

# 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](http://www.inahta.org)

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.

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# Introduction

The International Network of Agencies for Health Technology Assessment (INAHTA) is a global network linking 38 non-profit, governmental institutions from 19 countries (2002).

*INAHTA was established in 1993 with the aim*

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

*The mission of INAHTA is*

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

*The INAHTA membership is open to any organization which*

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

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

***Further information on INAHTA is available at [www.inahta.org](http://www.inahta.org)***



<b>Title</b>	<b>Treatment of Venous Leg Ulcers and Optimal Use of Apligraf™</b>
<b>Agency</b>	<b>AÉTMIS (formerly CETS), Agence d'évaluation des technologies et des modes d'intervention en santé</b> 2021 Union Avenue, Suite 1040, Montreal, Quebec, Canada H3A 2S9; tel:+1 514 873 2563, fax:+1 514 873 1369; aetmis@aetmis.gouv.qc.ca, www.aetmis.gouv.qc.ca
<b>Reference</b>	(AÉTMIS 2000-5 RE). Montréal: AÉTMIS, 2001, xiii-132 p. Available in French (ISBN 2-550-36940-8) and English (ISBN 2-550-37129-1)

## Aim

The Ministère de la Santé et des Services Sociaux du Québec asked AÉTMIS to document the clinical and economic value of the human skin substitute known as Apligraf™ used in treating venous leg ulcers. The resulting analysis is based on the epidemiology of venous leg ulcers, on current treatment options and their efficacy, and on estimated costs.

## Results and Conclusions

*Clinical issues:* 1) The evaluation and diagnosis of patients should be properly performed. 2) Treatment of venous leg ulcers with compression therapy is more effective than treatment without compression. 3) Compression therapy in conjunction with Apligraf™ provides faster healing times than compression alone. 4) Compression therapy in conjunction with Apligraf™ averts more ulcer days than does compression alone.

*Economic issues:* In the absence of validated data, the following statements remain provisional. 1) Compression therapy simultaneously with Apligraf™ generates high costs in reducing the number of ulcer days. 2) Compression therapy plus Apligraf™ for cases that are unresponsive to initial compression therapy is less costly than compression and Apligraf™ simultaneously and offers potential savings for the healthcare system in an optimistic scenario. 3) Identifying hard-to-heal ulcers with planimetry at week 4 of initial compression therapy and subsequently adding Apligraf™ to treatment can increase savings.

## Recommendations

1) To promote: (a) continued efforts to generalize the management of leg ulcer patients according to the recommendations of advisory panels and (b) the use of compression therapy in treating venous leg ulcers. 2) To recognize, at the clinical and administrative levels, the potential role of Apligraf™ in the treatment of venous leg ulcers that are resistant to initial compression and the possible savings that could be generated. 3) To maintain rigorous policies on the use of Apligraf™ by certified physicians in hospital outpatient clinics which are, or should start, planning for specific budgets for this specialized supply. 4) To promote the dissemination of clinical and administrative protocols on the use of Apligraf™, which some hospitals have developed and implemented, so that other institutions can consider and tailor them as needed.

## Methods

Literature review (MEDLINE, Cochrane, PubMed, Current Contents, World Wide Web, surveys, institutional documents); consultation of administrative databases.

## Further research required

1) To ensure that current developments on the indications of Apligraf™ be followed up and that this report be updated following the publication of results of the multicenter pan-Canadian randomized controlled trial in the summer of 2001. 2) To initiate the research necessary to document the epidemiology of leg ulcers in Quebec and the clinical effectiveness and costs of various treatment strategies in clinical, CLSC, and home care settings.



<b>Title</b>	<b>Intracoronary Brachytherapy</b>
<b>Agency</b>	<b>CEDIT, Committee for Evaluation and Diffusion of Innovative Technologies Assistance Publique Hôpitaux de Paris</b> 3, avenue Victoria, 75100 Paris RP, France; tel: +33 1 40 27 31 09, fax:+33 1 40 27 55 65, info.cedit@sap.ap-hop-paris.fr, http://cedit.ap-hop-paris.fr
<b>Reference</b>	CEDIT Report (in French) 01.09/Ra1/01/Recommendation 01.09/Re1/02.

## Aim

CEDIT was consulted by Professor Beaufile and Dr. Henry (Cardiology Department, Lariboisière Hospital) in association with Professor Maylin and Dr. Gozy (Radiotherapy Department, Saint-Louis Hospital) for an evaluation of intracoronary brachytherapy. This technique is used in cases of coronary restenosis following angioplasty and more generally as an adjuvant therapy for coronary atherosclerosis associated with angioplasty.

Intracoronary brachytherapy involves temporary insertion of a radiation source into the lumen of a vessel to be treated. Under optimal safety conditions for the operator, a radiation source, delivered by a radioactive source train, is inserted via the distal end of a catheter and then removed at the end of treatment. The procedure is conducted with radioscopic control. The equipment most widely used is the *GALILEO™ Intravascular Radiotherapy System* manufactured by GUIDANT and *Beta-Cath®* from NOVOSTE. Both are  $\beta$ -radiation systems used only in intracoronary brachytherapy.

## Results

Abundant data have been presented over the last 5 years on intracoronary brachytherapy. Our bibliographical search highlighted eight studies based on randomized treatment trials. They conclude that the arterial lumen in treated patients is favorably influenced by irradiation. Thus, a stenosis of over 50% during followup is far less frequent in treated groups than in control groups. However, it must be noted that for a non-negligible number of patients, data on control examinations are not available and followup modalities are rarely described.

The surplus cost of an intracoronary brachytherapy procedure as part of angioplasty is estimated at between 3800 EUR and 4600 EUR. This surplus cost includes equipment costs, consumables (the single-use catheter accounts for 90% of the overall surplus cost), and staffing costs. In light of results of randomized studies comparing brachytherapy to a placebo in the case of a first-time in-stent restenosis, our cost-effectiveness approach does not suggest that this surplus cost is offset by a significant reduction in clinical incidents.

## Recommendations

CEDIT is of the opinion that intracoronary brachytherapy has yet to be sufficiently evaluated. Since followup periods are not lengthy enough, its long-term effects are not fully known.

CEDIT emphasizes that the current development of coated stents, a promising technology, could well provide an alternative to intracoronary brachytherapy. However, followup information on the medium and long-term effects of such stents is insufficient, and their indications are yet to be clearly established.

CEDIT recommends that only one center of the AP-HP be designated for treatment with intracoronary brachytherapy for patients showing an in-stent restenosis.

## Methods

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



<b>Title</b>	<b>Intravascular Extraction of Chronically Implanted Permanent, Transvenous Pacing Leads, October 1999</b>
<b>Agency</b>	<b>MSAC, Medical Services Advisory Committee</b> Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia; tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au
<b>Reference</b>	MSAC application 1010. Assessment report, ISSN 1443-7120.

## Aim

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

## Conclusions and Results

*Safety:* Complications from the procedure are uncommon although near fatal/fatal adverse events are sometimes reported. No comparative safety profile with open heart surgery is available.

*Effectiveness:* The procedure is effective (78%–97%) with minimal invasiveness.

*Cost-effectiveness:* This was not completed due to insufficient data on comparative efficacy/effectiveness.

## Recommendations

- Additional funding should be supported for the procedure where the leads have been implanted for more than 3 months and require use of surgical tools and countertraction for their removal.
- The procedure should be restricted to cardiologists and cardiothoracic surgeons who have specialist training in the procedure and who are willing to participate in an audit program administered by the Cardiac Society of Australia and New Zealand to achieve accreditation.

## Method

MSAC conducted a systematic review of medical literature via MEDLINE and HealthSTAR from 1966 – June 1999.





**Title** **Effects of Education and Psychosocial Interventions for Adolescents with Diabetes Mellitus: A Systematic Review.**

**Agency** **NCCHTA, National Coordinating Center for Health Technology Assessment**  
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tel:+44 2380 59 5586, fax:+44 2380 59 5639, hta@soton.ac.uk, www.ncchta.org

**Reference** Health Technol Assess 2001;5(10) (April 2001); www.ncchta.org/htapubs.htm#510

## Aim

To examine the effectiveness of educational and psychosocial interventions for adolescents with type 1 diabetes, designed to improve their diabetes management. Research questions addressed were: Do educational and psychosocial interventions for adolescents with type 1 diabetes have beneficial effects on biological and psychosocial outcomes? Are there types or features of interventions that are shown to be more effective than others? What evidence exists on the cost-effectiveness of interventions?

## Results and Conclusions

- This systematic review found that educational and psychosocial interventions have small to medium beneficial effects on various diabetes management outcomes. Interventions are likely to be effective if they demonstrate the interrelatedness of the various aspects of diabetes management. However, well-designed trials are needed in the UK.
- It is not known whether interventions should be targeted (eg, modified for different disease stages, different types of diabetes management problems, or different age groups of adolescents).
- To obtain economic returns, interventions must show favorable, long-lasting effects on behavior and metabolic control, but we lack cost-effectiveness studies that fully address the resource implications and long-term consequences of educational interventions for adolescents with type 1 diabetes.

## Recommendations

This review recommends undertaking a phase program of primary research involving a consultation process in adolescents with type 1 diabetes, their families, doctors, nurses, health economists, and health psychologists to identify possible interventions seen as plausible and potentially effective by patients and their parents, feasible and practical in the context of the NHS diabetes services, and understood and accepted by doctors and nurses as key and integral parts of diabetes care.

## Methods

A search strategy was formulated, piloted, and refined. Three journals were handsearched, 11 electronic databases were searched, and personal contacts, flyers, conferences, and websites were used to notify the research community of the review to access further literature. This process generated 10 535 abstracts, which, after screening, resulted in 367 articles identified for retrieval. This number was augmented by hand-searching, personal contact, and exploding references, and a final total of 457 articles were scrutinized. Of these, 64 reports describing 62 studies were identified as empirical papers evaluating educational or psychosocial interventions. The relevant data were extracted from the papers and summary tables for each study were prepared. Where possible, effect sizes were computed for outcomes from studies that included a randomized control group (CG) and other relevant information.

## Further research/reviews required

Primary research of interventions based on sound behavioral principles that are acceptable to patients and have the potential to be cost-effective.



**Title** **Systematic Review of Dynamic Graciloplasty for the Treatment of Fecal Incontinence.**

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

Box 688, North Adelaide, SA 5006, Australia; tel +61 8 82391144, fax +61 8 82391244; [College.asernip@surgeons.org](mailto:College.asernip@surgeons.org)

**Reference** ASERNIP-S Report No. 14, ISBN 0 909844 437;  
[www.surgeons.org/open/asernip-s/publications.htm](http://www.surgeons.org/open/asernip-s/publications.htm)

## Aim

This systematic review aims to assess the safety and efficacy of dynamic graciloplasty compared to colostomy in the treatment of fecal incontinence.

## Results

No high-level evidence or comparative studies were available.

*Safety:* Mortality rates were around 2% for both graciloplasty and colostomy. Morbidity rates reported for graciloplasty varied widely across studies, with an average of one morbidity reported for each patient. Morbidity rates for colostomy were reported in a single study to be around 50%. There were no data available directly comparing the two surgical procedures.

*Efficacy:* Dynamic graciloplasty was clearly effective at restoring continence in 42% to 85% of patients, whereas colostomy is, by its design, incapable of restoring continence. Dynamic graciloplasty is associated with a significant risk of reoperation, with rates reported to range between 0.14 per patient up to 1.07 per patient. Reoperation rates for colostomy were reported at 0.13 per patient up to a cumulative risk of 0.17 at 11 years. No data directly compared the two procedures.

## Conclusions and Recommendations

The evidence base for dynamic graciloplasty was found to be inadequate to determine safety in comparison to colostomy, and a controlled clinical trial should be conducted although randomization would probably prove impractical for ethical reasons. Any such trial should also assess quality of life issues between the two procedures. Dynamic graciloplasty was found to be clearly more efficacious than colostomy for restoring continence in around 60% of patients. However, patients must be clearly informed of the high probability of failure of this operation.

## Methods

All original, published studies on dynamic graciloplasty and colostomy were identified by searching Current Contents, EMBASE, MEDLINE and the Cochrane Library from 1991 onward. Only studies of patients diagnosed with intractable fecal incontinence were included for review. English language papers were selected. Acceptable study designs included randomized controlled trials, controlled clinical trials, case series, or case reports.



**Title**      **Placement of Artificial Bowel Sphincters in the Management of Fecal Incontinence, December 1999**

**Agency**      **MSAC, Medical Services Advisory Committee**  
Commonwealth Department of Health and Aged Care GPO Box 9848 Canberra ACT 2601 Australia;  
tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference**      MSAC application 1023. Assessment report, ISSN 1443-7120.

## **Aim**

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

## **Conclusions and Results**

*Safety:* Could not be assessed due to insufficient data.

*Effectiveness:* Has not been demonstrated due to a lack of rigorous studies.

*Cost-effectiveness:* Could not be assessed.

## **Recommendations**

Public funding should not be supported at this time.

## **Method**

MSAC conducted a systematic review of the biomedical literature from 1966 to August 1999 by accessing biomedical electronic databases, the Internet, and international health technology agency websites. The manufacturer was consulted and reference lists of retrieved studies were searched.



- Title** **Invasive Aspergillosis: State of the Art in Diagnosis, Treatment, and Condition – an Assessment.**
- Agency** **ITA, Institute of Technology Assessment at the Austrian Academy of Sciences**  
Strohgasse 45, 1030 – Vienna, Austria; [www.oeaw.ac.at](http://www.oeaw.ac.at)
- Reference** ITA-Reports, June 2/2000

## Invasive Aspergillosis

Today, patients with life-threatening underlying diseases (acute leukemia, BMT, etc) and impaired immunologic status have a higher life expectancy. However, invasive aspergillosis (IA), a severe fungal infection, has emerged as a major cause of morbidity and mortality in departments of hemato-oncology and transplantation-medicine. Since aspergillosis spreads rapidly to other organs and can be lethal it is important to react quickly to the first clinical infestations of the infection. Amphotericin B is usually given at the slightest suspicion. In its lipid formulation, Amphotericin B is less toxic but much more costly.

## Aim

The project aims to provide information on available evidence concerning the effectiveness of different strategies to prevent and to effectively diagnose and treat IA.

## Results and Conclusions

- Since an ever-increasing number of patients (with tumors or undergoing transplantation, etc) receive immunosuppressive therapies, the incidence of IA has increased considerably and will increase in the future.
- To a certain degree, IA has to be accepted as a consequence of high-tech medicine.
- Since IA spreads rapidly, with lethal consequences, the main focus of intervention must be to prevent IA, ie, eliminating the fungus in the environment of immunosuppressed patients.
- Recent diagnostic developments (PCR and ELISA) make it possible to routinely screen risk-groups 2 to 3 times per week. A change in the diagnostic strategy should result in a change in treatment regimens toward preemptive therapy.
- The lipid Amphotericin B formulation is as effective as the conventional one, but is less nephrotoxic. However, it is 50 to 70 times more expensive and therefore can be used only selectively.
- An early diagnosis and treatment strategy must define which therapeutic approach – prophylactic, empiric, or preemptive – should be taken. A strategy plan must address medication, therapy start and dose, when to change medication, etc.

## Methods

Comprehensive HTA of epidemiological data, with a focus on high-risk groups, systematic review of methods for early diagnosis, treatment schemes, economic analysis, overview of EBM guidelines.

