA was significantly greater than that of combined CT and FDG-PET. Another study compared EBUS-TBNA to EUS-FNA. The Se, Sp, and NPV of these techniques were 85%, 100%, and 72% and 80%, 100%, and 62%, respectively. The accuracy of the combined approach was 100%.

An evidence-based clinical practice guideline on the initial diagnosis of lung cancer recommended that EBUS-TBNA could be one of the confirmation techniques in patients with suspected small cell lung cancer based on radiographic and clinical findings, in patients with extensive infiltration of the mediastinum based on radiographic findings, and in patients with lesions in multiple sites that are suspected of metastases, but in whom the biopsy of a metastic site would be technically difficult.

Methods

Systematic literature review conducted in November 2007, without time limits, in the following databases: MEDLINE, EMBASE, ISI Web of Knowledge, Cochrane Library Plus, NHS Centre for Reviews and Dissemination, and Tripdatabe. Articles were selected based on previously established inclusion/exclusion criteria. The search included grey literature and a manual search of reference lists.

Further research/reviews required

Further studies are needed to assess the real value of EBUS-TBNA compared to conventional (PET, TC) and new techniques (EUS-FNA, CT fluoroscopy-guided TBNA, electromagnetic navigation) used for diagnosis and lymph node staging and establish the diagnostic algorithm for suspected lung cancer and mediastinal involvement. Adequate follow-up studies are needed to determine its usefulness in estimating prognoses and guiding treatment choices.

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INAHTA Briefs

Issue 2009/166

Title **Photoselective Vaporization for Benign Prostatic Hyperplasia with KTP (Potassium-Titanyl-Phosphate) Laser or GreenLight**

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Reference Report no. CT 2007/04.
www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60058&uri=/Docs/Avalia-t/CT2007_04%20Laser%20Verde.pdf&hifr=900&seccion=0&seccion=0

Aim

To assess the efficacy, effectiveness, and safety of selective photovaporization using KTP or green laser in treating benign prostatic hyperplasia (BPH).

Conclusions and results

The bibliographic search retrieved 155 studies, of which 25 met the inclusion criteria. Most of the primary studies had a short follow-up time and corresponded to case series, except for one case-control study and a randomized controlled clinical trial (the latter study displayed low-quality methodological design and reported only preliminary results).

In the subjective (International Prostatic Symptom Score – IPSS- questionnaire and QoL) and objective (Qmax, VPR) parameters studied, the following improvements were observed when comparing preoperative and postoperative values: 49% to 88% in the IPSS; 86% to 93% in QoL; 150% to 246% in Qmax; and maximum values in VPR. As regards complications, the results of the respective studies showed low complication rates with the 80W green laser in both low- and high-surgical-risk patients (with oral anti-coagulants or large prostate volumes) thanks to its hemostatic properties and swift ablation of tissue with no increased risk of perioperative bleeding.

Evidence on the efficacy, effectiveness, and safety of treating BPH using 80W KTP or green laser is of low quality and based largely on uncontrolled clinical series and short follow-up times. Study results indicate that this technique is effective, leads to significant improvements in IPSS, Qmax, and VPR, requires a short hospital stay, and entails prompt withdrawal of the urethral catheter. Drawbacks include its unsuitability for taking histopathological specimens and the complexity involved in performing a total ablation of prostatic tissue.

It is a safe technique that has a low complication rate, requires no blood transfusion, and can be performed in the absence of postresection transurethral reabsorption syndrome. The most frequent complications are dysuria, polakyuria, retrograde ejaculation, urethral constriction, clot retention, and hematuria. The procedure can be performed with minimal risk of bleeding in patients having high surgical risk, oral anticoagulation therapy, or large glands. GreenLight laser has a short learning curve, but should nonetheless be performed by professionals with experience in the technique.

Further research/reviews required

Studies of good methodological quality are called for, as is a cost-effectiveness study to compare the results of this technique against those of transurethral resection of the prostate, the gold standard for treating BPH.

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INAHTA Briefs

Issue 2009/167

Title **Strategies for the Diffusion and Dissemination of Health Technology Assessment (HTA) Products**

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www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60570&uri=/docs/Avalia-t/EstDifMemFinal.pdf&hifr=1250&seccion=0

Aim

To analyze experiences in diffusion and dissemination of products issued and activities undertaken by HTA agencies and units at home and abroad.

Conclusions and results

Study results were divided into: Country-Specific Experiences and HTA Experience in Spain.

Country-Specific Experiences. We identified 37 agencies. The results were as follows:

Type of document: a percentage breakdown showed assessment reports (ARs) as being drawn up by all but one agency, CTs (38.88%), TDs (33.33%), CPGs (27.77%) and other types of documents (27.77%).

Audience: divided into administrative (100%), legislative (85.72%), clinical (82.85%), consumer (40%), and industrial segments (11.42%). Some agencies had included other profiles, eg, research community (17.45%), media (1.42%), and medical industry (8.57%).

Diffusion and dissemination strategies: all but one agency had their own Web pages. The language available was that of the country concerned, with English added in 69.4% of cases. Of all agencies, 48.38% reported publishing scientific papers, 32.25% reported publishing communications delivered to meetings, and 25.80% reported using the media. All had documents in specialized databases, but 5 agencies had no presence in general databases, 2 had no documents in MEDLINE, and 6 agencies had no presence in the Web of Knowledge database. Among their annual tasks, 21 agencies listed the provision and/or coordination of continuing education courses.

HTA Experience in Spain. The results obtained from this study were:

Type of document: ARs (100%), CTs (28.57%), and TDs (57.14%). Practically all agencies reported sporadically producing methodology documents, but only I+CS had compiled these documents into a formal series. In every case the complete text was available on the Internet in Spanish and/or the official language of the Autonomous Region (*comunidad autónoma)* in question.

Audience: legislative and administrative (100%), clinical (100%), general public (25%), and industrial (12.5%) audiences have been identified. In addition, other previously ignored sectors were located, eg, academics (12.5%) and the media (25%).

Diffusion and dissemination strategies: except for I+CS, Web pages were the most widely used method. All were available in Spanish, and four agencies also offered Web pages in English. Eight agencies reported publishing their studies in scientific papers and presenting their results at conferences, meetings, and symposia. All agencies had educational programs, eg, through participation in postgraduate courses.

Agencies focus their work on assessment reports, followed by technical consultation and technical dossiers. These documents target mainly an administrative audience. Apart from abridged and complete versions there appears to be no format specifically adapted to these users. The clinical audience ranks second, where the focus tends to center on clinicians. Other users (research community, media, etc.) appear to be sporadically reflected. Web pages are widely used and include information on mission, structure, and activities. Yet, users are seldom clearly specified. Nearly all of these documents are present in specialized databases, but not always in general databases.

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INAHTA Briefs

Issue 2009/168

Title **Endobronchial Valves in the Treatment of Diffuse Heterogeneous-Type Pulmonary Emphysema**

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www.sergas.es/MostrarContidos_N2_T01.aspx?IdPaxina=60058

Aim

To assess the efficacy and safety of reduction in pulmonary volume by bronchoscopic implantation of endobronchial valves in treating diffuse heterogeneous-type emphysema resistant to conventional medical treatment at maximum doses.

Conclusions and results

The following were selected: 3 case series and the randomized Emphasys Bronchial Valve for Emphysema PalliatioN Trial (VENT Study), undertaken using the Zephyr valve. At 6 months, the Zephyr group in this trial registered a 5.6 times higher risk of death or severe complications than did the control group. This risk declined to 2.23-fold at 12 months. Similarly, the Zephyr group displayed more COPD-related complications and thoracic-pulmonary problems than did the control group ($p<0.01$). The Zephyr group showed statistically significant improvements in forced expiratory volume (FEV1) versus the control group, with no differences observed in the other variables. Only 20% of the Zephyr group registered clinically significant improvements in FEV1 (>15%) versus 7.9% in the control group ($p=0.016$). During the procedure, 14.8% of valves were discarded, essentially due to problems in placement. This led to placement being modified by fitting a calibrator into the catheter holder. Bearing in mind that, on average, 3.8 valves were inserted into each patient, the estimated cost was about 21 333 euros (EUR) per patient.

The studies in this review were few and suffered from methodological shortcomings. Hence, rigorous conclusions cannot be drawn about the effectiveness and safety of endobronchial valves in treating diffuse heterogeneous-type emphysema. Treatment using endobronchial duckbill valves reflects a significantly higher number of adverse effects and rehospitalizations than what was observed for the control group. Reports of the preliminary results of the VENT study do not reflect overall clinically significant improvements among patients with diffuse heterogeneous-type emphysema. The procedure appears to display differing efficacy in line with patients' baseline status and the treatment strategy used. The current dearth of studies renders it impossible to draw conclusions about endobronchial umbrella valves.

Recommendations

Available scientific information does not allow for endobronchial duckbill valves to be recommended in treating diffuse heterogeneous-type emphysema. Moreover, the efficacy or appropriateness of these devices should be assessed in the context of other possible indications, eg, overdistension of the native lung following single-lung transplantation owing to emphysema or persistent bronchopleural fistulae irresolvable by surgical treatment.

Methods

The scientific literature was reviewed, stipulating no time limit and covering the following databases: MEDLINE; EMBASE; HTA (Health Technology Assessment); DARE (Database of Abstracts of Reviews of Effectiveness); NHSEED (National Health Service Economic Evaluation Database); Cochrane Library Plus; CSIC-Cindoc (*Consejo Superior de Investigaciones Científicas-Centro de Información y Documentación Científica*); and the Clinical Trials Registry. From the papers yielded by the search, we selected those that met the selection criteria, extracted data, and summarized the evidence.

Further research/reviews required

Quality studies of sufficient statistical robustness need to furnish definitive data on the efficacy and safety of this technique and enable firm conclusions to be drawn.

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INAHTA Briefs

Issue 2009/169

Title **Lung Cancer Screening**

Agency **AVALIA-T, Axencia de Avaliación de Tecnoloxías Sanitarias de Galicia**
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www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60056&uri=/docs/Avalia-t/CribCancerPulmonMemFinal.pdf&hifr=1250&seccion=0

Aim

To analyze the effectiveness of the different lung-cancer screening tests proposed (low-resolution computerized helical tomography, chest radiography, and sputum cytology) for early diagnosis of lung cancer; to ascertain the potential of other screening tests; and to estimate the population eligible for lung cancer screening in Spain, in total and by autonomous region (*comunidad autónoma*).

Conclusions and results

a) Since no lung cancer screening tests reduce mortality or increase the proportion of cures, the implementation of a lung cancer screening program is not to be recommended. b) The most appropriate method of lung cancer screening is selective screening of smokers. c) Of the tests available, imaging tests are the most appropriate for hypothetical screening. Computerized tomography is the test that affords greatest sensitivity and specificity. d) Imaging tests involve exposure to radiation. Care is called for when conducting repeated imaging tests and proper assessment should determine whether these are really necessary. e) Studies published on lung cancer screening display methodological deficiencies, and the presence of biases that may affect the results cannot be ruled out.

Recommendations

The best way to prevent lung cancer is to refrain from smoking. It is more useful to invest lung cancer screening program resources in well-designed smoking prevention and cessation programs. To ascertain the true efficacy of available lung cancer screening tests, well-designed randomized trials are needed, with uniform, sufficiently long follow-up periods and well-defined final points. The NELSON study and National Lung Screening Trial (NLST) will furnish sound data for measuring the efficacy of screening with low-dose computerized tomography. More detailed information is required on the characteristics of those smokers who would be best suited for inclusion in a lung cancer screening program.

To ascertain the effectiveness of a hypothetical screening program in Spain, good data are required on population tobacco use at a national level, broken down by autonomous region, intensity of tobacco habit, sex, and age. It would also be useful to have unified, population-based data on national and regional lung cancer mortality and incidence.

Methods

We conducted a systematic review of the scientific literature published until January 2009, targeting different databases, namely: a) specialized systematic-review databases; b) specific databases for Clinical Practice Guidelines; c) general databases, eg, MEDLINE (PubMed), EMBASE, ISI WEB of Knowledge, and Spanish medical index; and d) specialized Web pages. Specific search strategies were drawn up for each database using the relevant descriptors and different key words. Two independent reviewers examined and selected papers retrieved in accordance with pre-established selection criteria that specified, eg, language, design and type of publication, sample size and study objective. To ascertain the number of persons eligible for screening in Spain, by sex and autonomous region, we obtained data on the population aged 50 to 74 years, prevalence of smokers, and prevalence of smokers of over 20 cigarettes/day. This information was used to calculate how many smokers ought to be screened under a hypothetical lung cancer screening program.

Further research/reviews required

This report should be reviewed and revised in 2011, when there are new data on published studies and the effectiveness of any new biological or imaging tests.

Written by Alberto Ruano-Ravina, AVALIA-T, Spain

ISSN 1654-501X

INAHTA Briefs

Issue 2009/170

Title **Permanent and Semi-Permanent Dermal Fillers**

Agency **ASERNIP-S, Australian Safety and Efficacy Register of New Interventional Procedures – Surgical**
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Reference Report no. 55. ISBN 978-0-9806299-4-1.
www.surgeons.org/AM/Template.cfm?Section=ASERNIP_S_Publications&CONTENTID=30892&TEMPLATE=/CM/ContentDisplay.cfm

Aim

To assess the safety and efficacy of injectable semi-permanent and permanent dermal fillers compared to other injectable methods of facial augmentation for age-related wrinkle reduction, and for aesthetic improvement of human immunodeficiency virus (HIV)-associated facial lipoatrophy.

Conclusions and results

For-age related lines and wrinkles, and for HIV-associated facial lipoatrophy patients, permanent and semi-permanent dermal fillers increased skin thickness or improved subjective ratings of appearance and resulted in high patient satisfaction.

Long-term efficacy data were scarce, but appeared good in the few studies reporting it. The level of adverse-event reporting for both interventions varied greatly. Many adverse events were transient and mild, and most were associated with the injection process and resolved within a matter of days. Many of the studies in the review reported lumps, but this received little follow-up. Long-term safety was limited and hence could not be determined. The included studies varied in quality and did not employ similar study protocols. This variation prevented statistical pooling and limited the conclusions that could be drawn.

Methods

Studies were identified by searching EMBASE, CINAHL, PubMed, Cochrane Library, and Current Contents from inception to July 2008. Additional articles were identified through references in the retrieved studies. Twenty studies were included in this review, including 4 RCTs, 1 pseudo-RCT, and 2 nonrandomized comparative studies. Data from the included studies were extracted by an ASERNIP-S researcher using standardized data extraction tables developed *a priori* and checked by a second researcher. Statistical pooling was not appropriate due to the study and result heterogeneity.

Further research/reviews required

Long-term safety and efficacy, including quality of life outcomes, of permanent and semi-permanent dermal fillers. The development, and/or validation of assessment tools for use in cosmetic intervention studies. Development of training standards to aid physicians with injection techniques and product placement.

Written by Lana Sturm, ASERNIP-S, Australia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/171

Title **Systematic Review Update: 64-Slice or Higher Computed Tomography Angiography in the Investigation of Patients with Suspected Coronary Artery Disease**

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Reference HSAC Report 2009; 2(12). ISBN 978-0-9864551-7-9 (Online). ISSN 1178-5748 (Online)

Aim

To summarize the recent evidence pertaining to the clinical effectiveness of 64-slice, or higher, computed tomography angiography (CTA) as an alternative to invasive coronary angiography (ICA) in investigating patients with suspected coronary artery disease (CAD).

Conclusions and results

This report systematically reviewed the evidence for 64-slice CT angiography as a triage tool to identify significant stenosis (≥50%) in patients presenting with suspected CAD. In general, the pooled results of this meta-analysis update demonstrated the high diagnostic accuracy of 64-slice CTA in patients with suspected CAD. The included trials showed remarkable consistency in the sensitivity and NPV, considered the most important measures for this technology within this context. The base case meta-analysis (ie, studies with equivocal test results omitted excluded) at the patient-level, indicated a sensitivity of 98.2%, specificity of 81.6%, PPV of 88.9%, NPV of 96.8%, and overall diagnostic accuracy of 91.6%. Pooled diagnostic performance results at the vessel and segment level supported the patient-level findings. In all vessels, the pooled sensitivity was 95.0%, specificity 85.2%, PPV 69.4%, NPV 97.9%, and diagnostic accuracy 87.7%. At the individual artery level, overall diagnostic accuracy appeared to be slightly higher in the left and right coronary artery and slightly lower in the left anterior descending and circumflex. There has been considerable enhancement in temporal and spatial resolution of CTA over the past few years, and these improvements appear to have contributed to the fact that CTA now preserves a high rate of evaluable patients.

Methods

This systematic review update was based on a health technology assessment performed in the United Kingdom (UK) by Mowatt and colleagues (2008). A systematic method of literature searching and selection was employed in preparing this review update, with searches limited to English language material published from December 2006 onwards. The reference lists of key papers were searched to identify any peer-reviewed evidence that may have been missed in the literature search. The search identified 1438 citations. After applying study selection criteria, 28 studies were included for review. The included studies were quality assessed using the NHMRC diagnostic levels of evidence and a modified version of the QUADAS tool. Data were extracted onto specifically designed data extraction forms, and a summary of the study characteristics and calculated diagnostic performance (ie, sensitivity, specificity, positive predictive value [PPV], negative predictive value [NPV] and overall diagnostic accuracy) were provided in the results section. Results were also meta-analyzed and pooled sensitivity, specificity, PPV, NPV, and diagnostic accuracy results were presented at the patient, vessel, and segment level.

Written by Dan Paech, HSAC, Australia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/172

Title **Systematic Review and Individual Patient Data Meta-Analysis of Diagnosis of Heart Failure, with Modeling of the Implications of Different Diagnostic Strategies in Primary Care**

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Reference Volume 13.32. ISSN 1366-5278. www.hta.ac.uk/project/1509.asp

Aim

To assess the accuracy of clinical features and investigations in diagnosing heart failure and to determine: (1) whether a clinical scoring system based on symptoms and signs can usefully predict the presence of heart failure; (2) the optimum cut-off points for plasma natriuretic peptides (BNP); (3) whether diagnostic performance of BNP varies according to patient characteristics; and (4) the accuracy of the combination of BNP and electrocardiography (ECG).

Conclusions and results

In the systematic review, dyspnea was the only symptom or sign with high sensitivity (89%), but it had poor specificity (51%). Several clinical features had relatively high specificity, including history of myocardial infarction (89%), orthopnea (89%), edema (72%), elevated JVP (70%); cardiomegaly (85%), added heart sounds (99%), lung crepitations (81%), hepatomegaly (97%). However the sensitivity of all these features was low, ranging from 11% (added heart sounds) to 53% (edema). ECG, BNP, and NT-proBNP all had high sensitivities (89%, 93%, 93% respectively). CXR was moderately specific (76%-83%), but insensitive (67%-68%). BNP was more accurate than ECG, with a relative diagnostic odds ratio of ECG/BNP of 0.32, 95% CI 0.12–0.87. There was no difference between the diagnostic accuracy of BNP and NT-proBNP. In the individual patient data analysis, a model based upon simple clinical features (male gender, history of myocardial infarction, basal crepitations, edema) and BNP derived from one data set was found to have good validity when applied to other data sets, with AUC between 0.84 and 0.96, and reasonable calibration. A model substituting ECG for BNP was less predictive. From this, a simple clinical rule was developed:

In a patient presenting with symptoms such as breathlessness in which heart failure is suspected, refer straight to echocardiography if the patient has any one of: 1) history of MI, OR 2) basal crepitations, OR 3) male with ankle edema. See Executive Summary link at www.hta.ac.uk/project/1509.asp.