This assessment is available in German only. The full report can be obtained at <http://www.oeaw.ac.at/ita/hta/>



- Title** **Immunoglobulins in Transplant Medicine. Prevention and Therapy of Cytomegalovirus Infection.**
- Agency** ITA, Institute of Technology Assessment at the Austrian Academy of Sciences  
Strohgassee 45, 1030 – Vienna, Austria; [www.oeaw.ac.at](http://www.oeaw.ac.at)
- Reference** ITA-Reports, August 2/2001

## Aims and Background

Cytomegalovirus (CMV) infections are one of the most common infection complications in transplant recipients. The most important criteria for risk evaluation are: CMV – antibody constellation between donor and recipient, the type of immune-suppressive therapy, and the transplanted organ itself. The most favorable prophylactic treatment/therapy regime and the starting point of the intervention have been discussed for some time. The aim of this assessment is to analyze the clinical effectiveness of immunoglobulins (IG) in the prevention/therapy of CMV infections in transplant patients and to compare IG with other prevention/therapy regimes (virustatica, eg, Ganciclovir) with regard to clinical effectiveness and cost-effectiveness.

## Results

- With IG there is a significant reduction in CMV infections and diseases in comparison to placebo or no prophylactic treatment or therapy.
- A comparison of efficacy based on systematic reviews and meta-analyses offers no evidence that IG is more effective than virustatica. There is no evidence for additional effects of IG in antiviral therapy.
- A review of cost-effectiveness studies shows that virustatica are the most cost-effective option for prophylaxis and therapy of CMV.

## Conclusions

- Active CMV infection can be diagnosed by laboratory tests even before clinical symptoms appear. This allows for a combined CMV management consisting of risk-adapted prophylactic treatment in high-risk groups and the start of preemptive therapy.
- Despite lower toxicity of IG, this added value is only marginal because of the many times higher costs and the similar, inclining lower clinical efficacy in comparison to virustatica (eg, Ganciclovir).

## Methods

This assessment is based on a systematic review and meta-analysis of IG for prevention/therapy of cytomegalovirus. Additionally, basic knowledge on CMV infection, the frequency of transplantation, and cost issues are analyzed.

This assessment is available in German only. Full report at: [www.oeaw.ac.at/ita/hta](http://www.oeaw.ac.at/ita/hta)



**Title** Hepatitis C (HCV) Viral Load Testing, March 2000

**Agency** MSAC, Medical Services Advisory Committee

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference** MSAC application 1021. Assessment report, ISSN 1443-7120.

## Aim

To assess the safety and effectiveness of the service and under what circumstances public funding should be supported. Specifically, to assess whether certain tests for patients with HCV can inform clinical decisions to institute or continue interferon therapy.

## Conclusions and Results

*Safety:* The test is safe.

*Effectiveness:* Genotyping and viral load testing are predictive of the response to interferon therapy. As patients with a high viral load and more resistant genotypes can respond to interferon therapy, the predictive value of genotyping and viral load testing is insufficient to exclude a patient from treatment. Viral testing during interferon therapy has greater predictive value than pretreatment determinations and can guide decisions to continue therapy.

*Cost-effectiveness:* Cost savings would occur if 15% of patients tested decided not to proceed with interferon therapy as a result of testing. Although viral load testing and genotyping is expensive, it may be cost effective with careful patient selection.

## Recommendations

Public funding should be supported for these tests on patients with confirmed HCV where a consultant physician is managing treatment subject to the following new restrictions:

- Genotype testing be restricted to once only for each patient,
- Viral load testing is prior to treatment and used only once in a 12-month period,
- Viral detection testing be limited to patients undertaking antiviral therapy, and used once prior to treatment and no more than 3 times in the following 12 months, and
- A maximum of 4 viral detection tests for any course of treatment.

## Method

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

This review investigated the following in patients with HCV:

- Pretreatment genotyping/viral load testing predicts the response to interferon therapy,
- Polymerase chain reaction-based viral detection during antiviral therapy predicts sustained virological response.

Cost effectiveness was modeled by comparing the costs of genotyping and viral load testing with an empirical trial of therapy and a qualitative detection test at 12 weeks. The analysis indicates what proportion of patients need to decide not to proceed with interferon therapy – as a result of genotyping and viral load testing – for cost savings to result.





<b>Title</b>	<b>Brachytherapy Treatment of Localized Prostate Cancer</b>
<b>Agency</b>	<b>CEDIT, Committee for Evaluation and Diffusion of Innovative Technologies</b> <b>Assistance Publique Hôpitaux de Paris</b> 3, avenue Victoria, 75100 Paris RP, France; tel: +33 1 40 27 31 09, fax:+33 1 40 27 55 65, info.cedit@sap.ap-hop-paris.fr, http://cedit.ap-hop-paris.fr
<b>Reference</b>	CEDIT Report (in French) No. 01.06/Recommendation 1/01

## Aim

CEDIT received a request from Pr. Abbou (Urology Department at Henri-Mondor hospital, Paris), Pr. Leduc (Urology Department at Saint-Louis Hospital, Paris) and Pr. Boccon-Gibod (Urology Department at Bichat Hospital, Paris) for an opinion on the application of brachytherapy in treating localized prostate cancer in their departments.

## Results

CEDIT is of the opinion that there are too many reservations in terms of exact indications, methodology, effectiveness, and results on the quality of life for brachytherapy to be widely applied as treatment for localized prostate cancer. CEDIT believes that the effectiveness of this technique is still under evaluation, and therefore its use must be limited to one reference center where experience has already been acquired. As cooperation on this subject between the departments of Urology and Radiation Therapy at the Saint-Louis Hospital is operational and experience has been acquired, they are designated by CEDIT as a reference center for this treatment within AP-HP. It will be the role of this center to conduct rigorous evaluations to obtain clinical and economic results for a potentially wider application of the technique in AP-HP.

## Methods

A summary of the reports concerning this technique was published in 1999 by INAHTA, concluding that it was not possible to show that brachytherapy was more effective than other existing treatments, and that it might even be less effective. Since its side effects appeared to be less frequent, it was suggested that brachytherapy be reserved for low-risk localized cancers, at stage T1c, T2a, PSA $\leq$ 10, Gleason  $<7$  ng/ml, the risk of biological failure (rise in PSA) being three times higher if risk is average or high. CEDIT analyzed the literature available since 1999 and reports that: currently there is no prospective, randomized study that compares brachytherapy to other treatments, nor is a meta-analysis possible given the diversity of the various publications; brachytherapy requires a multidisciplinary organization and techniques where experience is acquired only after 30 patients have been managed at a rate of at least one treatment per week; comparisons between patients of the different series are not validated either in terms of results or side effects - follow-up indicates an increase in complications over time, particularly impotence in over 50% of patients in certain series; the fundamental concept of quality of life is largely under-evaluated; this technique is still under development as its indication as a *single treatment* for low-risk cancer T1 to T2a in 1999 seems to be restricted by the authors to cancer at stage T1; *the association of brachytherapy with hormone treatment and/or external radiation therapy* is yet to be evaluated for other stages of the disease; given the considerable variations in indications, techniques, doses, and associations, *the American Brachytherapy Society (ABS) in 1999 gave out clinical and dosimetric codes of conduct to uniformize treatment parameters and methods for data presentation.*



**Title**      **Brachytherapy for Prostate Cancer**

**Agency**    **CAHTA, Catalan Agency for Health Technology Assessment and Research**

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**Reference** CAHTA HTA report November 2000, Pages: 47, References: 51. Available only in Spanish at [www.aatm.es/cas/informes/i.html](http://www.aatm.es/cas/informes/i.html) (Report carried out on request of the Spanish Ministry of Health and Consumer Affairs under an agreement signed between the Instituto de Salud Carlos III and the CAHTA)

## Aim

To overview brachytherapy as applied to localized prostate cancer (PC) and to analyze the scientific evidence related to the efficacy, effectiveness, and clinical safety of this health technology. Another aim was to study the clinical practice of brachytherapy in Spain and related economic, organizational, and regulative issues.

## Results and Conclusions

The state of scientific knowledge about this therapy (efficacy, effectiveness, and clinical safety) is difficult to assess.

The literature search revealed no randomized, controlled clinical trials. The numerous studies performed in assessing the technique are limited to observational studies, most of which are retrospective, plus a few clinical series with non-equivalent comparison groups (without randomized grouping). Moreover, they vary widely in patient recruitment criteria (age, comorbidities, socio-economic class), tumor characteristics (staging, Gleason, PSA), implantation of different seeds and use of techniques, combination of treatments, followup time, and definitions concerning the progression of disease.

The intermediate short-term results of brachytherapy (biochemical control levels and disease-free survival) for patients selected with a low risk of extraprostatic progression seem to be comparable to those of other therapeutic options, eg, prostatectomy and external radiotherapy.

No long-term data are available, despite the fact that results from a sample (n=77) followed up for 12 years were recently published, showing the same rate of disease-free survival as was observed after 10 years of followup (66%). Among the complications secondary to brachytherapy described are prostatitis and acute urethritis, with greater frequency than after surgery. A smaller share of impotence and urinary incontinence were also found.

Brachytherapy seems to be indicated for patients with a low risk of extracapsular extension (stages T1, T2a; clearly differentiated and with low pretreatment rates of AST) with patients presenting prior irradiation of the pelvis, severe urethral obstruction, and transurethral prostatic resection excluded.

There is uncertainty as regards localized PC. Despite the evidence showing that this type of tumor tends to have a slow progression, it is unclear whether the type of treatment will or will not help all men with PC to live longer. On the other hand, it must be remembered that treatment can affect a patient's quality of life. Thus, random-design clinical trials are needed with prolonged followup to confirm the efficacy and safety of brachytherapy, assess patient quality of life, and define the role of this technique in the treatment of PC. In view of the lack of a therapeutic alternative that is clearly better than the rest, and due to the major side effects of some therapeutic options, it is becoming increasingly more necessary to consider the values and the preferences of patients when approaching this clinical condition.

## Methods

Qualitative systematic review of scientific evidence and external peer review process.





**Title** Photodynamic Therapy for Skin and Mucosal Cancer (PDT),  
May 1999

**Agency** MSAC, Medical Services Advisory Committee  
Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference** MSAC application 1008. Assessment report, ISSN 1443-7120.

## Aim

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

## Conclusions and Results

Safety: PDT is safe.

Effectiveness: Trials undertaken have been too small or lacked sufficient controls to provide firm evidence relating to the effectiveness of PDT relative to current treatment options. Long-term followup is necessary to resolve uncertainties pertaining to:

- The precise role of PDT in the management of non-melanoma skin cancers and related skin lesions,
- Appropriate indications for PDT,
- Selection of patients for PDT,
- Where to treat patients, and
- Unresolved issues associated with the physics and dosimetry of PDT.

Cost-effectiveness: No cost comparisons with other treatment are available. However, PDT has the potential to be very costeffective.

## Recommendations

PDT not be supported for public funding due to lack of sufficient evidence.

## Method

MSAC conducted a systematic review of medical literature via MEDLINE, EmBase, and HealthSTAR from 1993-1998.

## Further research

PDT trials are underway in Brisbane and at the Skin and Cancer Foundation in Melbourne. Research is continuing into the most appropriate light delivery system and photosensitizer for PDT.



<b>Title</b>	<b>Brachytherapy for the Treatment of Prostate Cancer, November 2000</b>
<b>Agency</b>	<b>MSAC, Medical Services Advisory Committee</b> Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia; tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au
<b>Reference</b>	MSAC application 1029. Assessment report, ISSN 1443-7120.

## Aim

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

## Conclusions and Results

*Safety:* Brachytherapy may offer less risk of impotence and urinary incontinence than other major treatment options for localized prostate cancer.

*Effectiveness:* There has not been a successful randomized controlled trial of the use of brachytherapy. The relative advantage of brachytherapy derives from perceived scope for potency preservation and the single session outpatient nature of the treatment.

*Cost-effectiveness:* Brachytherapy has slightly higher direct budgetary costs than other alternatives, but may involve less indirect costs associated with reduced hospitalization and time off work.

## Recommendations

Interim public funding should be supported at approved sites for patients with prostate cancer at clinical stages T1, T2a, or T2b, with Gleason Scores  $\leq 6$ , prostate specific antigen  $\leq 10$  ng/ml, a gland volume  $< 40$ cc, and with a life expectancy of more than 10 years, subject to a review within 3 years.

## Method

MSAC conducted a systematic review of the biomedical literature from 1990 to March 2000 using biomedical electronic databases, the Internet, and international health technology agency websites to identify relevant studies.



**Title** Conformal Radiotherapy, November 2001

**Agency** MSAC, Medical Services Advisory Committee

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference** MSAC application 1038. Assessment report, ISSN 1443-7120.

## Aim

To assess the safety and effectiveness of conformal radiotherapy (CRT) and intensity modulated radiation therapy (IMRT) using multileaf collimators (MLCs) to treat cancer and under what circumstances such services should be supported with public funding.

## Conclusions and Results

*Safety:* Tolerance of normal tissues is the limiting factor for the dose of radiation that can be delivered to the tumor. CRT aims to limit exposure of normal tissues to radiation and increase the dose to the tumor. In treating prostate cancer some randomized evidence suggests that delivery of similar doses using CRT may result in reduced toxicity than that experienced when using conventional radiotherapy.

*Effectiveness:* Based on a few randomized trials, data show that CRT efficacy is similar to conventional radiotherapy when delivering similar doses to treat prostate cancer. Higher doses delivered by CRT may result in greater efficacy for prostate cancer patients. However, further randomized evidence is needed in this area.

*Cost-effectiveness:* The main focus of the cost implications for conformal radiotherapy was the use of MLCs in treating patients with cancer. MLCs, in comparison to shielding blocks, can decrease the average duration of radiation treatment, increasing linear accelerator productivity and patient throughput. MLCs also reduce (or eliminate) the need to manufacture blocks, reducing labor and supply costs. Based on the additional costs of MLCs alone, CRT appears to be both more effective and less costly in some patient groups.

*Quality assurance, occupational health and safety:* The increased sophistication of technology, specifically in MLCs and electronic portal imaging, appears to provide some occupational health and safety benefits for both radiotherapy staff and patients.

## Recommendations

Public funding under the Australian Medicare Benefits Schedule should be supported for conformal radiotherapy. Intensity modulated radiation therapy should be reviewed at a later date when substantial additional data relating to safety, effectiveness, and cost-effectiveness are available.

## Method

MSAC conducted a systematic review of medical literature until the end of March 2001 using biomedical electronic databases, existing reviews, the Internet, and international health technology assessment organization websites. This review sought data on CRT, primarily in the treatment of prostate cancer, but also in the treatment of other cancer indications.



**Title** **Conductive Education for Children with Cerebral Palsy**

**Agency** **AHFMR, Alberta Heritage Foundation for Medical Research, HTA Unit**

3125 Manulife place, 10180-101 Street, Edmonton, Alberta, T5J 3S4, Canada;  
tel:+1 780 423 5727, fax:+1 780 429 3509, djuzwish@ahfmr.ab.ca

**Reference** ISBN 1-896956-33-5, full text downloadable [www.ahfmr.ab.ca](http://www.ahfmr.ab.ca)

## **Aim**

To assess the evidence on the effectiveness of conductive education as a treatment program focusing on children with cerebral palsy. This review was requested by three ministries to answer the question: Is conductive education as a learning approach or therapeutic intervention safe and efficacious for children with disabilities such as cerebral palsy that impact neuromotor functioning?

## **Results and Conclusions**

Evidence on the efficacy and effectiveness of conductive education (CE) is sparse and of poor quality. CE is a fast-developing educational approach. Its efficacy is not established nor is its nature well defined. The scientific literature does not show this approach to be superior to, or more effective than, other treatment methods. Research evidence, while not establishing CE as more effective than other forms of therapy for children with CP, indicates that children in the CE groups kept pace with their peers receiving other therapies. Other than decreased hip mobility identified in one study, no harm was identified from CE.

The report concludes that CE is developing rapidly, can be manifested in different ways in different social contexts, and is practiced differently in different countries. CE programs have been modified with components added from other approaches and special education. Most adaptations of CE have not involved residential treatment (as originally practiced in Hungary); some use conductors only, while others use multidisciplinary teams.