Recommendations

1) Patients with symptoms suggestive of heart failure, eg, breathlessness, should be referred straight for echocardiography if they have a history of myocardial infarction, or if they have basal crepitations on examination, or if they are male with ankle edema. 2) Otherwise, they should have a BNP test, and the decision to refer for echocardiography should depend on this result. 3) There is no need to perform an ECG as part of the assessment to determine whether or not heart failure is present.

Methods

See Executive Summary link at www.hta.ac.uk/project/1509.asp.

Further research/reviews required

See Executive Summary link at www.hta.ac.uk/project/1509.asp.

Written by Prof Jonathan Mant, University of Cambridge, UK

ISSN 1654-501X

INAHTA Briefs

Issue 2009/173

Title **A Multicentre Randomized Controlled Trial of The Use of Continuous Positive Airway Pressure and Non-Invasive Positive Pressure Ventilation in the Early Treatment of Patients Presenting to the Emergency Department with Severe Acute Cardiogenic Pulmonary Oedema: The 3CPO Trial**

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Reference Volume 13.33. ISSN 1366-5278. www.hta.ac.uk/project/1338.asp

Aim

To determine whether noninvasive ventilation (NIV) reduces mortality and whether outcomes differ substantially by treatment modality ie, continuous positive airway pressure (CPAP) or noninvasive positive pressure ventilation (NIPPV).

Conclusions and results

Noninvasive ventilation, ie, CPAP or NIPPV, appears to have benefits in the immediate treatment of patients with severe acute cardiogenic pulmonary edema and may reduce mortality.

Specifically we aimed to: (1) assess the clinical effectiveness of NIV in addition to standard therapy against standard therapy alone in early management of severe acute cardiogenic pulmonary edema; (2) assess whether the effectiveness of CPAP and NIPPV differ in the early management of acute cardiogenic pulmonary edema; (3) evaluate the safety of these interventions; (4) assess quality of life and patient satisfaction after treatment with NIV compared to standard therapy alone; and (5) assess the incremental cost effectiveness of NIV versus standard therapy from a health and social care perspective, in terms of cost per quality-adjusted life-year gained.

1069 patients (78±10 years; 43% male) were recruited to standard oxygen therapy (n=367), CPAP (n=346; 10±4 cmH,O) or NIPPV (n=356; 14±5/7±2 cmH,O). No difference was found between 7-day mortality for standard oxygen therapy (9.8%) and NIV (9.5%; p=0.87). The combined endpoint of 7-day death or intubation rate was similar irrespective of NIV modality (11.7% versus 11.1%, CPAP versus NIPPV respectively; p=0.81). In comparison to standard oxygen therapy, NIV was associated with greater reductions (treatment difference, 95% confidence intervals) in breathlessness (visual analogue score 0.7, 0.2-1.3; p=0.008) and heart rate (4/min, 1-6; p=0.004) and improvement in acidosis (pH 0.03, 0.02-0.04; p<0.001) and hypercapnia (0.7 kPa, 0.4-0.9; p<0.001) at 1 hour. There were no treatment-related adverse events or any differences in other secondary outcomes, eg, myocardial infarction rate, length of hospital stay, critical care admission rate, and requirement for endotracheal intubation. Economic evaluation showed that mean costs and QALYs up to 6 months were 3023 pounds sterling (GBP) and 0.202 for standard therapy, GBP 3224 and 0.213 for CPAP, and GBP 3208 and 0.210 for NIPPV. Modeling of lifetime costs and QALYs produced values of GBP 15 764 and 1.597 for standard therapy, GBP 17 525 and 1.841 for CPAP, and GBP 17 021 and 1.707 for NIPPV. These results suggest that both CPAP and NIPPV accrue more QALYs, but at higher costs than standard therapy. However, the estimates are subject to substantial uncertainty.

Recommendations

See Executive Summary link at www.hta.ac.uk/project/1338.asp.

Methods

See Executive Summary link at www.hta.ac.uk/project/1338.asp.

Further research/reviews required

See Executive Summary link at www.hta.ac.uk/project/1338.asp.

Written by Dr Alasdair Gray, Royal Infirmary of Edinburgh, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/174

Title **Methods to Identify Postnatal Depression in Primary Care: An Integrated Evidence Synthesis and Value of Information Analysis**

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Reference Volume 13.36. ISSN 1366-5278. www.hta.ac.uk/project/1521.asp

Aim

- To provide an overview of all available methods to identify postnatal depression (PND) and to assess their validity (in terms of key psychometric properties);
- To assess the acceptability of methods to identify PND and assess their clinical and cost effectiveness in improving maternal and infant outcomes;
- To identify research priorities and the value of further research into methods to identify PND, from the perspective of the UK NHS;
- To assess whether methods to identify PND meet minimum criteria outlined by the National Screening Committee (NSC) in the light of this evidence synthesis.

Conclusions and results

The Edinburgh Postnatal Depression Scale (EPDS) was the most frequently explored instrument across all of the reviews. In terms of test performance, postnatally the EPDS performed reasonably well: sensitivity ranged from 0.60 (specificity 0.97) to 0.96 (specificity 0.45) for major depression only; from 0.31 (specificity 0.99) to 0.91 (specificity 0.67) for major or minor depression; and from 0.38 (specificity 0.99) to 0.86 (specificity 0.87) for any psychiatric disorder. Evidence from the acceptability review indicated that, in most studies, the EPDS was acceptable to women and healthcare professionals when undertaken in the home, with due attention to training, with empathetic skills of the health visitor, and due consideration to positive responses to question 10 about self-harm. Suggestive evidence from the clinical effectiveness review indicated that use of the EPDS, compared with usual care, may lead to reductions in the number of women with depression scores above a threshold. In the absence of existing cost-effectiveness studies of PND identification strategies, a decision analytic model was developed. The results of the base-case analysis suggested that use of formal identification strategies did not appear to represent value for money, based on conventional thresholds of cost effectiveness used in the NHS. However, the scenarios considered demonstrated that this conclusion was primarily driven by the costs of false positives assumed in the base-case model.

Recommendations

In light of the results of our evidence synthesis and decision modeling we revisited the examination of PND screening against 5 of the NSC criteria. We found that the accepted criteria for a PND screening program were not currently met. The evidence suggested that there is a simple, safe, precise, and validated screening test, in principle a suitable cut-off level could be defined and that the test is acceptable to the population. Evidence surrounding clinical and cost effectiveness of methods to identify PND is lacking.

Methods

See Executive Summary link at www.hta.ac.uk/project/1521.asp.

Further research/reviews required

See Executive Summary link at www.hta.ac.uk/project/1521.asp.

Written by Professor Simon Gilbody, University of York, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/175

Title **A Double-Blind Randomized Placebo Controlled Trial of Topical Intranasal Corticosteroids in 4- to 11-Year-Old Children with Persistent Bilateral Otitis Media with Effusion in Primary Care**

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Reference Volume 13.37. ISSN 1366-5278. www.hta.ac.uk/project/1352.asp

Aim

To determine the effectiveness of topical intranasal corticosteroid in children with bilateral otitis media with effusion.

Conclusions and results

Of the topical steroid group, 40.6% (39/96) demonstrated tympanometric clearance (C1 or A type) in one or both ears at 1 month. The figure in the placebo group was 44.9% (44/98). The risk difference favoring placebo was 4.3% (95% CI -9.26% to 18.05%), making the number needed to treat (NNT) at least 11.The odds ratio (OR) was 0.84 (95% CI 0.48 to 1.48). Four covariates were prespecified for inclusion in logistic regression analysis: age as a continuous variable (p=0.94), season (p=0.70), atopy (p=0.61), and clinical severity (p=0.006). The adjusted odds ratio (AOR) at 1 month for the main outcome was 0.93 (95% CI 0.50 to 1.75). Secondary analysis at 3 months showed 58.1% of the steroid group had resolved and 52.3%of the placebo group, AOR 1.45 (95% CI 0.74 to 2.84). At 9 months, 55.6% of the treated group remained clear in at least one ear, but was higher at 65.3% of the placebo group, AOR 0.82 (95% CI 0.39 to 1.75). Adverse events were relatively minor and included nasal stinging, epistaxis, dry throat, and cough. Differences between groups were not significant. The OM8-30 scores reported hearing difficulty and days with otalgia were not significantly different between groups at 3 months (p=0.55, 0.08, 0.46 respectively). Cost effectiveness and health utilities analyses were not significant, but identified a trend toward increased benefits and lower costs in those aged 6.5 years or over, were male, and had milder disease (severity score>0.63) and a trend towards harm (reduced QALYs) in those under 6.5 years, female, and with more severe disease.

Recommendations

Topical nasal steroids are not likely to be an effective or worthwhile treatment for glue ear in primary care. Active monitoring in primary care for children with suspected glue ear is acceptable and satisfactory to children and families, but the current methods used to monitor children may require adaptation. Relatively few children with histories of ear problems attending the GP surgery have glue ear actually confirmed on both sides and need treatment. Children over 6.5 years have milder glue ear in primary care and while not actually showing significant benefit of topical steroids are an important group to consider regarding potential treatment benefits.

Methods

See Executive Summary link at www.hta.ac.uk/project/1352.asp.

Further research/reviews required

This large study of topical nasal steroids in a primary care population with null effect suggests that further studies, particularly in primary care populations, would not be worthwhile. However, a potential effect in children aged ≥ 6.5 years may be further evaluated. Other interventions feasible in the primary care setting, eg, autoinflation, need to be evaluated, but interventions for younger children in primary care remain problematic.

Written by Dr Ian Williamson, University of Southampton, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/176

Title **Breastfeeding Promotion for Infants in Neonatal Units: A Systematic Review and Economic Analysis**

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Reference Volume 13.40. ISSN 1366-5278. www.hta.ac.uk/project/1611.asp

Aim

To evaluate the effectiveness and cost effectiveness of interventions that promote or inhibit breastfeeding or feeding with breast milk for infants admitted to neonatal units; and to identify an agenda for future research.

Conclusions and results

Systematic review of effectiveness: 48 studies met the selection criteria, of which 65% (31/48) were randomized controlled trials (RCTs). Studies were heterogeneous in terms of design, intervention, participants, and outcomes measured. Six were rated as good quality and 28 as moderate quality. *Increased mother and baby contact:* Short periods of the kangaroo method of skin-to-skin contact increased the duration of breastfeeding among clinically stable infants in industrialized settings, and daily contact improved health outcomes at 2 and 6 months in all settings. *Interim feeding methods and related interventions:* The evidence for cup feeding vs bottle feeding is limited, but it may increase breastfeeding at discharge and reduce the frequency of oxygen desaturation. Lack of staff training is an important confounder. No evidence supports the use of gavage feeding vs bottle feeding, or the use of caregivers' fingers in place of pacifiers. *Methods of expressing breast milk:* Simultaneous pumping with an electric pump has advantages in the first 2 weeks. The mother may also benefit from a hand-operated pump or hand expression at home. *Enhancing breast milk production:* Pharmaceutical galactogogues have little role to play among mothers who have recently given birth. Some evidence supports the use of relaxation-related interventions for mothers. *Supporting optimal nutritional intake from breast milk:* Enhancing the composition of mothers' own milk offers an apparently simple method for optimizing protein and lipid intake, but good-quality evidence of effectiveness is lacking. *Breastfeeding education and support:* There is strong evidence for the effectiveness of community-led peer support in hospital and at home, and a more limited evidence base for the effectiveness of skilled professional support in neonatal units. *Staff training:* Limited evidence suggests that educational interventions delivered to a multidisciplinary staff group may increase healthcare professionals' knowledge, initiation rates, and duration of breastfeeding. Lack of staff training is an important barrier to implementation of effective interventions. *Early hospital discharge with home support:* This is unlikely to improve and may adversely affect the duration of breastfeeding. *Organization of care:* Baby Friendly accreditation of the associated maternity hospital resulted in improvements in several breastfeeding-related outcomes for infants in neonatal units. *Economic analysis:* Enhanced staff contact, which was additional skilled professional support in hospital, was found to be more effective and less costly (due to reduced neonatal illness) than normal staff contact in both the base case and the majority of sensitivity analysis scenarios.

Recommendations

See Executive Summary link at www.hta.ac.uk/project/1611.asp.

Methods

See Executive Summary link at www.hta.ac.uk/project/1611.asp.

Further research/reviews required

See Executive Summary link at www.hta.ac.uk/project/1611.asp.

Written by Professor Mary Renfrew, University of York, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/177

Title	**Neoadjuvant Radiochemotherapy for Rectal Cancer**
Agency	**ASERNIP-S, Australian Safety and Efficacy Register of New Interventional Procedures – Surgical** PO Box 553, Stepney SA 5069, Australia; Tel: +61 8 83637513, Fax: +61 8 83622077; asernips@surgeons.org, www.surgeons.org/asernip-s
Reference	Report no. 72. ISBN 978-0-9806299-7-2. www.surgeons.org/AM/Template.cfm?Section=ASERNIP_S_Publications&Template=/TaggedPage/TaggedPageDisplay.cfm&TPLID=17&ContentID=33666

Aim

To assess the high-level literature available on neoadjuvant radiochemotherapy (a preoperative, combined-modality treatment where both radiotherapy and chemotherapy are administered) for rectal cancer.

Conclusions and results

None of the reported complications were severe, and all were managed without rectal resection or extirpation. One systematic review stated that significantly more patients who received neoadjuvant radiochemotherapy had pathological complete response than patients who received neoadjuvant radiotherapy alone (11.8% vs 3.5%, p<0.001).

Recommendations

None.

Methods

The literature was systematically searched to identify available, current, English-language, systematic reviews and health technology assessments. Databases used were York CRD, Entrez PubMed, The Cochrane Library, Trip database, and NLH National Library of Guidelines. The quality of the identified systematic reviews was assessed using key items from the QUOROM statement. Three systematic reviews were identified.

Further research/reviews required

The evidence base is good (and includes a recent Cochrane systematic review) for judging the safety and effectiveness of neoadjuvant radiochemotherapy for rectal cancer. A further, full systematic review is unlikely to add value.

Written by Caryn Perera, ASERNIP-S, Australia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/178

Title **Endoscopic Thoracic Sympathectomy**

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www.surgeons.org/AM/Template.cfm?Section=ASERNIP_S_Publications&Template=/TaggedPage/TaggedPageDisplay.cfm&TPLID=17&ContentID=33666

Aim

To assess the high-level literature available on endoscopic thoracic sympathectomy (ETS) for hyperhidrosis.

Conclusions and results

A lack of high-quality randomized trial evidence on ETS makes it difficult to judge the safety and effectiveness of this technique. Several potential safety issues are associated with this procedure.

Recommendations

None.

Methods

The literature was systematically searched to identify available, current, English-language, systematic reviews and health technology assessments. Databases used were York CRD, Entrez PubMed, The Cochrane Library, Trip database, and NLH National Library of Guidelines. We used key items from the QUOROM statement to assess the quality of the identified systematic reviews. Two systematic reviews were identified.

Further research/reviews required

ASERNIP-S suggests that a full systematic review including all available comparative and case series information, together with clinical input, should be undertaken to provide an up-to-date and comprehensive assessment of the safety and effectiveness of ETS.

Written by Amber Watt, ASERNIP-S, Australia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/179

Title **Lower Respiratory Tract Infections of a Viral Origin in the Pediatric Population: Systematic Review of Spanish Literature**

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Reference ISBN 978-84-393-8072-6

Aim

To systematically collect and analyze the entire bibliography of works originating in Spain with respect to lower respiratory tract infections in the pediatric population and the identified viral causal agents.

Conclusions and results

The studies used show that lower respiratory tract infections and bronchiolitis represent a load in terms of morbidity, primarily with viral causes, among the infantile population and especially in those younger than 2 years of age or with an underlying pathology. However, the design of the studies analyzed and data collection had many shortcomings. The risk of hospitalization and seriousness are closely related to patients' associated morbidity. In healthy people, the variability of hospitalization rates is well known.

Identification of the etiological agent depends on multiple factors, especially the age of the child, the season of the year, and the thoroughness of the search for the causal viruses. Clinics are undifferentiated among the potential viral agents involved. It would be necessary to design and undertake multicenter and demographic studies with well-defined criteria that are explicit with respect to inclusion and seriousness to quantify and better specify the load of this illness and the role that respiratory syncytial virus and other causal agents play in it. An epidemiological surveillance system with a network of watch centers could help overcome these limitations and would provide data on these viruses, not only among the pediatric population, but also in the elderly.

Methods

A systematic search was carried out for articles published by Spanish researchers that made reference to aspects related to the etiology (causal agent) of respiratory or lower respiratory tract infections, in particular bronchiolitis. Criteria for inclusion were: articles published between 1995 and 2007; studies addressing a pediatric population (<14-16 years of age); Spanish health centers; identified etiological agent; more than 15 patients; and written in Spanish, English, or Catalan. Studies were excluded if, eg, they were performed on patients with serious pathologies or who were immunodepressed. Clinical case studies or reviews without primary data that compared diagnostic techniques or evaluated therapeutics and other types of bronchiolitis were not excluded. The studies included were analyzed using publication data (author, journal, year, language, study funding), the type of study (data collection, design, number of heath centers, study period), population and study location, selection criteria (definitions), examination of the etiological agent, and the evolution and main conclusions of the study.

Written by Pons Joan MV, CAHTA, Spain

ISSN 1654-501X

INAHTA Briefs

Issue 2009/180

Title **Artificial Liver Support Systems**

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Reference Report no. 2007/23

Aim

To describe the artificial support systems and evaluation of their efficacy and safety in patients with acute and acute on chronic liver failure.

Conclusions and results

After screening 436 references, we selected 10 control trials, of which 7 evaluated complete detoxification treatment. Eight included acute chronic liver patients and 2 included acute liver failure cases. MARS, Prometheus, and Biologic-DT interventions were analyzed. Efficacy was proven by a reduction in bilirubin, creatinine, and other toxic components after intervention compared to control. Clinical efficacy was measured in fewer studies, some showing an improvement in hepatic encephalopathy and survival. A few studies assessed intervention safety, based on adverse events, mainly coagulation disorders.

Recommendations

Reviewed evidence showed extracorporeal albumin dialysis-based systems were able to reduce toxic parameters in blood and improve clinical results. However, more studies are needed to further evaluate mortality and adverse events based on standardized notification. Two multicenter studies are currently in progress and aim to provide evidence on the safety and efficacy of these systems.

Methods

Trials were identified through electronic searches of the following databases: MEDLINE, The Cochrane Library Plus, EMBASE, and ISI Web of Knowledge. The articles with the most evidence, and which had been published in the last 10 years, were selected.