## **Recommendations**

Outcomes and conclusions from research conducted in other countries, or from other programs, may not be transferable to other settings, eg, Alberta.

## **Methods**

Systematic review and a critical appraisal of the clinical trials, randomized controlled trials, experimental methods, and empirical methods published in English from 1990 onward. Data sources included MEDLINE, CINHALL, HealthSTAR, EMBASE, ERIC database, PsycINFO, CBCA Fulltext Education, and Webspirs Current Contents. Six studies were analyzed, one RCT, three controlled studies, one pre/post design, and one case series.



- Title** **The Efficiency of Long-term Psychotherapy**
- Agency** **GR, Health Council of the Netherlands (Gezondheidsraad)**  
PO Box 16052, 2500 BB the Hague, the Netherlands; tel:+31 70 340 7520, fax:+31 70 340 7523;  
a.bolhuis@gr.nl, www.gr.nl
- Reference** Publication No. 2001/08E, 64 p.; full text available at [www.gr.nl](http://www.gr.nl)

## **Aim**

To review the current state of knowledge with regard to the efficacy, effectiveness, and efficiency of long-term psychotherapy.

## **Results and Conclusions**

- Efficacy of short-term psychotherapy has been demonstrated, however, long-term studies are scarce.
- Differences occur between efficacy and effectiveness of psychotherapy because in some cases the studied effects are of limited clinical significance, circumstances in practice may be different from the research setting, and comorbidity is found more often in the clinical situation.
- The cost-effectiveness of (long-term and short-term) psychotherapy is largely unknown. It appears that cost savings are considerable if hospitalization can be avoided.
- Psychotherapy in the Netherlands customarily involves more than 20 sessions. In view of the lack of evidence on efficiency, restraint needs to be exercised in administering such therapy.

## **Recommendations**

- Research is needed on the cost-effectiveness of long-term psychotherapy of patients with chronic relapsing depressions and personality disorders (especially the borderline type).
- Guidelines should contain criteria for determining the duration and frequency of psychotherapeutic treatments.
- A (national) monitoring system should be developed and implemented to assess the progress, efficacy, and quality of long-term psychotherapy.

## **Methods**

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

## **Further research/reviews required**

Research should be carried out to obtain more insight into the efficiency of psychotherapy, the effects of 'maintenance' therapy, and the degree of patient satisfaction.



**Title** Intensive Intervention Programs for Children with Autism

**Agency** AHFMR, Alberta Heritage Foundation for Medical Research

1500, 10104-103 Avenue, Edmonton, Alberta T5J 4A7, Canada; tel:+1 780 423 5727, fax:+1 780 429 3509,  
www.ahfmr.ab.ca

**Reference** February 2001, ISBN 1-896956-40-8, full text downloadable [www.ahfmr.ab.ca](http://www.ahfmr.ab.ca)

## Aim

To review the published research on the effectiveness of intensive intervention programs for children with an autism spectrum disorder (ASD).

## Results and Conclusions

Three critical reviews of intensive intervention programs for autism by ECRI, BCOHTA, and Smith were summarized. Of the three reviews, the one by ECRI was the most inclusive, analyzing studies on Lovaas therapy, TEACCH, the Rutgers Program, the Denver Program, LEAP, and the Autism Preschool Program. All critical reviews analyzed studies on Lovaas therapy and concluded that these studies were methodologically flawed. The outcome measurement instruments used in all of the studies assessed in the critical reviews were similar. Most researchers employed standardized measures of IQ tests, adaptive functioning, and language development.

Insufficient evidence is available to establish a relationship between the amount (intensity and duration) of any intensive intervention treatment program and outcome measures (intelligence tests, language development, adaptive behavior tests). It appears that children improve in functioning with intensive intervention programs, but it remains to be determined if any one program is more effective than another.

## Recommendations

Well-designed research studies using multiple independent measures are required. Optimal intensity and duration of intensive intervention programs for children with ASD remain to be determined through well-designed studies. Studies on the impact of these interventions on family members would also be useful to identify appropriate 'system changes' that would enhance quality of life for both the family members and the child with ASD.

## Methods

In light of recent work, it was decided to select and summarize published critical reviews. Systematic searches for critical reviews were conducted via MEDLINE, PreMEDLINE, Best Evidence, CINHAL, HealthSTAR, EMBASE, ERIC database, PsycINFO, HTA, EED, DARE, Cochrane, ISTAHC, CMA practice guideline, US National clearinghouse, and ECRI. In addition, a listing of outcome measures from the primary studies included in these critical reviews is detailed in relation to the validity and reliability of the measures.



- Title** **Psychosocial Aspects of Ultrasound Examinations During Pregnancy**
- Agency** **SWISS-TA, Center for Technology Assessment at the Swiss Science and Technology Council**  
Inselgasse 1, 3003 Bern, Switzerland; tel:+41 31 322 9963, fax:+41 31 323 3659, ta@swt.admin.ch  
www.ta-swiss.ch The study was carried out by the research groups of Professor Claus Buddeberg and Professor Renate Huch at the University of Zurich Hospital.
- Reference** Full report: TA 40 / 2001, in German, ISBN 3-908194-24-5. Short version: TA 40A / 200, in English, French, and German, also available under <http://www.ta-swiss.ch>

## Aim

In Switzerland, two ultrasound examinations are usually performed during a pregnancy. Both of these examinations are covered under the National Health Care Insurance Plan, but a revision of the Health Care Insurance Law with a view to reduce costs has brought this coverage into question. Against this background, the Swiss Federal Office for Social Insurance and the Centre for Technology Assessment decided to evaluate the psychological effects of ultrasound examinations and the attitude of expectant parents toward them. This study provides information that can serve as a basis for deciding whether these prenatal examinations should remain a part of health insurance coverage.

## Results and Conclusions

- The technical aspects of ultrasound testing receive good grades, and the prevailing assessment of ultrasound examinations for prenatal diagnosis is positive. Most of the women and men questioned believe that this technique should be an integral part of medical care for expectant mothers.
- Some of those questioned believed that the information they had received concerning the ultrasound examination had not been comprehensive, and some would have liked to have had more understandable explanations and more time for discussion.
- Many women mentioned the fear that a discovered disorder could possibly awaken in the parents. A few patients who were affected by positive findings were also burdened by a feeling of being left alone at a time when important decisions concerning the future of their pregnancy needed to be made.
- Approximately 30% of the women surveyed stated that they had not realized at the time of the first ultrasound examination that a suspicious diagnostic finding could force them into a decision-making crisis concerning termination of the pregnancy.

## Recommendations

- The conditions for more comprehensive and detailed counseling should be improved. It is of major importance that sufficient time be provided for discussions to allow the parents to come to terms with the information they have been confronted with.
- Counseling discussions are to be open, without placing the parents under pressure, and the doctors' basic approach is to be supportive and understanding.
- Guidelines should be developed for the correct means of caring for women who are confronted with a possible malformation of their unborn child. It is also necessary to work out concepts for cooperation among doctors, nurses, chaplains, social services, and psychologists.

*(continued next page)*





- Title** **Psychosocial Aspects of Ultrasound Examinations During Pregnancy**
- Agency** **SWISS-TA, Center for Technology Assessment at the Swiss Science and Technology Council**  
Inselgasse 1, 3003 Bern, Switzerland; tel:+41 31 322 9963, fax:+41 31 323 3659, ta@swr.admin.ch  
www.ta-swiss.ch The study was carried out by the research groups of Professor Claus Buddeberg and Professor Renate Huch at the University of Zurich Hospital.
- Reference** Full report: TA 40 / 2001, in German, ISBN 3-908194-24-5. Short version: TA 40A / 200, in English, French, and German, also available under <http://www.ta-swiss.ch>

## Methods

In this study, parents who came to the Ultrasound Center at the University of Zurich Hospital due to a suspected disorder in their unborn child were questioned. 128 women participated in the study. To learn more about how the psychological state of the affected women developed over time, they (and sometimes their partners) were questioned on three different occasions. The first questioning session involved an oral interview which took place shortly before an elucidating ultrasound examination, i.e. before suspected disorders had been confirmed or refuted. In addition to the interview, the participants also completed written question forms. The second session, a telephone interview which was also complemented with a written questionnaire, was held approximately 12 days later, at a point in time when the parents knew whether their suspicions had been confirmed or dispelled. In the third phase of the study, the participants were mailed a question form that was to be filled out by hand; this questionnaire was sent approximately 4 weeks after either the birth of the child or an eventual termination of the pregnancy.





- Title** **Chronic Fatigue Syndrome**
- Agency** **CAHTA, Catalan Agency for Health Technology Assessment and Research**  
Travessera de les Corts, 131-159, 08028 Barcelona, Spain; tel: +34 93 55 66 469, fax:+34 93 227 2998,  
diraatm@olimpia.scs.es, www.aatm.es
- Reference** CAHTA HTA IN01/2001 report April 2001, Pages: 62, References: 97. Available only in Catalan at <http://www.aatm.es/cas/informes/i.html>

## Aim

To review the scientific state of art for chronic fatigue syndrome (CFS). Specific goals are to know about specific diagnostic criteria, epidemiology, etiology, prognosis, and the general situation concerning CFS in Catalonia.

## Results and Conclusions

- CFS is characterized by debilitating fatigue persisting for 6 months or more, experienced as serious physical and mental exhaustion, which differs from somnolence and lack of motivation, and cannot be attributed to physical exercise or to any other medical or psychiatric disease. Apart from fatigue, there are several physical, constitutional, and neuropsychological manifestations: 1) short-term concentration or memory disorders, 2) pharyngitis, 3) painful cervical or axillary adenopathies, 4) myalgias, 5) multiarticular pain without arthritis, 6) headache of a new type, model, or severity, 7) non-reparative sleep, and 8) post-effort malaise lasting more than 24 hours.
- This syndrome is known by multiple names, although the term “chronic fatigue syndrome” is the most widely recognized over others (e.g. myalgic encephalomyelitis or chronic fatigue and immune dysfunction syndrome) due to the zero causal implication of the former, at least until the etiology of this condition can be ascertained. Also, some believe that reducing the entire syndrome complex to a single subjective symptom “fatigue” is inadequate. Although some people affected by CFS comply with fibromyalgia diagnostic criteria 2 (painful non-articular process mainly affecting the muscles), the latter is a clinical condition which differs from the former.
- Currently, no specific markers make it possible to establish or support the clinical diagnosis of CFS. Hence, in the clinical assessment of most patients with chronic fatigue, there is insufficient reason to systematically resort to a battery of laboratory tests. In fact, such tests are mainly indicated to assess concrete diagnostic alternatives which emerge from the case study and the physical exploration.
- The evolutional prognosis of CFS is difficult to establish, not only due to the absence of clear prognostic factors, but also because the fluctuating nature of its symptomatology may vary, even in the same person from one day to the next. In any event, the patient must be told that CFS, despite being chronic, is neither fatal nor does it increase the risk for acquiring other diseases. Despite the quantity of studies on the etiopathogenic base of CFS, neither the etiology nor the pathogeny are known with any certainty, even although available findings show the complex and multifactorial nature of this syndrome.
- CFS presently has no etiological treatment, nor one that leads to long-term remission despite the important number and diversity of therapies tested (pharmacological, non-pharmacological, and alternative medicine) and analyzed from many different methodological perspectives. Therefore, besides advising against total rest, the management of these patients is exclusively symptomatic, and the workable endpoint is their physical and social rehabilitation, where a good physician-patient relationship is regarded as crucial.

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Written by Dr.M. Dolors Estrada and Antoni Parada, CAHTA, Spain



- Title** **Chronic Fatigue Syndrome**
- Agency** **CAHTA, Catalan Agency for Health Technology Assessment and Research**  
Travessera de les Corts, 131-159, 08028 Barcelona, Spain; tel: +34 93 55 66 469, fax:+34 93 227 2998,  
diraatm@olimpia.scs.es, www.aatm.es
- Reference** CAHTA HTA IN01/2001 report April 2001, Pages: 62, References: 97. Available only in Catalan at <http://www.aatm.es/cas/informes/i.html>

- Only randomized controlled trials for cognitive behavioral therapy (in an ambulatory regimen and on an individualized basis) have shown benefits (improvement in physical function) compared to routine medical treatment in adults with CFS.
- The lack of studies and the contradictory results from other treatment methods (antiviral, immunological, active agents on the central nervous system, and metabolites) mean that these treatments cannot be recommended in regular clinical practice at the present time.

## Methods

Qualitative systematic review of scientific evidence and external peer review process.



- Title** **Mild Head Injury – Observation or CT Scanning?**
- Agency** **SBU, The Swedish Council on Technology Assessment in Health Care**  
PO Box 5650, Tyrgatan 7, SE-114 86 Stockholm, Sweden; tel: +46 8 412 32 00, fax:+46 8 411 32 60,  
management@sbu.se, www.sbu.se
- Reference** SBU Report 153, 2000. ISBN 91-87890-69-0.  
Available in Swedish and English at <http://www.sbu.se>

## Aim

This report reviews the scientific literature on two strategies for the acute management of mild head injury (MHI), mainly regarding patient benefits and risks, but also regarding the costs to health care and society.

## Results and Conclusions

- In Sweden, 17 000 patients per year (191/100 000) are hospitalized for MHI. All hospitals report using observation as a care strategy for MHI. Computed tomography (CT) is used in approximately 20% of the cases.
- An estimated 9% of all MHI patients who are received at a hospital have abnormal findings on CT scanning. On average, 1% of the patients need neurosurgery or other interventions. Mortality is low, 0.1%.
- No studies directly compare hospital observation to CT scanning and discharge. Based on large series of patients, the differences between the results of these strategies can be neither proved nor disproved.
- It is not known how many patients need to be admitted for ethical, social, and medical reasons although CT findings may be normal.
- The direct costs of acute care hospitalization for patients with MHI in Sweden are estimated at 100 million SEK per year. The indirect costs to society for production lost due to absenteeism, etc, cannot be estimated with reasonable accuracy.
- The cost of the CT scanning strategy is estimated to be substantially lower than the cost of hospital observation.

## Methods

A literature search was conducted in databases from 1966 to 2000. The keywords included combinations of various terms for brain concussion and minor head injury. Current clinical practice was surveyed, and national data on in-hospital care and costs were also analyzed.

## Further research required

Regardless of the treatment strategy, the risks for patients with MHI appear to be low, but potentially serious. No comparative studies on the two strategies are available. Using a study size of 2000 to 3000 patients, the hypothesis can be tested that the CT method does not give inferior long-term results as compared to hospital admittance. At the same time, it is possible to assess practical implementability and economics. Such a study is essential.



**Title** **Transcranial Magnetic Stimulation in Depression**

**Agency** **SMM, The Norwegian Centre for Health Technology Assessment**  
SINTEF Unimed, P.O. Box 124 Blindern, N-0314 Oslo, Norway; tel: +47 22 06 78 07,  
fax:+47 22 06 79 79, [smm@unimed.sintef.no](mailto:smm@unimed.sintef.no), [www.sintef.no/smm](http://www.sintef.no/smm)

**Reference** SMM Report No. 6/2001. ISBN 82-14-12616-4  
Available in Norwegian at <http://www.sintef.no/smm>

## Aim

To undertake a critical and systematic review of the clinical effectiveness of repetitive transcranial magnetic stimulation (rTMS) in depression and obsessive-compulsive disorder. rTMS has been offered to patients with major depression who do not respond to other treatment modalities (resistant and refractory depressions). Electroconvulsive treatment (ECT) is an established treatment option for these patients. ECT requires general anesthesia and muscle relaxation and is an expensive procedure. Legal constraints also restrict the application of ECT. In contrast, rTMS can be used without sedatives to patients. rTMS is delivered in daily sessions for a duration of weeks. An important question in this review has been whether rTMS can replace or supplement ECT.