Written by Bertrán Maria Jesús, Unidad de Evaluación, Soporte y Prevención (UASP), CAHTA, Spain

ISSN 1654-501X

INAHTA Briefs

Issue 2009/181

Title **Clinical Effectiveness and Cost Effectiveness of Different Models of Managing Long-Term Oral Anticoagulation Therapy: A Systematic Review and Economic Modeling**

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Reference Volume 11.38. ISSN 1366-5278. www.hta.ac.uk/project/1495.asp

Aim

To systematically review the clinical and cost effectiveness of patient self-testing / self-management of oral anticoagulation treatment compared with clinic-based management.

Conclusions and results

The principle research question was: How does the safety, effectiveness, and cost effectiveness of patient self testing/-management compare to clinic-based management?

Sixteen randomized trials were included. Patient self-monitoring of oral anticoagulation therapy was more effective than poor-quality, usual care provided by family doctors. Poor quality of anticoagulation control managed by family doctors was particularly associated with a greater proportion of time spent below the target therapeutic clotting range. This was reduced by patients self-monitoring. Patient self-monitoring was as effective as good-quality, specialized clinics in maintaining the quality of anticoagulation therapy. In meta-analysis of randomized trials, no significant differences appeared in risk of major bleeding events between patient self-monitoring and usual care controls (RD -0.0039, 95% CI -0.0154 to 0.0077). Pooled analyses found that, compared to primary care or anticoagulant clinics, self-monitoring was associated with statistically significant fewer thromboembolic events (RD -0.0224, 95% CI -0.0334 to -0.0115) and deaths (RD -0.017, 95% CI -0.0287 to -0.0053). However, the reduction in complication events and deaths was not consistently associated with improved anticoagulant control.

Recommendations

For selected and successfully trained patients, self-monitoring is effective and safe for long-term oral anticoagulation therapy. Self-monitoring may enhance the quality of life for some patients who are frequently away from home, who are in employment or education, or those who find it difficult to travel to clinics. In general, patient self-monitoring is unlikely to be more cost effective than the current high-quality care provided by specialized anticoagulation clinics in the UK.

Methods

See Executive Summary link at www.hta.ac.uk/project/1495.asp.

Further research/reviews required

Research leading to better dose-algorithms and other procedures could lead to improved patient self-monitoring performance beyond that currently achieved.

Evidence is lacking on whether patient education alone is sufficient to reduce the risk of bleeding, thromboembolic complications, and death in patients who receive long-term anticoagulation therapy. The clinical and cost effectiveness of patient education and training in long-term, oral anticoagulation therapy needs to be investigated.

Written by Dr David Moore, University of Birmingham, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2009/182

Title **The Effect of Fatigue on Surgeon Performance and Surgical Outcomes**

Agency **ASERNIP-S, Australian Safety and Efficacy Register of New Interventional Procedures – Surgical**
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Reference Report no. 68. ISBN 978-0-9806299-5-8.
www.surgeons.org/AM/Template.cfm?Section=ASERNIP_S_Publications&CONTENTID=33301&TEMPLATE=/CM/ContentDisplay.cfm

Aim

To investigate the effect of fatigue on surgeons and surgical outcomes, and to investigate the impact of fatigue on the cost of surgery and surgical training.

Conclusions and results

Results were grouped into four areas of performance: clinical, academic, cognitive, and psychomotor skills. There is a paucity of evidence investigating the effects of sleep loss and fatigue on the performance of surgeons and subsequent clinical outcomes. The overall weight of (poor) evidence shows that performance is not proven to be affected by sleep deprivation or fatigue and that psychomotor performance may or may not be. Variations in results were, in some cases, attributable to the level of training of participants and between-subject differences. Many studies used surrogate markers to measure performance, although the relationship between these markers to actual clinical performance is unclear. It appears that fatigue can be compensated for in the acute operating room setting, but the impact it has on normal functions is unclear. The search strategy did not identify any economic evaluations, resulting in an inability to comment on the financial effect of fatigue on surgery and surgical training.

Recommendations

None.

Methods

We systematically reviewed the literature. Studies were identified by searching EMBASE, CINAHL, PubMed, The Cochrane Library and Current Contents from inception to June 2008. Additional articles were identified through reference sections of the retrieved studies. Data from the included studies were extracted by an ASERNIP-S researcher using standardized data extraction tables developed *a priori* and checked by a second researcher. Statistical pooling was not appropriate due to the study and result heterogeneity. Twenty studies were included for review: 2 RCTs, 7 nonrandomized comparative studies, and 11 case series (pretest/posttest outcomes). Studies were of variable quality and differed in study design.

Further research/reviews required

Further research is recommended to identify surrogate markers, if any, to actual clinical performance and the relationship with actual clinical performance; to develop a clearer definition of fatigue and its relationship to sleep deprivation; to identify the effects of acute sleep deprivation with and without chronic partial sleep loss on performance; to compare performance at difference times of day to assess outcomes at different circadian points; to compare performance of inexperienced surgeons with experienced surgeons with respect to fatigue and sleep loss; and to determine the impact of fatigue on the cost of surgery and surgical training.

Written by Lana Sturm, ASERNIP-S, Australia

ISSN 1654-501X

INAHTA Briefs

Issue 2009/183

Title **Interspinous Implants and Pedicle Screws for Dynamic Stabilization of Lumbar Spine: Rapid Assessment**

Agency **KCE, Belgian Health Care Knowledge Centre**
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Reference Report no. 116 (C), 2009. www.kce.fgov.be/index_en.aspx?SGREF=5223&CREF=14081

Aim

To synthesize available clinical and economic evidence for lumbar, nonfusion, posterior stabilization devices.

Conclusions and results

Lumbar, nonfusion, posterior stabilization devices are an alternative to decompression surgery and/or fusion surgery in treating degenerative conditions of the spine that have not responded to conservative treatment.

Nonfusion Pedicle screws (Dynesys: Prospective studies reported improvements in back and leg pain, quality of life, walking distance, and return to work. However, a significant proportion of operated patients required a surgical re-intervention needing device removal. Complications reported were malpositioned screws and broken screws leading to screw loosening.

Interspinous devices (X STOP and Wallis): One RCT concluded to the higher effect of X STOP on pain relieving 2 years after surgical intervention, on walking ability, and on patients' satisfaction. However, a trend of regression in pain was observed toward baseline levels. Methodological weaknesses questioned the reliability of results. Prospective studies on X STOP and Wallis reported an improvement in pain, physical function, and walking distance. Complications associated with the devices were device migration.

Economic evaluation: No full economic evaluation of interspinous implants and pedicle screw systems was identified. Information was insufficient to perform a cost-effectiveness analysis.

International comparison: In Belgium, the prices for X STOP and Dynesys are close to the prices in 5 neighboring countries (approximately 2500 euros). Different countries apply different reimbursement mechanisms.

Conclusion: There is low quality evidence on the clinical effectiveness and the safety of nonfusion dynamic stabilization devices in treating degenerative pathologies of the lumbar spine.

Recommendations

The lumbar nonfusion dynamic stabilization devices must be considered experimental.

- Randomized prospective studies are needed to define the place of these devices as therapeutic means in degenerative lumbar spine surgery.
- Evidence is insufficient to recommend reimbursement for lumbar nonfusion posterior stabilization devices.

Methods

This rapid assessment followed the standard methodology of HTA reports, without considering patient, ethical, and organizational issues. We searched the following databases: HTA agencies, databases of CRD, Cochrane Library, MEDLINE, Embase, Psychinfo, Econlit, and the NHS Economic Evaluation Database. An international comparison aimed to compare prices and reimbursement practices among sampled European countries.

Written by Sabine Stordeur, KCE, Belgium

ISSN 1654-501X

INAHTA Briefs

Issue 2010/001

Title **Long-Acting Beta2-Agonist and Inhaled Corticosteroid Combination Therapy for Adult Persistent Asthma: Systematic Review of Clinical Outcomes and Economic Evaluation**

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Reference CADTH Technology Report, Issue 122, November 2009.
ISBN 978-926680-24-8 (print), ISBN 978-1-926680-25-5 (online)

Aim

To evaluate the clinical efficacy, safety, and cost effectiveness of long-acting beta2-agonist and inhaled corticosteroid (LABA-ICS) combination therapy for adults (12 years of age or older) diagnosed with persistent asthma.

Conclusions and results

For most patients with persistent asthma, the initial and only therapy needed is inhaled corticosteroid (ICS). The clinical review found statistically important, but not clinically meaningful, benefits from switching to combination therapy in managing most asthma not controlled by ICS. A primary economic analysis from a Canadian perspective found that the later a long-acting beta2-agonist (LABA) is introduced into therapy, the more cost effective the treatment strategy becomes. The analysis suggests that introducing LABA before patients have tried high-dose ICS therapy is not justified.

Recommendations

Not applicable.

Methods

Clinical and economic analyses were conducted. For the clinical analysis, RCTs comparing LABA-ICS with ICS monotherapy or another LABA-ICS combination therapy for managing persistent adult asthma were identified, and meta-analyses were performed when appropriate. For the economic analysis, we conducted a systematic review of economic evaluations comparing the use of LABA-ICS combination therapy with ICS monotherapy in patients (12 years of age or older) with asthma. A Markov model was created to estimate the long-term costs and quality-adjusted life-years (QALYs) associated with four strategies relating to the optimum time to introduce LABA: in combination with ICS as initial therapy; after lack of control on low-dose ICS; after lack of control on medium-dose ICS; or after lack of control on high-dose IC.

Further research/reviews required

More comparative research seems warranted, eg, to provide evidence on potential clinical benefits after using fixed versus variable dosing.

Written by Bond K, Coyle D, O'Gorman K, Coyle K, Spooner C, Lemière C, Vandermeer B, Tjosvold L, and Rowe BH, CADTH, Canada

ISSN 1654-501X

INAHTA Briefs

Issue 2010/002

Title **Development and Testing of Search Filters to Identify Economic Evaluations in MEDLINE and EMBASE**

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Reference CADTH Technology Report, October 2009.
ISBN 978-1-926680-10-1 (print), ISBN 978-1-926680-11-8 (online)

Aim

To develop search filters that will identify economic evaluations in the MEDLINE and EMBASE databases with maximum sensitivity and levels of precision to meet the needs of health technology assessment researchers; and to obtain data on the relative performance of new and published search filters.

Conclusions and results

Filters produced by NHS EED, NHS QIS, and Royle and Waugh continue to perform with high sensitivity in MEDLINE. None of the published or new filters meet the objectives of high sensitivity (more than 0.95) with a precision of 0.20, or lower sensitivity (greater than 0.79) and enhanced precision (at least 0.50).

Recommendations

Not applicable.

Methods

Several search filters were developed using sets of economic publication records to identify terms that best discriminated economic evaluations from other economic publications. We selected a set of gold-standard citations using the NHS EED filter for identifying economic evaluations. Comparator sets were created by applying this filter to the MEDLINE and EMBASE databases. Sensitivity, specificity, and precision were calculated for each search filter. The relative performance of new and existing filters was tested.

Further research/reviews required

Further analysis of the data and gold-standard records in this report may lead to improved filters. Additional analyses could focus on the performance of lower-frequency terms (below the selected cut-off frequency used in this project) and analysis of phrases and terms in close proximity in the title and abstracts of records.

Written by Glanville J, Fleetwood K, Yellowlees A, Kaunelis D, and Mensinkai S, CADTH, Canada

ISSN 1654-501X

INAHTA Briefs

Issue 2010/003

Title **Reassessment of Health Technologies: Obsolescence and Waste**

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Reference CADTH Technology Report, December 2009.
ISBN 978-1-926680-28-6 (print), ISBN 978-1-926680-29-3 (online)

Aim

To promote discussion about practical and policy issues related to health technology obsolescence and to offer a framework for advancing reassessment and decommissioning of health technologies in Canada.

Conclusions and results

A model is proposed for managing obsolescence of health technologies, including a description of structures, processes, and outcomes.

Recommendations

Not applicable.

Methods

A discussion paper was written to propose a policy framework for reassessing and decommissioning health technologies in Canada. This is a narrative summary based on a focused literature review and input from experts; not a systematic review of the literature.

Written by Joshi NP, Stahnisch FW, and Noseworthy TW, CADTH, Canada

ISSN 1654-501X

INAHTA Briefs

Issue 2010/004

Title **Brief Review: Fast-Track Surgery and Enhanced Recovery after Surgery (ERAS) Programs**

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Reference Report no. 74. ISBN 978-0-9806299-5-8. www.surgeons.org/Content/NavigationMenu/Research/ASERNIPS/ASERNIPSPublications/Fast_track_surgery_a.htm

Aim

To assess the safety and efficacy of fast-track surgery programs on patient outcomes; and to qualitatively explore the status of fast-track surgery in Australia.

Conclusions and results

In relation to safety, 2 studies reported that optimized patients had significantly lower mortality and morbidity than conventionally treated patients, with the remainder of studies either reporting no difference between the groups, or not reporting any statistical analyses. There appeared to be little difference in patient-reported pain, although patients in the optimized groups may have had less pain shortly after surgery.

Optimizing conditions before, during, and after surgery reduced the length of hospital stay for patients with no increase in readmission rates. Using the mobilization protocols, patients mobilized faster and spent more time out of bed shortly after surgery. Optimized patients generally had a faster return of gastrointestinal function than conventional patients.

A search of ongoing trials demonstrated that this an area of increasing interest. Some trials currently underway might not be recorded in a manner that notes fast-track surgery to be part of the research, and might instead incorporate it into a study in a different area.

Surgeon interviews showed that many surgical units are investigating some aspects of optimized surgery. General principles were similar, although some followed protocols more strictly than others. Education of all staff in fast-track surgery principles was acknowledged to be important.

Recommendations

None.

Methods

Systematic literature review: Studies were identified by searching MEDLINE, PubMed, and the Cochrane Library from inception to January 2009. One systematic review, 11 RCTs, and one guideline document were included for review. Data were extracted by an ASERNIP-S researcher using standardized data extraction tables developed *a priori* and checked by a second researcher. Statistical pooling was not appropriate due to the study and result heterogeneity.

Survey of surgeons: Surgeons from Australia and New Zealand who conduct fast-track surgery were identified via literature searches or through personal referrals. Responses from informal semi-structured interviews were deidentified, grouped into themes, and reported narratively.

Further research/reviews required

Further work is required to define the key aspects of optimized surgery, the indications, and the patient groups most likely to benefit.

Written by Lana Sturm, ASERNIP-S, Australia

ISSN 1654-501X

INAHTA Briefs

Issue 2010/005

Title **Labor Care in Healthy Women: Study of Variability and Systematic Review**

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Reference Report no. 2007/03. ISBN 978-84-95463-61-6.
www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60056&uri=/docs/Avalia-t/MemAsistParto.pdf&hifr=1250&seccion=0

Aim

- To describe types of delivery and existing variations in the use rates of different childbirth-related procedures; and to study the variability among Autonomous Regions, provinces, and types of Spanish hospitals (2001-2006).
- To systematically review the current state of knowledge on the effectiveness and safety of aspects linked to normal delivery in low-risk women, and to draw evidence-based conclusions for their use in clinical practice.

Conclusions and results

Conclusions

- *Variability in childbirth:* Our results highlight the variability of childbirth care in Spain in terms of time, geography, and clinical practice.
- *Systematic review:* The conclusions reflect the scientific evidence available on care of normal childbirth in low-risk women. Our methodology was appropriate and reproducible and could serve as a basis to draw clinical practice recommendations that would improve integral care and results, both maternal and neonatal, in normal deliveries.

Results

- *Variability in childbirth:* From 2001 to 2006, childbirths increased at a rate of 10 000 to 15 000 per annum. The percentage breakdown of the mean number of deliveries was: noninstrumented, 62.7%; instrumented, 15.1%; and cesarean section, 22.2%. Procedures varied widely at the different levels of hospitals, provinces, and autonomous regions; even among some that were in close proximity.
- *Systematic review:* The first search located 2 clinical practice guidelines, both from 2007; one by the National Institute for Clinical Excellence (NICE) and the other by the Institute for Clinical Systems Improvement using the AGREE (Appraisal of Guidelines for Research & Evaluation) tool for their assessment. The NICE guideline answered most of the group's questions and displayed high overall quality. It was rated "highly recommended" and adopted as reference. The searches targeting systematic reviews posed 7 blocks of questions: care during childbirth; pain-relief methods; fetal monitoring and control of fetal wellbeing; first stage of delivery; second stage of delivery; third stage; and care of neonate immediately after birth. Evidence was collected on each, and pertinent conclusions were drawn.

Methods

- Assessment strategy: Variability in childbirth and systematic review.
- Type of analysis: Decision analysis, and social/ethical implications considered.
- Data sources: Search of clinical practice guidelines on childbirth in specific databases (Tripdatabase, PUBGLE, GUIASALUD, and FISTERRA) and general databases (EMBASE and MEDLINE). For each question, we conducted a specific search of systematic reviews and meta-analyses in specialized (Cochrane Library Plus and NHS Centre for Reviews and Dissemination: HTA and DARE) and general databases (MEDLINE). If the reference guide or systematic reviews did not answer the questions, or failed to obtain level-1 evidence on the Scottish Intercollegiate Guidelines Network (SIGN) scale, we searched the Cochrane Library Plus Clinical Trial, MEDLINE, and EMBASE databases for clinical trials.
- Types of studies assessed: clinical practice guidelines, systematic reviews, meta-analyses, and ECA.

Written by Mª del Carmen Maceira Rozas, Ángel Salgado Barreira, and Gerardo Atienza Merino, AVLIA-T, Spain

ISSN 1654-501X

INAHTA Briefs

Issue 2010/006

Title **Dementia – Etiology and Epidemiology**

Agency **SBU, Swedish Council on Health Technology Assessment**
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Reference Report no. 172E/1. ISBN 978-91-85413-23-2.
www.sbu.se/en/Published/Yellow/Dementia--Etiology-and-Epidemiology/

Aim

To systematically review dementia in terms of, eg, incidence and prevalence, risk factors, diagnostics, drug therapies, caring, ethical considerations, ethnicity, and health economics.

Conclusions and results

Old age is the major risk associated with dementia. Good control of hypertension during middle age and an active life with intellectual activities during old age may reduce the risk of dementia.

Screening is not an option for diagnosing dementia at an early stage. A good clinical examination, combined with a caregiver interview and a clock test, will identify patients needing further investigation involving CT or MRI. Neuropsychological testing and cerebrospinal fluid biomarkers offer additional options for testing.

Patients with mild to moderate Alzheimer's disease may benefit from acetylcholinesterase inhibitors. The effect on cognition is small and lasts for some time, but adverse events are frequent.

Good care requires a good relationship between patient and caregiver. Psychoeducational interventions and skills-training programs may be helpful for informal caregivers.

Societal costs from dementia are high. Cost effectiveness cannot be reported for any treatment or intervention.

Recommendations

Not applicable.

Methods

The systematic literature search included databases and hand searching reference lists.

Included papers in English were published from 1966 to 2004, with the exception of updated consensus criteria on Lewy body dementia from 2005.