## Methods

Studies were identified by searches in Medline and Embase (up to February 2001) and from handsearching selected journals. Outcome measures were mainly psychometric scales that assess mood and vegetative symptoms.

## Results and Conclusions

The 12 included studies were small and varied in scientific quality. The subjects were often inadequately characterized as regards previous depressive illness and treatment, diagnosis, and therapeutic setting.

- Three of 12 scientific studies found no clinical effects from rTMS on depressions. Seven studies reported clinical effects of limited magnitude (less than 50% reduction in depression). Two studies demonstrated a good clinical response to treatment with rTMS (more than 50% reduction in depression).
- None of the studies documented the effect of rTMS beyond the treatment period.
- Two studies compared rTMS with ECT. These studies found differences in favor of ECT. The patients were not followed after the treatment period.
- The cost of ECT and rTMS treatment was comparable.
- rTMS was well tolerated and had few side effects.

In summary, clinical documentation is insufficient to justify rTMS in widespread management of depressed patients. Antidepressive efficacy is low in most studies, and treatment gains were not sustained beyond the treatment period. To maintain the antidepressive efficacy, daily treatment seems to be required. Indeed, the antidepressive efficacy was not consistent. Comparisons with ECT indicate superiority for ECT with respect to clinical effects. Some patients had good, albeit short-lived, responses to rTMS. The value of such a response can be to give hope in an otherwise hopeless situation, but beyond this there is no certain clinic.



**Title** Deep Brain Stimulation (DBS) for Symptoms of Parkinson's Disease, April 2001

**Agency** MSAC, Medical Services Advisory Committee

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia; tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference** MSAC application 1031. Assessment report, ISSN 1443-7120.

## Aim

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

## Conclusions and Results

*Safety:* Limited evidence suggests that DBS has less frequent, less severe adverse effects relative to ablative surgery. One of the benefits of DBS is the reversibility of the procedure. Long-term studies are needed.

*Effectiveness:*

- DBS relative to ablative surgery. More randomized controlled trials focusing on patient quality of life are required to assess the long-term effectiveness of DBS. Some evidence shows that thalamic stimulation significantly improves certain aspects of quality of life.
- DBS relative to medical treatment. Although two studies show some added effect of DBS over medical therapy, no conclusions can be made due to deficiencies in the studies available. Long-term studies of improved methodological quality are needed.

*Cost-effectiveness:* One study regarding thalamic DBS compared to thalamotomy indicates that DBS costs \$17,000 to \$51,000 more than ablative surgery over 5 years.

## Recommendations

- Interim funding of DBS should be supported for patients whose response to medical therapy is not sustained and is accompanied by unacceptable motor fluctuations.
- Technology is to be reviewed in 3 years.

## Method

MSAC conducted a systematic review of the biomedical literature from 1966 to September 2000 using biomedical electronic databases, the Internet, and international health technology agency websites to identify studies which compared DBS to ablative surgery or medical treatment. This review sought data on forms of DBS (thalamic stimulation, pallidal stimulation, and subthalamic stimulation) that targeted different areas of the basal ganglia for control of different symptoms.

## Further studies

Two trials are underway, and one will commence soon, comparing DBS to ablative surgery:

1. Kings Healthcare R&D consortium.
2. University Hospital, Birmingham, NHS Trust.
3. University College London Hospitals NHS Trust (due to commence in 2002).

Queens College London is investigating potential cognitive gains and losses from DBS, and the Medical University of South Carolina is investigating the mood effects of DBS.



**Title** **Low Intensity Ultrasound (LIUS) Treatment for Acceleration of Bone Fracture Healing – Exogen™ Bone Growth Stimulation, November 2001**

**Agency** **MSAC, Medical Services Advisory Committee**  
Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference** MSAC application 1030. Assessment report, ISSN 1443-7120.

## Aim

To assess the safety and effectiveness of LIUS treatment for acceleration of bone fracture healing (Exogen™ bone growth stimulator) and under what circumstances such services should be supported with public funding.

## Conclusions and Results

*Safety:* The intervention appears safe for use in adults, however, it should not be used prior to skeletal maturation, or in patients with pacemakers.

*Effectiveness:* The results of two high-quality, randomized, placebo-controlled studies conducted on the treatment of distal radius and tibial fractures with LIUS are contradictory. It is not possible to conclude that LIUS is consistently more efficacious than current treatment of fresh fractures. Evaluation of comparative effectiveness against current Australian treatments of fracture non-union was not possible.

*Cost-effectiveness:* The cost effectiveness of LIUS in the treatment of fresh tibial, distal radius, and scaphoid fractures does not compare favorably with a range of other common healthcare interventions.

## Recommendations

Public funding under Australian Medicare benefits arrangements should not be supported for this service.

## Method

MSAC conducted a systematic review of the medical literature from 1996 to October 2000. This review sought data on the use of LIUS to treat closed and/or grade 1 open fresh fractures and existing fractures exhibiting non-union. Further information was sourced from the applicant.

Randomized controlled clinical trial evidence was available for tibial, distal radius, and scaphoid fresh fractures. Only non-comparative case series and registry data were available for fracture non-union. Evidence was classified and scored with respect to study design, patient characteristics, minimization of bias, outcome measures, and statistical analyses. The primary outcome measure was time to healing defined as independent radiological confirmation of bridging of three of four cortices.

Valid comparators were determined by a review of current Australian practice. The comparator for fresh fractures of the tibia, distal radius, and scaphoid was cast immobilization (with or without closed reduction). In addition, for tibial fractures specifically, the use of an intramedullary rod was also an appropriate comparator. The comparator for fracture non-union in the publicly funded health sector was open reduction and internal fixation with bone grafting.

Economic evaluations were undertaken to determine the cost effectiveness and cost utility ratios of LIUS treatment of fresh fractures, relative to current Australian practice. Direct and indirect costs were considered. With respect to non-unions, the cost-effectiveness of LIUS relative to current Australian practice could not be investigated due to the lack of comparative efficacy data.





**Title** Hospital or Physician Volume and Quality of Health Care.

**Agency** SMM, The Norwegian Center for Health Technology Assessment  
SINTEF Unimed, P.O Box 124 Blindern, N-0314 Oslo, Norway; tel: +47 22 06 78 08,  
fax:+47 22 06 79 79, smm@unimed.sintef.no, www.sintef.no/smm

**Reference** SMM Report No. 2/2001. ISBN 82-14-02407-2

## Aim

To aid in organizational planning of health services, the Norwegian Ministry of Health asked SMM to summarize research results concerning the relationship between volume of hospital or physician activities and quality of care.

## Results and Conclusions

The report reviews the literature published from 1997 to 2000 and summarizes a systematic review from 1997 (CDR-report 8: The relationship between hospital volume and quality of health outcomes, University of York). Studies on volume and quality of care are mainly observational in design. Information from such studies must be interpreted with caution since various sources of bias may flaw the results. RCTs on the other hand are not a suitable study design to answer these questions. Each study was graded according to the level of case-mix adjustment, and conclusions were based on studies with adjustment for age, sex, severity of illness, and/or comorbidity.

There is no evidence to suggest a general relationship between volume and quality of care. The relationship must be studied separately for each procedure or diagnosis. For the following conditions, patients treated in high volume hospitals and/or surgeons have better outcomes in terms of mortality, morbidity, or organ survival: cancer in the esophagus, pancreas, and liver, abdominal aorta aneurysms, carotid endarterectomy, congenital heart disease, acute myocardial infarction and PTCA, organ transplantation, and AIDS.

In trauma treatment, no relationship was found between hospital volume and mortality. For orthopedic procedures (hip or knee arthroplasty or hip fracture) the results are inconsistent.

## Methods

The CRD and Cochrane databases were searched to identify systematic reviews. Primary literature was identified after searches in MEDLINE, EMBASE, and HealthSTAR for the period 1997 through 2000.

## Relevance to Norwegian health services

The challenge for Norwegian hospitals is to maintain high volume or easy access to services. The current volume levels for Norwegian hospitals are presented for selected procedures and discussed in relation to the evidence on the volume-outcome relationship. High-risk elective procedures (cancer, coronary heart diseases) were performed in very low volume hospitals (1-2 procedures per year), and centralizing these services may benefit the patients. Continuous monitoring of the quality of care should be introduced to establish knowledge about the performance of Norwegian hospitals.



<b>Title</b>	<b>Computer-Based Patient Records</b>
<b>Agency</b>	<b>SWISS-TA, Center for Technology Assessment at the Swiss Science and Technology Council</b> Inselgasse 1 3003 Bern, Switzerland; tel:+41 31 322 9963, fax:+41 31 323 3659, ta@swr.admin.ch www.ta-swiss.ch
<b>Reference</b>	TA Study «Computerbasierte Patientendossiers. Chancen und Risiken», TA-36/2000 Short version «The patient in the data network – advantages and risks of computer-based patient records» TA-36A/2000, 8 p., available in English, French and German); www.ta-swiss.ch

## Aim

Computer-based patient records are electronically managed health records. In Switzerland they are being used in certain cases as they are more easily managed than bulky paper files and more easily available and accessible for analyses, eg, for scientific purposes, preventive medicine programs, or insurance companies. Furthermore, computer-based patient records can facilitate the use of telemedicine. However, potential risks, principally concerning data protection and IT security, must also be considered when introducing the system. This report gives detailed information on the advantages and risks of computer-based patient records.

## Results and Conclusions

Computer-based patient records are part of the future in healthcare, medicine, and medical information technology. Conflicts of interests will appear when computer-based patient records replace written medical records. It will be necessary, eg,

- To ensure greater efficiency in medical treatment, but not at the patient's expense,
- To have more information generally accessible, eg, for epidemiological purposes, without comprising data protection,
- To ensure more transparency in healthcare procedures without excessive control of those directly involved,
- To improve quality assurance without limiting the scope of activity of medical staff, and
- To guarantee competition for small and medium-sized manufacturers of medical software while ensuring reliable, internationally compatible systems.

## Recommendations

- Existing regulations governing data protection and security are general as regards computer-based patient records. Hence, it would be useful to have guidelines for handling personal data in the medical sector, help with regard to the application of electronic systems, and recommendations for those responsible in the healthcare sector.
- All those directly affected by computer-based patient records should have input on design and introduction procedures. This would particularly include those who use computer-based patient records and representatives of patient organizations.
- Patients should play an active role in deciding which data may be accessible to third parties and which data are to be kept confidential.
- Computer-based patient record systems in Switzerland have mainly come about through individual initiative. In the next few years, increased coordination and planning will be called for, involving specialists from a broad range of disciplines and those directly involved, eg, representatives of patient and professional organizations.

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- Title** **Computer-Based Patient Records**
- Agency** **SWISS-TA, Center for Technology Assessment at the Swiss Science and Technology Council**  
Inselgasse 1 3003 Bern, Switzerland; tel:+41 31 322 9963, fax:+41 31 323 3659, ta@swr.admin.ch  
www.ta-swiss.ch
- Reference** TA Study «Computerbasierte Patientendossiers. Chancen und Risiken», TA-36/2000  
Short version «The patient in the data network – advantages and risks of computer-based  
patient records» TA-36A/2000, 8 p., available in English, French and German); www.ta-swiss.ch

## Methods

The international (scientific) literature was studied extensively, and over 20 experts were interviewed in Switzerland. The individuals and institutions considered were mainly doctors, medical IT specialists, lawyers, and others employed in the healthcare system.

## Further research/reviews required

It is recommended to support further research on computer-based patient records as regards rights, economic aspects, and the provision of health care.



**Title** **Low-end Scanners**

**Agency** **CEDIT, Committee for Evaluation and Diffusion of Innovative Technologies**  
**Assistance Publique Hôpitaux de Paris**  
3, avenue Victoria, 75100 Paris RP, France; tel: +33 1 40 27 31 09, fax:+33 1 40 27 55 65,  
info.cedit@sap.ap-hop-paris.fr, http://cedit.ap-hop-paris.fr

**Reference** CEDIT Report 97.03/Re-2/01

## Aim

CEDIT was called upon in 1997 by three chiefs of the Department of Radiology at Hospital Saint-Antoine, Saint-Vincent-de-Paul, and Tenon in Paris to evaluate the role of low-end scanners<sup>1</sup>. These devices have a lower investment cost, but their technical characteristics are inferior to high-end scanners<sup>2</sup>.

During its plenary session of October 28, 1997, following an examination of the first report, CEDIT did not recommend the widespread use of low-end scanners at the AP-HP. It recommended conducting a study to evaluate the medical and economic impact of these scanners in the AP-HP, particularly since an evaluation process was underway at the time within various official bodies to dissociate authorization of low-end scanners from specific needs as defined for the healthcare coverage map. The potential use of these scanners was either to replace high-end scanners at a lower price in medium-sized hospitals, or to supplement high-end scanners in larger hospitals.

## Results and Conclusions

- Numerous technical problems were encountered during this study. Tube capacity and its cooling speed, lower on the low-end scanners, limited use of these machines to tests not requiring quick consecutive use of several spirals (a problem encountered particularly when contrast agents were injected). Reconstruction times and the absence of a second control panel further limited their use.
- Due to differences between individual low-end scanners and technical improvements in newer machines, it is therefore impossible to generalize results over all machines in this category. Most importantly, however, the technological leap represented by multi-slice scanners raises the question of whether a second low-end machine in addition to a first is of any benefit.
- According to classifications of the expert group, many patients might benefit from a test conducted on a low-end machine. However, frequent breakdowns on the Philips and Toshiba scanners discouraged radiologists and operators in the departments, and for the sake of caution, contributed toward eliminating a large number of patients.
- When low-end scans were conducted, responses to clinical questions were obtained in 99.4 % of cases at SVP and 91.7% of cases at Tenon.
- We might also note that major discrepancies appeared in the technical performance of the machines as specified by manufacturers and what was actually obtained.
- The number of patients concerned by the indications on list B were also measured in an exhaustive manner over 1 month in two General Radiology departments with high activity levels (Cochin and Beaujon). The rates of use for low-end scanners varied between 31% and 78% depending on the department. It is therefore not possible to draw general conclusions regarding the potential impact of these machines at the AP-HP in terms of number of patients. Departmental evaluation would be necessary before any future installation.

<sup>1</sup> = class 1 according to CNAM price classifications.

<sup>2</sup> = class 3 according to CNAM price classifications.

*(continued next page)*



**Title**      **Low-end Scanners**

**Agency**    **CEDIT, Committee for Evaluation and Diffusion of Innovative Technologies**  
**Assistance Publique Hôpitaux de Paris**  
3, avenue Victoria, 75100 Paris RP, France; tel: +33 1 40 27 31 09, fax:+33 1 40 27 55 65,  
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**Reference**   CEDIT Report 97.03/Re-2/01

- Concerning the economic aspects for a site with low activity (4500 procedures per year), substituting a high-end with a low-end scanner offers moderate financial advantages: a savings of 5% in total operating costs. In a hospital with high activity levels, (14 000 procedures per year), supplementing a low-end with a high-end scanner does not seem economically well founded since multi-slice scans have made their appearance on the market. In the AP-HP, it seems more financially advantageous to renew the high-end, single-slice scanners with multi-slice scanners (or upgrade the machine depending on its age) rather than to buy a low-end machine in addition to a main scanner.

## Recommendations

The restricting factor of the healthcare card, the lack of any economic justification, and differences between class 1 machines are all arguments against the widespread use of these scanners in the AP-HP, either to replace or to supplement main scanners.

## Methods

Systematic review using the following databases: Medline, Current Contents, Embase, and Cochrane Library.

A call for participation was launched with manufacturers to make three scanners available, and given the authorization of official bodies, the following machines were installed: an Elscint (Select) in Saint-Vincent-de-Paul (SVP), a Philips (Tomoscan M) in Tenon, and a Toshiba (Auklet) in Saint-Antoine. The evaluation was performed in two stages:

- First, an expert group, using CERF<sup>3</sup> classifications, selected indications that would be impossible to assess on small scanners (list A) for technical reasons, while they retained other indications for phase 2 of the protocol involving patients (list B).
- In the second stage, investigators conducted a prospective study with patients at the three sites to measure for which indications from list B, tests on the low-end scanners would enable responses to the clinical questions posed. This study also aimed to evaluate the number of patients concerned by these indications and to assess the potential impact of these scanners at the AP-HP, including financial aspects.

<sup>3</sup> CERF : *College of French Radiology Professors*, who wrote a list for acknowledged indications for scanner use.



- Title** **Ventilation in Operating Theatres**
- Agency** **SMM, The Norwegian Centre for Health Technology Assessment**  
SINTEF Unimed, P.O Box 124 Blindern, N-0314 Oslo, Norway; tel: +47 22 06 78 07,  
fax:+47 22 06 79 79, [smm@unimed.sintef.no](mailto:smm@unimed.sintef.no), [www.sintef.no/smm](http://www.sintef.no/smm)
- Reference** SMM Report No. 5/2001. ISBN 82-14-402433-1  
Available in Norwegian at <http://www.sintef.no/smm>

## Aim

SMM's expert group has now completed the second part of a technology assessment dealing with hygienic initiatives aimed at preventing post-operative surgical site infections. This new assessment is a systematic literature review of all identified relevant clinical trials of conventional versus ultraclean ventilation.

## Methods

From over 4000 abstracts reviewed in this assessment, 183 scientific articles were collected and 11 were included in the final report. The main bulk of literature was assembled through Medline (1966–2001), Embase (1974–2000), DARE, NHS EED, and HTA database. NZHTA Information Specialist Susan Bidwell assisted in the literature search. In addition to some smaller databases, library catalogues and websites were checked, and a handsearch was conducted. The literature search was completed in June 2000 with an update of Medline by January 2001.

## Conclusions and Results

The rationale for keeping the bioburden (the number of microorganisms) in the air of operating theatres as low as possible is that microorganisms are a necessary, but not sufficient condition, for the development of surgical site infections. In general, ventilation with ultraclean air will provide a lower concentration of microorganisms in the air ("bacterial air counts") than conventional positive-pressure ventilation. However, the increased and directed airflow may in some instances lead to increased bacterial wound contamination.

- The association between the number of microorganisms in the air during surgery and the frequency of surgical site infections is not well documented.
- There is no documentation for the claim that ventilation with ultraclean air (less than 10 colony forming units pr m<sup>3</sup>) yields lower rates of surgical site infections than conventional positive-pressure ventilation.
- The recommended maximum limits for bacterial air contamination proposed by The Norwegian National Board of Health are not supported by scientific documentation.
- Whether ventilation with ultraclean air is cost-effective depends on several uncertain factors. If the risk of surgical site infection is high with traditional ventilation, and if ultraclean air is effective in reducing this risk, the net cost of ultraclean air may be negative (ie, cost savings).

Sufficient documentation has not been found to support the contention that ultraclean ventilation results in infection rates that are lower than with conventional ventilation.

## Further research/reviews required

Large and well-designed studies are needed to establish the effectiveness of various ventilation measures in reducing the incidence of surgical site infections.



<b>Title</b>	<b>Systematic Review of the Endoscopic Modified Lothrop Procedure for the Treatment of Chronic Frontal Sinusitis</b>
<b>Agency</b>	<b>ASERNIP-S, Australian Safety and Efficacy Register of New Interventional Procedures - Surgical</b> Box 688, North Adelaide, SA 5006, Australia; tel +61 8 82391144, fax +61 8 82391244; <a href="mailto:College.asernip@surgeons.org">College.asernip@surgeons.org</a>
<b>Reference</b>	ASERNIP-S Report No. 12, ISBN 0 909844 410; <a href="http://www.surgeons.org/open/asernip-spublications.htm">www.surgeons.org/open/asernip-spublications.htm</a>

## Aim

To compare the safety and efficacy of the endoscopic modified Lothrop procedure (EMLP), performed either wholly intranasally or in combination with an external approach, against the current benchmark treatment, the osteoplastic flap procedure with or without fat obliteration (OPF).

## Results

The limited comparative data suggested that EMLP caused fewer adverse postoperative outcomes but was more likely to generate a perioperative cerebrospinal fluid leak than OPF. However, none of the morbidity traditionally associated with OPF was evident following EMLP. EMLP appeared to have a shorter operative time and a lower perioperative blood loss than OPF, but little could be determined regarding the long-term efficacy and durability of EMLP because of the relatively short followup in most studies.

## Conclusions and Recommendations

The evidence base for EMLP was found to be inadequate, and a national audit with standardized data reporting should be conducted to establish safety and efficacy. A concurrent national audit of the osteoplastic flap procedure was also recommended. The following clinical recommendations were made to guide the development of EMLP during this audit phase:

1. Otolaryngological surgeons should obtain institutional support and appropriately inform their patients before commencing EMLP.
2. EMLP should be performed only on appropriately selected patients by a properly trained otolaryngological surgeon who is accredited in the use of the procedure. Before performing EMLP, the surgeon should participate in a formal training workshop that includes surgical theory, endoscopic anatomy, and cadaver dissection. A minimum prescribed number of cadaver dissections and supervised surgical procedures should be performed before full accreditation is awarded.

## Methods

All original, published studies on the endoscopic modified Lothrop procedure and the osteoplastic flap, with or without fat obliteration, were identified by searching Current Contents, EMBASE, MEDLINE, and The Cochrane Library. Only studies of patients diagnosed with chronic frontal sinusitis were included for review. English language papers detailing randomized controlled trials, controlled clinical trials, case series, or case reports were included.



**Title** Treating Asthma and COPD – a Systematic Review

**Agency** SBU, Swedish Council on Technology Assessment in Health Care

PO Box 5650, Tyrgatan 7, 114 86, Stockholm, Sweden; tel:+46 8 412 3200, fax:+46 8 411 3260;  
management@sbu.se, www.sbu.se

**Reference** SBU Report 151, 2000 ISBN/ISSN 91-87890-67-4

## Aim

To systematically review the evidence on the current treatment methods for asthma and COPD (chronic obstructive pulmonary disease) in adults and children. Socio-economic and cost-effectiveness analyses are also included.

## Results and Conclusions

- The cause behind the increase in asthma is unknown. However, the dominant, confirmed cause behind COPD is tobacco smoking. To prevent the advancement of COPD, it is important to detect the disease early. The most important preventive measure is to intervene effectively against smoking.
- COPD is associated with substantial limitations in everyday life and a lower quality of life despite medication. Although asthma also leads to a lower quality of life, individuals with asthma have a greater chance of becoming symptom-free through modern medication. To assess the treatment of asthma and COPD, it is essential to use outcome measures that reflect the impact of the disease on an individual's life (health-related quality of life, symptom scales, need for acute care, mortality).
- The new drugs for treating asthma have major advantages. They also have contributed toward a dramatic decline in the cost of hospitalization for asthma patients.
- Smoking cessation is the single most important intervention against COPD. Smoking cessation increases survival substantially and reduces symptoms. For many individuals with severe COPD, drugs provide only limited relief for their medical, psychological, and social situation.
- Current maintenance treatment for asthma using long-acting beta-2 stimulants and inhaled steroids is based on solid scientific evidence that shows a positive effect.
- Treatment as needed with short-acting beta stimulants for asthma symptoms and exacerbations is well founded.
- Other treatment principles for asthma such as chromoglicate, antileukotrienes, and immunotherapy have documented effects.
- The benefits of cough medications in obstructive lung diseases are inadequately studied.
- Treatment with theophylline tablets is not beneficial
- Continual treatment with short-acting beta stimulants is not effective.
- Preventive measures against asthma symptoms, such as allergen elimination, need to be assessed.
- Scientific evidence on alternative medicine as a complementary treatment method for asthma and COPD is either weak or completely lacking.

## Methods

The search was based on MEDLINE, 1996 through 1999, and a review of reference lists. For some chapters additional searches were conducted through the Cochrane Library, CATS, Cinahl, Embase, Psycinfo, Swemed, and Spriline. Selection was based on protocol-defined criteria. The literature was searched for 1966 through 1999.

## Further research/reviews required

There is a major need for controlled, well-executed studies on complementary treatment methods. Methods for improving patient compliance with treatment regimens need to be developed and can be strengthened when patients themselves participate in decisions on treatment methods. There is also a major need to assess special asthma clinics and home treatment methods for severe COPD. Different forms of COPD rehabilitation play an important role, but need to be developed and assessed.

Written by Dr. Mats Eliasson, SBU, Sweden





**Title** Lung Volume Reduction Surgery (LVRS), February 2001

**Agency** MSAC, Medical Services Advisory Committee

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference** MSAC application 1011. Assessment report, ISSN 1443-7120.

## Aim

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

## Conclusions and Results

*Safety:* The test is safe.

*Effectiveness:* Genotyping and viral load testing are predictive of the response to interferon therapy. As patients with a high viral load and more resistant genotypes can respond to interferon therapy, the predictive value of genotyping and viral load testing is insufficient to exclude a patient from treatment. Viral testing during interferon therapy has greater predictive value than pretreatment determinations and can guide decisions to continue therapy.

*Cost-effectiveness:* Cost savings would occur if 15% of patients tested decided not to proceed with interferon therapy as a result of testing. Although viral load testing and genotyping is expensive, it may be cost effective with careful patient selection.

## Recommendations

1. Funding should not be supported for this procedure until international clinical trial data is available.
2. Surgeons who wish to continue performing this procedure should seek in principle approval from hospital ethics committees or equivalent.
3. Patients should be informed of the risk of the procedure.

## Method

MSAC conducted a systematic review of the biomedical literature from 1998 to April 2000 using biomedical electronic databases, the Internet and international health technology agency websites. The two primary sources of information were:

1. A systematic review by the University of Birmingham in 1999.
2. A systemic review of Australian Safety and Efficacy Register of New Interventional Procedures-Surgical (ASERNIP-S) in 1998.

Assessment of clinical effectiveness relied heavily on one controlled randomized trial (Geddes et al) and one controlled trial (Licker et al) that compared patients with LVRS and those receiving standard medical treatment or pulmonary rehabilitation. One UK study (Young et al) that also examined cost-effectiveness was considered as a possible framework for evaluation.

## Further research

Four trials are ongoing and should report within the next 2 years: NETT (USA), CLVR (Canada), OBEST (USA), Lomas et al. (UK) and VOLREM (Sweden).



**Title** **Positron Emission Tomography (PET) Scanning Technology.**

**Agency** **CMS, Coverage and Analysis Group, Center for Medicare & Medicaid Services**  
7500 Social Security Boulevard, Woodlawn, Maryland 21244, USA;  
tel +1 410-786-0245, fax +1 410-786-9286, [www.hcfa.gov/coverage](http://www.hcfa.gov/coverage)

**Reference** Decision Memorandum; Administrative File # CAG-00090A; Issue date: June 29, 2001.

## Aim

To review and consider the evidence regarding differences between full-ring PET and gamma camera imaging and to issue a decision on the appropriate equipment to use with PET indications currently covered by the Medicare program.

## Results and Conclusions

- Most of the evidence submitted to CMS and available in the scientific literature regarding the diagnostic performance of PET was derived from use of dedicated full-ring PET scanners with bismuth germanate (BGO) crystals. Thus, all the data used to gain recent Medicare coverage approval of FDG-PET for certain oncological and other indications was based on the imaging performance of full-ring systems compared to conventional anatomic imaging.
- Review of the available published studies on camera-based PET shows that these systems miss a non-trivial number of small (2 cm or less), but potentially clinically significant, malignant lesions compared with full-ring PET scanners.
- The clinical utility of PET was premised on the additional information provided by dedicated full-ring PET compared to CT, MRI, and other conventional anatomic imaging studies. CMS has drawn conclusions about the clinical utility of partial-ring scanners based on the evidence for full-ring systems, due to the fundamental design similarities for these two types of systems. However, such design characteristics are significantly different from gamma cameras modified to perform PET.
- Accurate information about sensitivity and specificity for camera-based PET systems is not available. Without studies providing more confident sensitivity and specificity estimates, it is not possible for clinicians to properly interpret the findings from these imaging studies, nor is it possible to determine the clinical significance of diagnostic errors that might result from use of camera-based PET technologies.
- The extension of coverage from full-ring PET to camera-based systems, while anecdotally supported by nuclear medicine experts, cannot be clearly justified based on existing clinical and scientific data.
- Medicare coverage of FDG-PET for new indications (as of July 1, 2001) is limited to use of partial and full-ring PET scanners. Coverage of camera-based systems has been restricted, subject to review over time.

## Methods

- Further studies of the technical and clinical performance of gamma camera-based systems will be necessary to determine whether these systems offer net medical benefit or might inadvertently cause harm.
- Technology in this area is changing rapidly, and CMS is anxious to review any available data comparing the image quality, resolution, sensitivity, and specificity of newer PET scanners to that relating to full-ring PET scanners currently available.
- Standards for PET performance measurement recently released by the National Electric Manufacturers Association (NEMA), the NU 2-2001 standards, may provide a framework for comparing the performance of PET systems with different design features.

Written by Carlos Cano, CMS, USA





**Title**      **Diagnostic Ultrasound in Primary Care**

**Agency**    **SMM, The Norwegian Center for Health Technology Assessment**

SINTEF Unimed, Postboks 124 Blindern, 0314 Oslo, Norway; tel:+47 22 06 7961, fax:+47 22 06 7979

**Reference**   SMM Report 4/2001, ISBN 82-14-024323, [www.sintef.no/smm](http://www.sintef.no/smm)

## Aim

The development of small, diagnostic ultrasound devices will most probably lead to increased use among general practitioners. This raises questions of professional competence and organization, which have given cause for this early warning report.

## Results and Conclusions

Literature addressing the use of ultrasound in primary health care is sparse. Only a few studies mention the clinical significance for the patient. Several studies show that when general practitioners have access to the equipment, the use of ultrasound increases more than with the usual practice of direct referrals to the secondary health service. The widest area of use is prenatal care. Some clinical examinations concern maxillar sinusitis, abdominal pain, and stone formation in the gallbladder and kidneys.

- An abundance of literature addresses the use of diagnostic ultrasound in specialist health services (incl. hospitals). The transfer value is uncertain regarding experiences from the specialist to the primary care service.
- The report raises questions regarding; 1) the use of ultrasound in a population where the prevalence of a disease is low, 2) problems concerning false positive and false negative findings related to ultrasound examinations, and 3) consequences for the specialist health services (due to increased referrals because of false positive ultrasound examinations and uncertain results, or fewer referrals).
- The result of the examination depends on the examiner's education and experience.
- If general practitioners are to use ultrasound in their practice, it is essential to look into basic and further medical education, accreditation, and re-certification
- The use of ultrasound in primary care services will entail increased costs, depending on the number of general practitioners who use the method. The cost-effectiveness is not known.

## Methods

SMM based the present work on the Spanish AETS report: "Ultrasonography in primary health care – systematic review 1998". An updated search of the literature for 1998 – 2000 was added, together with empirical data from the Norwegian health services.

## Further research/reviews required

Clinical studies are needed on the diagnostic value and clinical effect (including the cost-effectiveness) of ultrasonography use in general health care.



**Title** Prenatal Screening: Down Syndrome, Neural Tube Defects, Routine Ultrasonography

**Agency** GR, Health Council of the Netherlands (Gezondheidsraad)

PO Box 16052, 2500 BB the Hague, the Netherlands; tel:+31 70 340 7520, fax:+31 70 340 7523; wj.dondorp@gr.nl, www.gr.nl

**Reference** Publication No. 2001/11; full text (in Dutch) available at www.gr.nl; 9 p. executive summary (English) also available separately

## Aim

- To synthesise current knowledge on methodological, psychological, and ethical aspects of various forms of antenatal screening for Down syndrome (DS) and neural tube defects (NTDs) and of routine ultrasound (US) examination during pregnancy.
- Report prepared in response to a request by the Minister of Health in view of evaluation of current policy in the Netherlands. This policy includes: age-based screening for DS, no screening for NTDs, no routine US. The gap is widening between policy and practice in this field.