For search terms used in the systematic review, please see www.sbu.se.

Further research/reviews required

Additional research on dementia disorders is required in several areas: Progression of various dementia disorders; development of diagnostic methods; better instruments for identifying and measuring cognitive and related symptoms; methods to assess quality of life in people with dementia; evaluation of drugs (including adverse effects) for all categories of dementia; and studies examining the long-term effects and costs of pharmacotherapies in combination with programs of caring.

Written by Anders Norlund and Oksana Petersen, SBU, Sweden

ISSN 1654-501X

INAHTA Briefs

Issue 2010/007

Title **A Randomized Controlled Trial to Compare Minimally Invasive Glucose Monitoring Devices to Conventional Monitoring in the Management of Insulin-Treated Diabetes Mellitus (MITRE)**

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Reference Volume 13.28. ISSN 1366-5278. www.hta.ac.uk/project/1306.asp

Aim

To evaluate the clinical efficacy, acceptability, and economic impact, in the long and medium term, of two minimally invasive, continuous glucose monitors in poorly controlled, insulin-requiring people with diabetes.

Conclusions and results

The percentage change in HbA1c from baseline to 18 months was the primary indicator of long-term efficacy in this study. The percentage change in HbA1c from baseline to 6 months and baseline to 12 months assessed efficacy in the medium term. The change to 3 months assessed the short-term effects. No differences between any of the groups were found in the percentage changes in HbA1c at any of the assessment times. Likewise, no differences were found in the percentage of participants achieving what was defined as a clinically important change of 12.5% in HbA1c percent at each of the assessment times. Although not significant, the Glucowatch group produced the smallest change in HbA1c and the lowest numbers achieving a clinically meaningful change at all time points. The findings on change in HbA1c, in the group studied, indicated no advantage from having a continuous glucose monitoring device. The economic analysis showed no advantage pertaining to the groups that received continuous blood glucose monitoring devices. Using health economic tools, a lower cost and higher benefit was found in the attention control arm during the trial period. A comparison of the use and acceptability of devices indicated that, overall, the Glucowatch was used less (20% vs 57% by 18 months), had more side effects, was found to interfere more with daily activities, and was perceived as being more difficult to use compared to the Continuous Glucose Monitoring System (CGMS).

Recommendations

The findings indicate that continuous glucose monitors, as assessed in this study, do not improve clinical outcomes in individuals with poorly controlled, insulin-requiring diabetes. In terms of health economics, no benefits accrued from use of the two continuous glucose monitoring devices assessed in the study. The findings also indicate differences in the acceptability to participants of the two devices. On acceptability grounds alone, the data suggest that the Glucowatch technology assessed in this study will not be frequently used by individuals with diabetes.

Methods

See Executive Summary link at www.hta.ac.uk/project/1306.asp.

Further research/reviews required

The findings emphasize the importance of examining acceptability. Devices may demonstrate clinical value, but if potential users find them unacceptable – or choose not to use them – then it is unlikely that they could be introduced into routine clinical care.

Written by Professor Stanton Newman, UCL, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2010/008

Title **Rehabilitation of Older Patients: Day Hospital Compared to Rehabilitation at Home. A Randomized Controlled Trial**

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Reference Volume 13.39. ISSN 1366-5278. www.hta.ac.uk/project/1218.asp

Aim

To test the hypotheses: a) Older people and their informal carers are not disadvantaged by home-based rehabilitation (HBR) relative to day-hospital rehabilitation (DHR); and b) Home-based rehabilitation is less costly.

Conclusions and results

We found no new published randomized controlled trials (RCT) since 1999, and the review conclusions provide justification for a further RCT. Of 480 NHS Trusts in England at the time of the survey, 368 (77%) completed an initial questionnaire. Of these, 322 (87.5%) trusts reported providing rehabilitation services; 181 (46.2%) provided both HBR and DHR; 80 (20.5%) provided HBR but not DHR; and 61 (15.6%) provided DHR but not HBR. Comparison with a previous survey from 1998 suggested recent increase in home-based rehabilitation teams. Originally, a sample of 460 subjects (230 in each participating site) was proposed for the RCT. However, as well as time consuming difficulties in recruiting participating sites and implementing research processes, we experienced lower than anticipated rates of recruiting subjects into the trial in participating sites. We developed an exit strategy and stopped recruiting after 89 subjects had been randomized between the services.

Recommendations

Statistical analyses of the trial outcomes do not provide sufficient evidence to conclude that patients receiving home-based rehabilitation were disadvantaged compared to those receiving day-hospital rehabilitation. This finding is complemented by the observation that the cost of providing HBR is not markedly different from providing rehabilitation in hospital. Neither the new evidence provided by this RCT, nor the existing evidence from previous trials, suggests any advantage or disadvantage from providing rehabilitation in a day hospital versus providing it in the patient's home.

Methods

A systematic literature review and a national survey of NHS Trusts were followed by a two-arm RCT conducted in 4 trusts in England that provide both HBR and DHR. In each setting, clinical staff reviewed consecutive referrals to identify subjects who were potentially suitable for randomization according to the defined inclusion criteria. Patients were randomized to receive either HBR or DHR. The primary outcome measure was the Nottingham Extended Activities of Daily Living (NEADL) scale. Secondary outcome measures included the EuroQol 5 dimensions (EQ-5D), Hospital Anxiety and Depression Scale (HADS), Therapy Outcome Measures (TOMs), hospital admissions, and the General Health Questionnaire (GHQ-30) for carers.

Further research/reviews required

Future research, rather than comparing these settings for efficacy, might focus on identifying those services that are better provided in one or other setting and will take account of the current commissioning environment in the UK, which explicitly supports choice in the provision of health services for patients.

Written by Professor Stuart Parker, University of Sheffield, NETSCC, United Kingdom

ISSN 1654-501X

INAHTA Briefs

Issue 2010/009

Title **Methodology: Development of Continuous Improvement Plans for Quality Management**

Agency **ETESA, Department of Quality and Patient Safety of the Ministry Health of Chile**
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Reference Report no. 23.
www.redsalud.gov.cl/portal/url/item/703fdc65125826 3ee04001011f013b08.pdf

Aim

To synthesize the best evidence on methodologies, tools, and interventions for generating and implementing improvement plans and to develop an evidence-based methodological guide.

Conclusions and results

This guide provides a tool to support healthcare facilities in designing and implementing plans for improvement in areas where it is necessary to respond to periodic performance assessments, eg, accreditation, nosocomial infection programs, or incident reporting systems.

Methods

Research commissioned.

The development of the guide was based on general literature on the subject, and a systematic review of the literature on studies that have evaluated the effectiveness of interventions for improving quality in health care.

A literature search included MEDLINE, Lilacs, Database of Abstracts of Effectiveness (DARE), Health Technology Assessment Database (HTA), and Cochrane Database of Systematic Reviews (CDSR).

Further research/reviews required

Further randomized clinical trials are needed to measure the impact of plans and determine whether they are effective in improving quality in health care.

Written by Luis Vera, Patricia Kraemer, ETESA, Chile

ISSN 1654-501X

INAHTA Briefs

Issue 2010/010

Title **Methodology for Developing Health Checklist**

Agency **ETESA, Department of Quality and Patient Safety of the Ministry Health of Chile**
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Reference Report no. 24.
www.redsalud.gov.cl/portal/url/item/7cf9e499a55c4cc7e0400101f016c69.pdf

Aim

To offer an approach concerning the structure of methodology for developing checklists in healthcare.

Recommendations

This review offers methodology to develop checklists. It considers both quantitative and qualitative aspects that must be present in this instrument to support the activities of healthcare personnel and deliver safer health services.

Checklists are important tools for reducing medical errors and raising standards of patient care and procedures, especially under stress conditions when memory and monitoring of cognitive functions may be affected.

Checklists should not be static, but processes in which expert groups participate to transform a range of knowledge and information on a specific theme in the particular content to which they relate.

Methods

Research commissioned.

The investigator reviewed bibliographic databases and websites of organizations to collect grey literature; Cochrane Database of Systematic Reviews (CDSR), World Health Organization (WHO), Pan-American Health Organization, Ministry of Health Chile, and MEDLINE.

Further research/reviews required

The application of checklists is a relatively new issue in health care. Further studies are needed to assess the effectiveness of implementing this instrument.

Written by Luis Vera, Patricia Kraemer, ETESA, Chile

ISSN 1654-501X

INAHTA Briefs

Issue 2010/011

Title **Patient Involvement Between Ideals and Reality**

Agency **DACEHTA, Danish Centre for Health Technology Assessment**
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Reference 2008; 8(3). ISBN 978-87-7676-703-7.
www.sst.dk/Udgivelser/2008/Patient%20involvement%20between%20ideals%20and%20reality%20-%20an%20empirical%20study%20of%20shared%20decision%20making%20and%20orinary%20encounters%20between%20patients%20doctors%20and%20nurses%20summary%20-%20a%20Health%20technology%20Assessment.aspx

Aim

To open a debate with healthcare professionals and decision makers about how to shape and develop patient involvement.

Conclusions and results

Several parameters affect patient involvement in decision making. The report shows that patient involvement in everyday clinical practice depends on:

1. Expectations of patients and healthcare professionals
2. The specific clinical situation
3. Type of treatment and treatment decisions

The correlation between these parameters creates both possibilities and barriers for patient involvement – and interaction between patients and healthcare professionals is shaped in the interplay between these parameters. An understanding of the interplay between the parameters, as shaped in the context of each department and clinic, is a necessary prerequisite for generating greater patient involvement. This conclusion is substantiated by several empirical analyses that illustrate how such interplay is shaped in cardiac rehabilitation and arthritis clinics.