## Results and Conclusions

- The report contains an extensive cost-effectiveness analysis comparing various strategies for antenatal DS screening. Comparison of screening based on the triple test with maternal age-based screening (on which DS screening in the Netherlands is currently based) shows that the former approach is much more cost-effective. A further conclusion from the analysis is that some newly developed risk-assessment strategies, eg, the combination of nuchal translucency measurement and a first trimester serum test, appear to be more cost-effective than triple-test screening. However, the scientific data in support of these alternative risk-assessment tests is not yet as strong in every respect as for the triple test.
- Other than the triple test, risk-assessment tests for DS in the first trimester cannot also be used to screen for NTDs. Ultrasound screening between 18 and 21 weeks has been proposed as an alternative, with the advantage of a one-step approach. It remains to be seen whether the sensitivity of this approach (for spina bifida) measures up to that of MSAFP screening; the costs will most likely be higher.
- The scientific literature does not provide sufficient hard evidence to support the use of US screening for structural abnormalities other than neural tube defects. Nor has routine US in pregnancy been shown to have any conclusive effect on clinical outcome measures. Given the limited nature of the research in this area, however, such an effect cannot be ruled out.
- No evidence shows that the psychological effects of risk-assessment screening are so serious as to make it unacceptable to offer such a test. Further research is needed into certain aspects, focusing on the quality of counselling and support. To date, scarcely any research has been conducted into the psychological consequences of risk-assessment screening in the first trimester of pregnancy (eg, nuchal translucency measurement).
- Antenatal screening for conditions such as DS or NTDs can be morally justified if the purpose is either to enable pregnant women and their partners to have the pregnancy terminated in the event of an abnormal result, or to prepare them for the birth of a handicapped child. The routine nature and the complexity of risk-assessment screening make it all the more challenging to meet the requirement of informed consent. The report advocates a phased approach.

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Written by Dr. Wybo J. Dondorp, GR, The Netherlands



**Title** Prenatal Screening: Down Syndrome, Neural Tube Defects, Routine Ultrasonography

**Agency** GR, Health Council of the Netherlands (Gezondheidsraad)  
PO Box 16052, 2500 BB the Hague, the Netherlands; tel:+31 70 340 7520, fax:+31 70 340 7523;  
wj.dondorp@gr.nl, www.gr.nl

**Reference** Publication No. 2001/11; full text (in Dutch) available at www.gr.nl; 9 p. executive summary (English) also available separately

## Recommendations

- Introduction of risk-assessment screening for DS, based on the triple test as the most tried and tested method, and organisationally the least ambitious, approach. The test should be offered to all pregnant women. Stimulation of research into newly emerging screening possibilities through regional trial population screening projects.
- Introduction of screening for NTDs. This should be based on the MSAFP test as long as triple-screening (including MSAFP) is the standard approach for DS. Where (in trial projects) first trimester DS screening is offered, it is advocated to offer US screening at 18 to 21 weeks as a test for NTDs, also as a trial screening program.
- As long as NTD screening is based on MSAFP, there is no scientific reason for offering routine US in pregnancy. However, the report recommends offering one dating scan to all pregnant women 'on pragmatic grounds'.
- The professional groups involved need to draw up guidelines for the various components and aspects of the screening program, including counselling. Educational programs are required for caregivers involved in the program.
- Prenatal screening for DS and NTDs needs to be subject to ongoing evaluation (ie, monitoring) to be conducted on a national level. Program results should be nationally recorded.

## Methods

- Systematic review of published scientific literature. Expert Committee. Peer review of draft report.
- Cost-effectiveness analysis (appendix to the report) of strategies for prenatal DS screening.

## Further research/reviews required

- Methodological/psychological/ethical: first-trimester screening for Down syndrome.
- Psychological: dynamics of decision making throughout the entire screening process; impact of false-negative outcomes of risk-assessment screening; consequences of abnormal US outcomes whose clinical significance is either unclear or uncertain.
- Ethical: informed consent for risk assessment screening.



**Title**      **Population Screening for Colorectal Cancer**

**Agency**    **GR, Health Council of the Netherlands (Gezondheidsraad)**

PO Box 16052, 2500 BB the Hague, the Netherlands; tel:+31 70 340 7520, fax:+31 70 340 7523;  
www.gr.nl

**Reference** GR 2001/01. ISBN 90-5549-356-2

## **Aim**

To review the epidemiology of CRC and to assess the scientific evidence regarding the efficacy and cost-effectiveness of different screening strategies.

## **Results and Conclusions**

Colorectal cancer (CRC) is the second leading cause of cancer-related mortality in the Netherlands, resulting in approximately 4400 deaths in 1998. Three randomized trials have shown that screening by fecal occult blood testing (FOBT) every 2 years has the potential to reduce mortality by up to 21%. According to a meta-analysis, the number needed to screen to prevent one death from CRC over 10 years is 1200 (700 to 2800). The real number is probably lower.

We do not have proof that other screening strategies for CRC can reduce mortality. However, much clinical and epidemiological evidence suggests that flexible sigmoidoscopy (FS) or total colonoscopy and removal of colonic polyps may effectively reduce CRC-related mortality and incidence. Screening programs based on FS may be more cost-effective than those based on FOBT. FS screening could even result in a net savings of direct healthcare costs due to prevention of cancer treatment costs.

Colonoscopic screening may be less cost-effective than FS screening, unless delivered at less frequent intervals (10-year or a one-time examination).

A recent contender for screening is virtual colonoscopy. This developing technology (computed tomography or MRI colography) has several potential advantages as a screening test. An economic analysis indicates that to become cost-effective, virtual colonoscopy would need to be offered at a very low price or result in compliance rates superior to those associated with conventional colonoscopy.

## **Recommendations**

It is recommended that a national policy on population screening for CRC be developed. A first priority is to resolve remaining issues, such as: which screening test should be used, at what ages, how often, and who is going to do these investigations. Other important questions are the acceptability of screening for CRC, the GP's role, the program organization and evaluation, quality assurance, and the indications for surveillance colonoscopy of those who screen positive.

It is recommended that feasibility studies and pilot trials be conducted and that a simulation model be developed to make well-founded judgements about screening strategies. The most uncertain aspects of the present models are the dwelling time distribution of adenomas that grow into cancer, and the percentage of cancers not preceded by adenomas. Simulation outcomes depend heavily on assumptions about the natural history of CRC. Better estimates can be made after analysis of observational data from CRC screening trials and surveillance studies. Such an analysis is being conducted in Rotterdam, taking advantage of emerging data in this area. It is recommended that these validation studies and more detailed modeling be used, and that feasibility studies and pilot trials also be conducted in planning for a possible national CRC screening program.

## **Methods**

The relevant literature was surveyed and experts were consulted. The draft report was subjected to independent peer review.

Written by Willem A van Veen, M.D., GR, The Netherlands



<b>Title</b>	<b>Glycemic Holter</b>
<b>Agency</b>	<b>CEDIT, Committee for Evaluation and Diffusion of Innovative Technologies Assistance Publique Hôpitaux de Paris</b> 3, avenue Victoria, 75100 Paris RP, France; tel: +33 3 40 27 31 09, fax:+33 1 40 27 55 65, info.cedit@sap.ap-hop-paris.fr, http://cedit.ap-hop-paris.fr
<b>Reference</b>	CEDIT Report (in French) 01.04/Ra1/01/Recommendation 01.04/Re1/01.

## Aim

CEDIT was requested by Professor JL Selam (Diabetes Department – Hôtel-Dieu Hospital – Paris) to conduct an evaluation of the glycemic Holter sold by the MiniMed company under the name CGMS (Continuous Glucose Monitoring System).

The CGMS is an investigation tool used to followup diabetic patients with glucose imbalance. It is a functional exploration tool designed to measure glucose concentration in the interstitial fluid through a continuous recording period in an outpatient setting. Occasionally, it is used (like a Holter) to supplement the standard glucose monitoring method.

## Results

The glycemic Holter analyzes the glucose profile outside customary self-monitoring periods and detects infraclinical hypoglycemia and short-lived incidents of hyperglycemia. It is therefore believed that the Holter corresponds, at least theoretically, to the requirements established by scientific societies for the followup of diabetic patients who are thus more involved in the management of their disease.

However, reservations are expressed with regard to the performance criteria of the device currently sold. Experts agree on the need for evaluation studies on the indications and benefits of the glucose control obtained. Although data in the literature are sparse, they show that continuous recording of glucose highlights glucose variations not detected by standard monitoring methods, which in turn leads to adjustments in treatment.

## Recommendations

CEDIT considers that this device for continuous glucose recording has not been sufficiently evaluated. Therefore, CEDIT does not recommend widespread use of the device at the AP-HP (Assistance Publique Hôpitaux de Paris). However, CEDIT holds the opinion that the proposed protocol is of very high quality and therefore supports the proposed protocol particularly since it would involve four teams and provide expert evaluation from within the institution.

## Methods

The Minimed Glucose Sensor would be evaluated through a randomized study involving approximately 100 type 1 diabetic patients. Four centers in Paris (France) would participate: Hôtel-Dieu, Pitié-Salpêtrière, Bichat, and Saint-Louis. This would be a medical-economic comparison of two methods re-establishing diabetic balance. One would be hospitalization for 1 week with glycemic monitoring conducted several times in 24 hours. The other would be outpatient glucose monitoring using the Holter. The goal would be to demonstrate with certainty that continuous outpatient recording of glucose does indeed provide glucose control of a quality that is at least as good as that provided by hospitalization for 1 week.

One of the study's secondary criteria for judgment will involve evaluating the cost of both methods from the standpoint of hospitals. The cost per patient using each of the two methods will thus be linked to the criteria of effectiveness considered.



**Title** Patient's Bedside Biological Analyzer

**Agency** CEDIT, Committee for Evaluation and Diffusion of Innovative Technologies  
Assistance Publique Hôpitaux de Paris  
3, avenue Victoria, 75100 Paris RP, France; tel: +33 3 40 27 31 09, fax:+33 1 40 27 55 65,  
info.cedit@sap.ap-hop-paris.fr, <http://cedit.ap-hop-paris.fr>

**Reference** CEDIT Report (in French) 98.04/Ra3/01/Recommendation 98.04/Re3/01.

## Aim

The CEDIT was consulted in April 1998 by the Director General of AP-HP on the benefit for the institution of delocalized biochemical analyzers placed near the patient's bed.

## Results

The speed in obtaining high-quality results with this type of device is confirmed. Delocalized biology near the patient is seen to enable real-time treatment of patients in outpatient or day-hospital settings.

This device, which is time-consuming for healthcare professionals, should be compared to a system for the rapid transfer of samples (pneumatics, etc). Its installation requires the establishment of a quality control system where the biologist writes down procedures and validates them, monitors and controls disfunctionalities, and trains users.

## Recommendations

The CEDIT is of the opinion that widespread use of the device in hospitals must be limited to emergency services, intensive care units, and operating rooms which do not always have the option to rapidly transfer biological samples. The installation and choice of a patient bedside device must be submitted to a competent commission consisting of biologists, prescribing clinicians, a nursing representative, a biomedical engineer, and a hospital management representative.

## Methods

A multidisciplinary working group formed by the CEDIT in 1998 gave an opinion on the validity of the technical performances of the main device involved (i-STAT<sup>®</sup>), on its conditions of use, and on the degree of use of this type of device within AP-HP.

The working group then recommended supplementary studies to evaluate the practical effects of such a bedside biological analyzer in AP-HP hospitals once a primary study had verified the device's reliability.

After the technical results were validated, a protocol was set up in the emergency room of the Louis-Mourier hospital (Colombes – France) to analyze the practical effects of biological analyzers at the patient's bedside. This was a single-center, longitudinal study comparing 2 months of activity: May 1999, when the assays were still conducted in customary biochemical laboratory conditions (242 patients included) and May 2000, when the i-STAT<sup>®</sup> system became available along with the customary method (293 patients included).





**Title** **The Benefit of Population Screening for Breast Cancer With Mammography**

**Agency** **GR, Health Council of the Netherlands/Gezondheidsraad**  
P.O. Box 16052, 2500 BB Deb Haag, The Netherlands; tel: +31 70 340 7520, fax:+31 70 340 7523,  
www.gr.nl

**Reference** GR Report 202/03E. ISBN 90-5549-420-8.

## Aim

The Health Council of the Netherlands (GR) was asked by the Dutch Minister of Health to advise her whether a recent Cochrane review (undertaken by Ole Olsen and Peter Göttsche) nullifies the practice of screening for breast cancer in women aged over 50 years.

## Results

The GR agrees with the Danish reviewers that the RCTs examined can be criticized in some respects. However, with one exception, the GR finds that the nature of these shortcomings do not render the published data unusable. Moreover, the GR opinion is that insufficient arguments are used to score four of the RCTs much lower on methodological grounds than two other RCTs.

Although the Cochrane review notes possible sources of bias, the reviewers have not shown that bias greatly effects the trial results. The GR considers as too extreme the conclusion that breast cancer mortality is an unreliable outcome that is biased in favor of screening. The GR does not agree with the conclusion that breast cancer mortality must be replaced by overall mortality. The GR does, however, find that the use of breast cancer mortality as the only endpoint can lead to incorrect interpretation – total cancer mortality, deaths from other major causes, and overall mortality must also be taken into consideration.

If data from all eligible trials (flawed studies excluded) are considered for women aged over 50 years, then the relative risk for breast cancer mortality is 0.74 (95% CI 0.62–0.89) after 7 years and 0.75 (0.66–0.86) after 13 years. In the same way, the relative risk for overall mortality is 0.97 (0.93–1.00) after 7 years and 0.99 (0.97–1.02) after 13 years. The Cochrane review does not report separately on the relative risk for cancer mortality in women aged over 50 years.

## Conclusion

The GR sees no basis, in the light of the Cochrane review, for the conclusion that population screening for breast cancer among women aged over 50 years has no survival benefit.

## Methods

A committee of scientists not involved in the screening program prepared the advisory report. As part of its work, the committee held a hearing that was attended by Dutch experts either involved in, or opposed to, the screening program.





**Title** **Advanced Breast Biopsy Instrumentation (ABBI), May 1999**

**Agency** **MSAC, Medical Services Advisory Committee**

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference** MSAC application 1001. Assessment report, ISSN 1443-7120.

## **Aim**

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

## **Conclusions and Results**

*Safety:* ABBI is safe.

*Effectiveness:* Available evidence does not suggest that ABBI is superior to conventional core biopsy diagnostic testing.

*Cost-effectiveness:* This was not undertaken.

## **Recommendations**

ABBI should continue to be funded under existing arrangements as additional funding is not currently warranted. MSAC conducted a systematic review of medical literature on ABBI from 1982 until May 1998 via Medline, HealthSTAR, EmBase, Austrom, Austhealth, the Cochrane Library, Biosis, CANCERLIT, IAC Health & Wellness, Pascal, and Elsevier Biobase databases. In addition, information was sought from the Internet, international technology assessment agencies, from references quoted in retrieved articles, and from the distributor for ABBI.



<b>Title</b>	<b>OctreoScan® Scintigraphy for Gastro-entero-pancreatic (GEP) Neuroendocrine Tumors, August 1999</b>
<b>Agency</b>	<b>MSAC, Medical Services Advisory Committee</b> Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia; tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au
<b>Reference</b>	MSAC application 1003. Assessment report, ISSN 1443-7120.

## Aim

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

## Conclusions and Results

*Safety:* OctreoScan is safe at recommended doses.

*Effectiveness:* OctreoScan has the advantage of being able to image the whole body. It can detect extrapancreatic tumors and metastatic lesions outside of the abdomen and chest, and MEN-1 tumors. It is less sensitive in detecting insulinomas.

Sensitivity and specificity could not be determined as test results were not compared in blind fashion with an acceptable 'gold standard'. There is some evidence that OctreoScan changes patient management, but no evidence to suggest increased cure rates and survival time.

*Cost-effectiveness:* It was not possible to assess cost-effectiveness due to lack of validated data on test accuracy and impact on clinical outcomes.

## Recommendations

Public funding should be supported for OctreoScan where:

- Biochemical evidence indicates a GEP neuroendocrine tumor and conventional radiology produces negative or equivocal structural imaging, or
- Biochemical and conventional imaging indicates a surgically amenable disease to rule out further metastatic disease.

However, the evidence is insufficient to support public funding for octreotide therapy as a viable therapeutic option.

## Method

MSAC conducted a systematic review of the biomedical literature from 1989 to 1999 by accessing biomedical electronic databases, the Internet, and international health technology agency websites. Reference lists of reviews and other articles were also searched. Data was also available from unpublished trials conducted by a manufacturer of the technology (Mallinckrodt Medical Petten).



**Title** **Oto-acoustic Emission Audiometry (OAEA), August 1999**

**Agency** **MSAC, Medical Services Advisory Committee**

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference** MSAC application 1002. Assessment report, ISSN 1443-7120.

## Aim

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

## Conclusions and Results

*Safety:* The only risks relate to false positive/false negative test results.

*Effectiveness:* OAEA has relatively high sensitivity and specificity, although studies show significant variation in results. As the tests require no behavioral response it is very useful for prelingual children. The negative predictive value of the test (where a negative test result for impairment proves to be accurate) is much higher than the positive predictive value. False positives increase with an infant's age (beyond 48 hours).

*Cost-effectiveness:* A detailed economic evaluation was not undertaken.

## Recommendations

Public funding should be supported for detection of permanent congenital hearing impairment (PCHI) for children identified to be in a high risk group because of:

- Admission to a neonatal intensive care unit,
- A family history of hearing impairment,
- Perinatal infection,
- A birthweight below 1.5 kg,
- Craniofacial deformity,
- Birth asphyxia,
- Chromosomal abnormality, including Down syndrome, or
- Exchange transfusions.

## Method

MSAC conducted a systematic review of the biomedical literature from 1998 to April 2000 by accessing biomedical electronic databases, the Internet, and international health technology agency websites.

## Further research

If OAEA is funded, effectiveness monitoring will be needed, especially with respect to:

- The age of diagnosis,
- The commencement of habilitation,
- The effectiveness of early intervention,
- The prevalence and consequences of mild or unilateral PCHI, and
- The prevalence and consequences of temporary conductive hearing loss (currently the subject of a randomized controlled trial by the UK Medical Research Council).



**Title** Directional Vacuum-assisted (DV) Breast Biopsy, October 1999

**Agency** MSAC, Medical Services Advisory Committee

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference** MSAC application 1015. Assessment report, ISSN 1443-7120.

## Aim

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

## Conclusions and Results

*Safety:* DV breast biopsy is safe.

*Effectiveness:* Comparative studies (level III-3 evidence) suggest that compared to core biopsy, DV breast biopsy:

1. Has a higher success rate in the removal of microcalcifications,
2. Is able to obtain larger numbers of specimens at biopsy, and
3. Has increased sensitivity in detecting ductal carcinoma in situ and atypical ductal hyperplasia.

DV breast biopsy seems to be a more effective diagnostic method for non-palpable breast abnormalities.

*Cost-effectiveness:* This was not undertaken. Some items used in DV are more expensive than with core biopsy.

## Recommendations

DV breast biopsy for non-palpable breast lesions should receive higher remuneration than currently available, pending a review of the costs of the procedure.

## Method

MSAC conducted a systematic review of medical literature on DV from 1975 until August 1998 using the MEDLINE, HealthSTAR, and Cochrane Library databases.



<b>Title</b>	<b>Positron Emission Tomography (PET) for a Number of Services, March 2000</b>
<b>Agency</b>	<b>MSAC, Medical Services Advisory Committee</b> Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia; tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au
<b>Reference</b>	MSAC application 1025. Assessment report, ISSN 1443-7120.

## Aim

To assess the safety and effectiveness of the services and under what circumstances such services should be supported with public funding.

## Conclusions and Results

*Safety:* PET is noninvasive and generally accepted as a safe diagnostic procedure. A large US study found no adverse reactions to over 80 000 doses of positron emitting radiopharmaceuticals.

*Effectiveness:* PET has improved diagnostic accuracy over conventional imaging for several indications:

- Detection of mediastinal and distant metastases not detected by conventional imaging in the staging of non-small cell lung cancer (NSCLC),
- Detection of metastatic disease in patients with potentially resectable metastatic melanoma;
- Detection of local recurrence, hepatic metastases, and extrahepatic metastases in patients with suspected recurrence of colorectal cancer; medically refractory epilepsy, and
- Assessment of viable myocardium that may respond to reperfusion in patients being considered for coronary revascularization.
- However, as with other imaging modalities, PET still has low sensitivity for the detection of early (ie, low volume or microscopic) metastatic disease.

[There are documented examples of where the results of PET have led to changes in patient management in these indications. There is, however, no direct evidence available at this time that can demonstrate that improvements in diagnostic accuracy provided by PET, and any subsequent management changes, lead to improvements in long-term health outcomes for patients. As such, it is difficult to establish the true clinical effectiveness of PET. In the case of residual/recurrent mass in patients treated for malignant glioma, there was no evidence PET was superior to SPECT imaging.]

*Cost-effectiveness:* Evaluating cost-effectiveness of PET is problematic due to uncertainties regarding the true clinical effectiveness (ie, patient health outcomes) and the true cost of PET. It is likely that the ongoing randomized trials will provide valuable information to help address these issues.

## Recommendations

The evidence is currently insufficient concerning the clinical and cost effectiveness of PET to warrant unrestricted funding. Despite this, the evidence suggests that PET is safe, potentially clinically effective, and potentially cost effective for the indications reviewed. MSAC recommended PET receive interim funding in clearly specified clinical scenarios (see report).

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- Title**      **Positron Emission Tomography (PET) for a Number of Services, March 2000**
- Agency**    **MSAC, Medical Services Advisory Committee**  
Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au
- Reference**   MSAC application 1025. Assessment report, ISSN 1443-7120.

## Method

The National Health and Medical Research Council (NHMRC) Clinical Trials Centre at the University of Sydney conducted a systematic review of the literature (with eligibility criteria defined a priori) on the role of FDG PET. The following sources were searched from commencement to March 2001: MEDLINE, PreMedline, National Library of Medicine Health Services Research Databases, CINAHL, Australian Medical Index, Biological Abstracts, Best Evidence, Current Contents, EmBase, the Cochrane Library, ISTAHC, and the NHS Databases, DARE, EED and HTA. Internet and health technology assessment agency sources were searched and studies were also identified from MSAC applications and members of the Supporting Committee.

## Further research

Trials are currently underway that will provide information on the link between improvements in diagnostic accuracy from PET, subsequent patient management changes, and improvement to the health outcomes of patients. In addition, a detailed cost study is being conducted as part of a randomized trial in NSCLC which should provide a more accurate estimate of the likely cost of PET. Interim funding of prescribed clinical scenarios should produce useable data on clinical and cost effectiveness of PET in the future.



**Title**      **Positron Emission Tomography (PET) for a Number of Services, May 2001**

**Agency**    **MSAC, Medical Services Advisory Committee**

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia; tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference**   MSAC application 1027. Assessment report, ISSN 1443-7120.

## Aim

To assess the safety and effectiveness of the services and under what circumstances such services should be supported with public funding.

## Conclusions and Results

*Safety:* PET is non-invasive and generally accepted as a safe diagnostic procedure. A large US study found no adverse reactions to over 80 000 doses of positron emitting radiopharmaceuticals.

*Effectiveness:* PET has improved diagnostic accuracy over conventional imaging for several indications:

- Assessment of suspected recurrent disease in patients with ovarian cancer;
- Detection of nodal and distant metastatic involvement in the pretreatment staging of patients with cervical cancer;
- Detection of nodal and distant metastatic involvement in the pretreatment staging of patients with esophageal cancer; and
- Detection of nodal and distant metastatic involvement in the pretreatment staging of gastric and gastroesophageal cancer.
- It was not possible to evaluate the role of PET in the staging of endometrial cancer due to a paucity of data.

*Cost-effectiveness:* There are documented examples of where the results of PET have led to changes in patient management in these indications. It is difficult to establish long-term clinical effectiveness due to lack of direct evidence on consequent improved health outcomes for patients. In the clinical scenarios evaluated in this review, PET is used to provide incremental information over conventional imaging. At present, the evidence is insufficient concerning the impact of PET on long term clinical outcomes to be able to provide any reliable estimates of cost effectiveness.

## Recommendations

Currently the evidence is insufficient on the clinical and cost effectiveness of PET to warrant unrestricted funding. Despite this, the evidence suggests that PET is safe, potentially clinically effective, and potentially cost effective for the indications reviewed. As such, interim funding was recommended for:

1. Assessment of disease following initial therapy in patients with suspected recurrence of epithelial ovarian carcinoma based on equivocal anatomical imaging findings or an elevation of CA-125,
2. Staging of disease in patients with a pathological diagnosis of primary carcinoma of the uterine cervix, prior to planned radical radiation therapy or combined modality therapy,
3. For staging of a patient with proven esophageal carcinoma where curative surgery or chemoradiation is planned, and
4. For staging of a patient with proven gastric cancer where curative surgery is planned.

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**Title**      **Positron Emission Tomography (PET) for a Number of Services, May 2001**

**Agency**    **MSAC, Medical Services Advisory Committee**

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference**   MSAC application 1027. Assessment report, ISSN 1443-7120.

## Method

The National Health and Medical Research Council (NHMRC) Clinical Trials Centre at the University of Sydney conducted a systematic review of the literature (with eligibility criteria defined *a priori*) on the role of FDG PET. The following sources were searched from commencement to March 2001: MEDLINE, PreMedline, National Library of Medicine Health Services Research Databases, CINAHL, Australian Medical Index, Biological Abstracts, Best Evidence, Current Contents, EmBase, the Cochrane Library, ISTAHC, and the NHS Databases, DARE, EED, and HTA. Internet and health technology assessment agency sources were searched, and studies were also identified from MSAC applications and members of the Supporting Committee.



**Title** **Advanced Breast Biopsy Instrumentation (ABBI) System for Nonpalpable Breast Lesions, July 2001**

**Agency** **MSAC, Medical Services Advisory Committee**

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference** MSAC application 1037. Assessment report, ISSN 1443-7120

## Aim

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

## Conclusions and Results

*Safety:* Safety data differ widely. Adverse events associated with ABBI often relate to technical or equipment failure. Most other adverse events reported in case series and comparative studies are of low incidence and health significance.

More common adverse event	# studies/12	% of patients
Hematoma	11	1–12.5%
Wound infection	6	0–3%
Dehiscence/wound problems	3	1–3%
Bleeding	3	0.4–4.2%

*Effectiveness:* In the absence of randomized controlled trials, evaluation was based on comparative studies and case series. These show:

- Discordant biopsy rates were lower for ABBI compared to core needle biopsy and Mammotome,
- Technical success was slightly lower for ABBI compared to core needle biopsy, Mammotone, and open wire localized biopsy,
- Mean blood loss was considerably less than for needle localization with excisional breast biopsy, and
- Margins for ABBI were generally positive.

*Cost-effectiveness:* The evidence is insufficient for cost-benefit analysis. Some cost savings may result from using ABBI, but this may not necessarily translate into a better cost-benefit ratio.

## Recommendations

1. Public funding of ABBI diagnosis should be supported where fees do not exceed existing comparators.
2. The evidence is insufficient to assess a therapeutic role for ABBI against breast cancer.
3. The use of ABBI equipment shall be limited to surgeons and radiologists with training and expertise in the procedure.
4. A costing study should be carried out to assess the appropriate Medicare Rebate.

## Method

MSAC expanded on the existing review (MSAC 1999). The current review included a systematic review of the biomedical literature from 1999 to March 2001 by accessing biomedical electronic databases, the Internet, and international health technology agency websites. Relevant data from the manufacturer (subject to independent confirmation), textbooks, and conference proceedings were also considered.



**Title** Evaluation of Near Patient Cholesterol Testing Using the Cholestech LDX, August 2001

**Agency** MSAC, Medical Services Advisory Committee

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia; tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference** MSAC application 1026. Assessment report, ISSN 1443-7120.

## Aim

To assess the safety and accuracy and precision of the Cholestech LDX and under what circumstances public funding should be supported for the service.

## Conclusions and Results

*Safety:* The Cholestech LDX device does not come into contact with the individual undergoing lipid testing and no direct safety concerns were identified.

*Effectiveness:* Under ideal conditions the evaluation found the Cholestech LDX to be precise and accurate in its measurement of TC, HDL-C and TG. Although the pooled estimates for %bias and CV did not always fall within the NCEP guidelines for TC, HDL-C and TG, the pooled TE for these three measures always met the NCEP criteria. No clear conclusions can be drawn about the influence of site on the accuracy and precision of the Cholestech LDX because only a small number of studies were available and those that were available were not designed to assess differences in this parameter. In terms of operator, no relevant articles could be found in the literature reporting the effect of operator on results obtained by the Cholestech LDX. The evaluation found that lipid determinations derived from either fingerstick derived or venous blood samples are equivalent.

*Cost-effectiveness:* A decision analytic modeled evaluation was used to determine the costs and effectiveness of NPT for total cholesterol using the Cholestech LDX compared to current laboratory testing. In comparison to laboratory testing, the use of near patient testing resulted in an extra cost of \$1.17 per patient presenting for a GP consultation. The incremental cost per additional patient detected with elevated cholesterol was \$392; per additional patient achieving target lipid levels was \$1,287; and per life year gained was \$132,934. Sensitivity analysis indicated that these ratios were influenced most by the rate of growth of cholesterol testing due to the presence of NPT and the population in which the new tests were being performed.

## Recommendations

The restricted use of near patient cholesterol testing, as an alternative to laboratory testing of lipids, should be considered in settings or circumstances where there is adequate training, accreditation and quality assurance. It is strongly recommended that further information be collected on the diagnostic performance of the NPT devices in the community setting and the impact of near patient testing on patient outcomes including changes in lipid management, compliance with lipid lowering therapies and amount of doctor visits.

## Method

The medical literature was searched to identify relevant studies published on the Cholestech LDX that examined the accuracy and precision of the device or the influence of site, operator or sample type (fingerstick blood compared with venous blood) on the accuracy and precision of the device. Nineteen studies were reviewed in order to provide evidence regarding the accuracy and precision of the Cholestech LDX.



**Title**      **Positron Emission Tomography (PET) for a Number of Services, August 2001**

**Agency**    **MSAC, Medical Services Advisory Committee**

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia; tel: +61 2 6289 6811, fax: +61 2 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference**   MSAC application 1027. Assessment report, ISSN 1443-7120.

## Aim

To assess the safety and effectiveness of the services and under what circumstances such services should be supported with public funding.

## Conclusions and Results

*Safety:* PET is non-invasive and generally accepted as a safe diagnostic procedure. A large US study found no adverse reactions to over 80 000 doses of positron emitting radiopharmaceuticals.