The report discusses the potential benefits from supporting explicit, patient-involving dialogue. Research on patient involvement has led to development of several tools for this type of communication support. The report concludes with a proposal to work toward adapting these tools to the conditions of the Danish healthcare system and society.

Recommendations

This HTA offers recommendations at the department level and to the individual health professional. It emphasizes the importance of keeping in mind that the goal of patient involvement is not for the patient to know everything and make decisions about everything. However, the following objectives should be central:

- Patients must know about the treatment system, potential risks, and the progress of the procedure
- Patients should be able to understand the purpose of the clinical dialogue, that they themselves contribute important knowledge, and what kind of choice they are part of
- Patients should be encouraged to engage in dialogue and ask questions.

Such efforts will strengthen both the patient and healthcare professionals in making decisions regarding treatment.

Methods

The empirical study is a qualitative case study. In total, 50 cases from cardiac rehabilitation and arthritis treatment units were chosen for observation and further analysis. In addition, 21 qualitative interviews were conducted with patients and 17 with their nurses and doctors. The interviews were conducted and analyzed in a narrative perspective. Observations were analyzed with special attention to how knowledge is exchanged between patients and healthcare professionals, and how the dialogue affects and shapes the course of treatment and treatment decisions.

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INAHTA Briefs

Issue 2010/012

Smoking Cessation in General Practice

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Reference 2009; 9(2). ISBN 978-87-7676-904-8.
www.sst.dk/Udgivelser/2009/Rygestop%20i%20almen%20praksis%20kursus%20internetbaseret%20program%20eller%20samtale%20-%20en%20Medicinsk%20Teknologi%20Vurdering.aspx

Aim

To find the most cost-effective intervention on smoking cessation in general practice.

Conclusions and results

We found no significant effect of GP referral to free smoking cessation groups or an Internet-based smoking cessation program as compared with usual smoking cessation activities in general practice. Although both the patients and the GPs were positive toward the study and referral to other smoking cessation activities, few actually made use of them. Hence, we concluded that routine referral is not cost effective, and we cannot recommend changing usual practice. However, we cannot exclude that the selection of doctors and patients could have influenced the results of the study. We suppose that the brief intervention offered in general practice, ie, a few minutes of smoking cessation counseling, is not sufficient to increase the smoking cessation rates in general practice. Intensifying counseling for smoking cessation and, eg, arranging a date for a smoking cessation group before the smoking patient leaves the practice, could possibly increase the quit rates.

Methods

All general practitioners in a selected area in a suburb of Copenhagen were prerandomized to 1 of 3 groups (A, B, or C). GPs allocated to *group A* were to briefly talk with all smokers about smoking and refer all motivated smokers to a smoking cessation group for an 8-week period. GPs allocated to *group B* were to briefly talk about smoking with all smokers and refer all motivated smokers to an Internet-based smoking cessation program (interactive, individual advice) for an 8-week period. GPs allocated to *group C* (control group) were to continue to give smoking cessation advice and assistance to quit "as usual" (not necessarily to all smokers). Only 40% of the GPs agreed to participate in the study, and those who agreed to participate were a selected group, already more active in smoking cessation counseling. Furthermore, registered smoking prevalence among patients was only 17%, which was almost 10% lower than the national smoking prevalence. This could represent a selection in patients. More than 1500 smokers were included. About half expressed a wish to join a smoking cessation group, or to try the Internet-based smoking cessation program. However, only 7% attended the smoking cessation groups, and only 16% of those given the opportunity tried the Internet-based smoking cessation program. We measured both self-reported and validated abstinence and corrected for baseline differences in sex, age, socioeconomic status, motivation to quit, and tobacco consumption in the 3 groups.

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INAHTA Briefs

Issue 2010/013

Title **Systematic Review of the Effects of Home Telemonitoring in the Context of Diabetes, Pulmonary Diseases, and Cardiovascular Diseases**

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Reference ETMIS 2009, 5(3). Printed French edition ISBN 978-2-550-55794-4, English summary (PDF) ISBN 978-2-550-55795-1. www.aetmis.gouv.qc.ca/site/en_publications2009.phtml

Aim

To determine the effects associated with home telemonitoring in light of studies on 3 main categories of diseases and their associations: diabetes (types 1, 2, and gestational), pulmonary diseases (asthma and chronic obstructive pulmonary disease), and cardiovascular diseases (heart failure and hypertension) and explore the conditions for success in this care delivery method.

Conclusions and results

Analysis of the 119 identified studies on home telemonitoring reveals that the effects of this care delivery method are, in general, highly encouraging, especially at the clinical, behavioral, and structural levels. In general, telemonitoring is clinically effective in patients with diabetes, hypertension, or asthma and allows for a better understanding of the patient's health, better control of symptoms, greater compliance with pharmacotherapy, and greater patient empowerment. It also leads to a reduction in demand for health care, with 50% of the studies reporting a significant decrease in service consumption. The other half of the studies report that both modalities (telemonitoring and conventional home follow-up) are equivalent in this regard. The analysis also identified 3 main categories of conditions for successful implementation of telemonitoring: 1) those associated with the patients in question, 2) those associated with the technological devices used, and 3) those associated with the organization of a home telemonitoring program. The highly encouraging results observed at all levels, together with demographic changes, the prevalence of chronic diseases, and the anticipated shortage of nurses in Québec warrant a gradual implementation of home telemonitoring for all healthcare services provided to the chronically ill. However, the success of such projects depends on adopting a holistic view and proactively managing the various issues and risks involved, since the technological devices provided to the patients cannot, alone, guarantee that the desired effects will be achieved.

Only by meeting all conditions listed in the report can the likelihood of observing these positive effects be significantly increased.

Methods

The systematic review covers January 1966 to December 2007 and concerns the clinical, behavioral, structural, and economic effects associated with home telemonitoring and its main conditions for success. MEDLINE (PubMed interface), The Cochrane Library, and the INAHTA (International Network of Agencies for Health Technology Assessment) database were consulted, and the Copernic and Google search engines were queried.

Further research/reviews required

Given the paucity of evidence and the ambiguity of the results obtained thus far, no firm conclusions can be drawn regarding the economic viability of home telemonitoring. More thorough and more rigorous economic studies are therefore recommended.

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INAHTA Briefs

Issue 2010/014

Title	**Screening Mammography for Women Aged 40 to 49 Years: Update**
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Reference	ETMIS 2009, 5 (8). Printed French edition ISBN 978-2-550-56663-2, English summary (PDF) ISBN 978-2-550-56662-5. www.aetmis.gouv.qc.ca/site/en_publications2009.phtml

Aim

To review the new mortality reduction estimates for screening starting from 40 years of age; to assess the magnitude of screening-related adverse effects, especially those associated with radiation exposure, additional diagnostic tests, and overdiagnosis; to enable Québec's Department of Health and Social Services (MSSS) and women and their physicians to make informed decisions regarding participation in screening mammography starting from 40 years of age.

Conclusions and results

Mammographic screening starting from 40 years of age reduces breast cancer mortality by about 15% for all women invited to screening, but the reduction is around 25% among women who are actually screened, and this is the relevant consideration for women weighing the benefits and harms of screening. Although screening mammography reduces mortality, it also has drawbacks, eg, exposition to ionizing radiation. These drawbacks significantly counterbalance the benefits that women in this age group could gain from participating in a systematic screening program. Hence, it is not advisable to extend the screening program to all women aged 40 to 49 years. Currently, doctors can recommend mammographic screening to some women in that age group after assessment of their individual risk. Other recommendations were made on the organization of the *Programme québécois de dépistage du cancer du sein* (Québec's Breast Screening Program) and on ways to strengthen its quality-assurance measures to optimize the net benefits for women screened.

Methods

Pool the results of the UK Age Trial with those of the other randomized mammography trials conducted in women younger than 50 years; present these results by comparing the expected outcomes for a cohort of 1000 women aged 40 years assumed to participate in annual screening for 10 years, with the outcomes of unscreened women; examine the amount of radiation absorbed during a mammogram and its carcinogenic effects, according to different modeling analyses, and also look at the additional adverse effects arising from diagnostic investigations and overdiagnosis; compare the conditions and parameters of Québec's organized breast screening program with programs implemented during the major clinical trials from which the estimates were derived in order to evaluate the extent to which these trials' outcomes might be reproduced in the Québec program.

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INAHTA Briefs

Issue 2010/015

Laser Technology for Removal of Caries

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Aim

To evaluate the scientific evidence on laser technology in removing carious tissue.

Conclusions and results

Limited scientific evidence suggests that laser is as effective as rotary bur in removing carious tissue. Treatment time is prolonged. Limited scientific evidence suggests that adults prefer laser treatment. No conclusions can be drawn regarding biological or technical complications, children's perception of laser treatment, or cost effectiveness of the method.

Three medium-quality studies evaluated erbium laser in cavity preparation and caries excavation. Time required to remove carious tissue was evaluated in 5 studies assessed as medium quality for this outcome. Four studies included the effect of laser treatment on dental pulp as an outcome, but quality was assessed as low due to short follow-up time. Two studies, which included longevity of the restoration as an outcome, were also assessed as having low quality due to inadequate follow-up time. Three studies that evaluated patient response were assessed as having medium quality with respect to this outcome. The economic model showed that compared to excavation by rotary bur, laser excavation increases the cost by about 31 euros.

Methods

The literature search identified 23 papers that addressed treatment effects and economic aspects of laser technology. We found no relevant studies on economic aspects. Hence, a simplified model was used to calculate a cost per intervention. Regarding the effect of treatment, 16 papers were selected for assessment according to established criteria.

Further research/reviews required

Additional studies need to investigate biological and technical complications, children's perception of laser treatment, and cost effectiveness of the method.

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