*Effectiveness:* PET has improved diagnostic accuracy over conventional imaging for several indications:

- Staging, restaging, and assessment of residual mass in patients with lymphoma (Hodgkin's disease and non-Hodgkin's lymphoma),
- Evaluation of primary and nodal metastatic involvement in the pretreatment staging of patients with squamous cell carcinoma (SCC) of the head and neck; assessment of residual and recurrent disease for patients with SCC of the head and neck; and detection of occult squamous cell primary tumors in patients diagnosed with SCC cervical node metastases, and
- Detection of visceral metastases in patients with soft tissue sarcoma and assessment of locally recurrent disease in patients with sarcoma.
- However, as with other imaging modalities, PET still has low sensitivity for the detection of early (ie, low volume or microscopic) metastatic disease.

*Cost-effectiveness:* There are documented examples of where the results of PET have led to changes in patient management in these indications. It is difficult to establish long-term clinical effectiveness due to lack of direct evidence on consequent improved health outcomes for patients. In the clinical scenarios evaluated in this review, PET is used to provide incremental information over conventional imaging. At present, there is insufficient evidence of the impact of PET on long-term clinical outcomes to be able to provide any reliable estimates of cost effectiveness.

## Recommendations

There is currently insufficient evidence on the clinical and cost effectiveness of PET to warrant unrestricted funding. Despite this, the evidence suggests that PET is safe, potentially clinically effective, and potentially cost effective for the indications reviewed. As such, interim funding was recommended for:

1. Staging of newly diagnosed or previously untreated disease, evaluation of residual mass after treatment and restaging of suspected recurrent/residual Hodgkin's and non-Hodgkin's lymphoma,
2. Primary staging, suspected residual or recurrent SCC of the head and neck and evaluation of metastatic SCC involving cervical nodes from an unknown primary site, and
3. Guiding biopsy of suspected bone or soft tissue sarcomas where structural imaging suggests lesion heterogeneity, staging of biopsy-proven bone or soft tissue sarcoma being considered for resection of the primary or limited metastatic disease, evaluation of suspected residual or recurrent sarcoma on the structural imaging after definitive therapy.

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***Title***      **Positron Emission Tomography (PET) for a Number of Services, August 2001**

***Agency***      **MSAC, Medical Services Advisory Committee**

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

***Reference***      MSAC application 1027. Assessment report, ISSN 1443-7120.

## **Method**

The National Health and Medical Research Council (NHMRC) Clinical Trials Centre at the University of Sydney conducted a systematic review of the literature (with eligibility criteria defined a priori) on the role of FDG PET. The following sources were searched from commencement to March 2001: MEDLINE, PreMedline, National Library of Medicine Health Services Research Databases, CINAHL, Australian Medical Index, Biological Abstracts, Best Evidence, Current Contents, EmBase, the Cochrane Library, ISTAHC, and the NHS Databases, DARE, EED and HTA. Internet and health technology assessment agency sources were searched and studies were also identified from MSAC applications and members of the Supporting Committee.



<b>Title</b>	<b>Magnetic Resonance Imaging for Staging Cervical and Endometrial Cancer, November 2001</b>
<b>Agency</b>	<b>MSAC, Medical Services Advisory Committee</b> Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia; tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au
<b>Reference</b>	MSAC reference 7B. Assessment report, ISSN 1443-7120.

## Aim

To assess the safety and effectiveness of Magnetic Resonance Imaging (MRI) for staging cervical and endometrial cancer and under what circumstances such services should be supported with public funding.

## Conclusions and results

*Safety:* Effects of magnetic fields during MRI are insufficient to result in irreversible or hazardous biological effects in patients undergoing the procedure, although MRI is contraindicated in some patients. Intravenous contrast agents sometimes administered during MRI are considered safe and generally well tolerated by patients.

*Effectiveness:* The potential for bias should be borne in mind when interpreting this review as it is based on data from case series.

Cervical cancer:

- The diagnostic accuracy of MRI appears to be relatively high for the detection of parametrial invasion, although there is a lack of data directly comparing MRI with other imaging modalities. In the detection of vaginal invasion, MRI has lower sensitivity, but relatively high specificity.

Endometrial cancer:

- While MRI appears to have improved or comparable diagnostic accuracy over some modalities in the differentiation of extensive early disease, the positive predictive value of MRI does not appear to be high enough to suggest that it should replace current staging practices.
- There was insufficient evidence to compare MRI with computed tomography in detecting extensive endometrial cancer from early disease.

*Cost-effectiveness:* A modeled cost analysis was conducted based on modest improvements in the diagnostic accuracy of MRI over computed tomography (CT) in staging cervical cancer. Using these estimates, for every 100 patients where MRI was used to assess disease extent, the incremental cost per 100 patients would range from saving A\$1300 to costing an extra A\$17 000. This improvement in diagnostic accuracy over CT would also result in five fewer false positive results and five fewer false negative results, potentially avoiding inappropriate treatments and their associated costs.

## Recommendations

- Public funding should be supported for MRI staging of histologically proven cervical cancer at FIGO stages IB or greater following assessment by examination under anesthesia. At present, the evidence is insufficient to support public funding for MRI in patients with recurrent cervical cancer, but further studies may require this issue to be reviewed in the future.
- Public funding should not be supported for MRI staging of endometrial cancer at this time.

## Method

MSAC conducted a systematic review of medical literature between January 1997 (prior to this date MRI technology was considered sufficiently different to currently available technology as to make comparison inappropriate) and August 2001 using biomedical electronic databases, the Internet, and international health technology organization websites. This review sought data on the use of MRI for staging cervical and endometrial cancer.





**Title** **Fragile X Syndrome: The Place of Molecular Diagnosis and Screening Within an Integrated Service Approach**

**Agency** **AÉTMIS, Agence d'évaluation des technologies et des modes d'intervention en santé**  
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fax:+1 514 873 1369; aetmis@aetmis.gouv.qc.ca, www.aetmis.gouv.qc.ca

**Reference** (AÉTMIS 2001-1 RF). Montréal: AÉTMIS, 2001, xxvii-191 p.

## Aim

- 1) To review the current state of knowledge with regard to the molecular analysis for the diagnosis and carrier identification of the fragile X syndrome.
- 2) To assess the utility, feasibility, and acceptability of implementing various diagnostic/screening strategies for this syndrome in the Quebec healthcare system.

## Results and Conclusions

- The molecular analysis of the FMR1 gene constitutes a substantial gain over earlier cytogenetic analyses since it clearly establishes the diagnosis in symptomatic individuals and identifies individuals at risk of transmitting the syndrome. It therefore provides an important contribution to genetic counseling, despite residual gaps in current knowledge.
- The reference method for the molecular analysis consists of the Southern blot, followed, if needed, by PCR. None of the alternative approaches has been rigorously and systematically compared with the reference method.
- The analysis of the regional context highlights several shortcomings in the provision of services to affected individuals and their families with respect to diagnosis and management. Consequently, no proactive population screening strategy can be recommended at this time. Such strategies also raise ethical issues and scientific problems which need to be resolved.

## Recommendations

- Molecular tests should be available for: 1) molecular diagnosis of fragile X syndrome in symptomatic individuals, 2) cascade screening of an affected individual's relatives, 3) confirmation of carrier status in a pregnant woman with a family history of signs associated with the syndrome, and 4) prenatal diagnosis if the mother carries a mutation.
- Necessary medical, social, and educational resources should be available to meet the needs of families with fragile X syndrome in a timely and appropriate fashion. Partners in the health, social service, and educational sectors should reinforce intersectorial collaboration to improve the early identification and diagnostic workup of children with signs consistent with fragile X syndrome and the coordination and continuity of available services.

## Methods

Systematic review of published scientific literature; review of administrative and research data regarding regional service provision; consultation with key informants and experts.

## Further research required

Research should be pursued to develop and validate genetic tests better suited to wide-scale use and to further document the epidemiology of the syndrome, the phenotype-genotype correlation, and the psychosocial impact of genetic counseling. Pilot projects need to evaluate any high- or low-risk-population diagnostic/screening strategy that might be considered for implementation.





**Title** DNA Chips: Analysis Systems of DNA Sequence Variations

**Agency** CEDIT, Committee for Evaluation and Diffusion of Innovative Technologies

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info.redit@sap.ap-hop-paris.fr, http://redit.ap-hop-paris.fr

**Reference** CEDIT Report 01.08 (in French).

## Aim

This report, based on a literature review, aims to estimate the benefit of using DNA chips in a hospital diagnostic laboratory.

## Conclusions and Results

Working with DNA chips requires combining different components: the chip itself with its special surface, the device for producing DNA chips by spotting the nucleic acids onto the chip or for their *in situ* synthesis, a fluidic system for hybridization to target DNA, a scanner to read the chips, and sophisticated software programs to quantify and interpret the results. Special equipment is now commercially available for each of these components. Moreover, complete systems currently commercially available should move this technology from its current standing as a laboratory-based research tool toward becoming an analytical method for clinical use.

Two primary techniques are used to prepare DNA chips:

- The *in situ* synthesis technique is based on the synthesis of nucleotides directly on the chips using a photolithographic mask. These chips need to be purchased from manufacturers, eg, Affymetrix®, which currently markets a range of GeneChips aimed at specific applications and a complete workstation.
- In the second technique, probes are prepared and spotted onto the chip array by the laboratory. Nanogen® currently markets the complete “NanoChip™ molecular biology workstation” and the cartridges containing the DNA chips. The innovative character of the current technique lies in the use of electronic addressing and hybridization, which are entirely automated. Moreover, it is the only complete workstation currently manufactured that presents such adaptable characteristics, with a particular focus on the diagnosis of rare diseases such as hereditary diseases. The limitation of the technique is actually the small number of spots (100 spots) by chip.

The DNA chip technology is currently available essentially for research applications: gene expression analysis, detection of new point mutations, insertions or deletions, detection of single nucleotide polymorphisms (SNP), etc. Diagnostic applications involve detection of hereditary or acquired (cancer) human diseases and detection and identification of microorganisms (bacteria, viruses, or parasites). DNA chips allow simultaneous analysis of a considerable number of sequences:

- Analysis of the majority of described point mutations for a single human disease, as long as all existing point mutations are known,
- Classification of individual tumors and analysis of gene mutations involved in cancer, and
- Isolation, identification, and detection of specific virulence or drug-resistance markers of microorganisms in a single step.

Numerous molecular biology methods used so far are time-consuming, whereas using DNA chips could reduce the diagnostic time from a few days to a few hours.

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**Title** DNA Chips: Analysis Systems of DNA Sequence Variations

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**Reference** CEDIT Report 01.08 (in French).

Since the technology is new and essentially used in research applications, no economic evaluation has been found in literature. It has been suggested that this technology would be economically competitive for sustained use.

### **Recommendations**

CEDIT emphasizes that DNA chips are an extremely exciting development. The evaluation of the NanoChip™ molecular biology workstation in a hospital biochemistry and genetic laboratory will be supported by CEDIT. This evaluation will first focus on human diseases with several points of mutation.

### **Method**

A literature search was performed in MEDLINE, and contacts with manufacturers and experts were also used in the assessment.



<b>Title</b>	<b>Cellular Xenotransplantation</b>
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<b>Reference</b>	TA 39 / 2001: Zelluläre Xenotransplantation, complete report, 331 pages, in German, and TA 39 April / 2001 (short version): The birth of a new type of treatment – Cells extracted from other species for use in treating diseases in humans; 12 pages, in English, also available under <a href="http://www.ta-swiss.ch">http://www.ta-swiss.ch</a>

## Aim

Since animal organ transplants give rise to problems of a scientific, technical, ethical, legal, and social nature, an intense, controversial debate on xenotransplantation of organs has developed. In contrast, xenotransplantation of cells and tissues, referred to here as “cellular xenotransplantation” is barely discussed although it appears to conceal a wider potential for application than xenotransplantation of organs. Also, it has advanced further in clinical trials, and certain aspects of cellular xenotransplantation make it possible to avoid serious problems associated with the xenotransplantation of organs.

This first technology assessment of cellular xenotransplantation examines the common ground and differences between cellular xenotransplantation and xenotransplantation of organs, how to evaluate these issues, and their ultimate consequences. For this purpose, the current status of xenotransplantation of animal tissue and cells to humans, their perspectives and problems areas, are determined, evaluated, and recommendations are derived. This report aims to provide a factual and comprehensive information base on cellular xenotransplantation and contribute toward a sophisticated social discussion on xenotransplantation.

## Results and Conclusions

Clinical experience is available particularly for the treatment of diabetes, damage to the central nervous system, and acute liver failure. However, cellular xenotransplantation represents a long-term option where the chances of success are uncertain. At the same time, cellular xenotransplantation is considered to be a transitional option until medical alternatives such as gene therapy, tissue engineering, stem cell technologies for regenerative systems for cell, tissue, and organ replacement are introduced. In contrast to the xenotransplantation of organs, cellular transplantation offers the possibility – through the use of cell lines and cell cultures, their genetic change, and immune isolation of animal transplants – to reduce the use of source animals, avoiding rejection, reducing the risk of infection, and optimizing the transplant’s ability to function.

The analysis revealed, however, that the potentials of cellular xenotransplantation are seldom used in clinical testing. Furthermore, they have not been sufficiently tested scientifically, are not technically mature, and the scientific proof that they actually have the desired effects has not been furnished.

In terms of the range of problems, cellular xenotransplantation applications are comparable to or even add new issues to the difficulties related to xenotransplantation of organs – an example is the potential personality changes associated with xenotransplantation of neural cells or tissue to the brain, unless fixed limits are drawn for cerebral xenotransplantations. Thus, cellular xenotransplantation unites several different development lines, each with specific advantages and disadvantages, prospects of success and risk profiles requiring a different type of assessment.

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- Title** **Cellular Xenotransplantation**
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## Recommendations

The report recommends that cellular xenotransplantation should be handled on a social level, clearly and openly, that less problematic approaches in cellular xenotransplantation should be explored, and that the search for less problematic alternatives to cellular xenotransplantation should be encouraged. With respect to regulation of xenotransplantation, both cellular and organ xenotransplantation must be subject to a compulsory approval procedures with strict requirements. With respect to biosafety issues, the present state of science and technology does not allow a differentiation between different forms (ie, cellular vs. organ) of xenotransplantation in the law.

## Methods

The international scientific literature was extensively studied, and 20 experts were interviewed in Switzerland and Germany.

## Further research/reviews required

There is a need for more detailed analyses of the possible risk of infections involved in cellular xenotransplantation. Research is required on the characteristics and specific advantages of cellular xenotransplantation since most advantages voiced to date are only hypothetical and not proven to exist in practice.



<b>Title</b>	<b>Systematic Review of Treatments of Atopic Eczema</b>
<b>Agency</b>	<b>NCCHTA, National Coordinating Center for Health Technology Assessment</b> Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom; tel:+44 2380 59 5586, fax:+44 2380 59 5639, hta@soton.ac.uk
<b>Reference</b>	Hoare C, Li Wan Po A, Williams H. Systematic review of treatments of atopic eczema. <i>Health Technol Assess</i> 2000;4(37) (published Jan 2001)

## Aim

To produce an up-to-date coverage 'map' of randomized controlled trials (RCTs) of treatments of atopic eczema (syn. atopic dermatitis) and to assist in making treatment recommendations by summarizing the evidence from RCTs using qualitative and quantitative methods.

## Results and Conclusions

- This systematic literature review found a lack of evidence supporting many of the products used in preventing and treating atopic eczema. Most studies are short-term trials of 'me too' products, and the standards of clinical trial reporting are poor.
- Little research has evaluated commonly used treatments compared with each other or in combination.
- Also lacking are common outcome measures for issues that are important to patients and data on questions that physicians and people with atopic eczema deem important.

## Recommendations

Urgent primary research priorities include RCTs of wet-wrap treatments, the clinical benefit of allergy testing, the use of water softeners, the role of specialist nurses, comparisons of tacrolimus and ascomycin against topical corticosteroids, studies of disease prevention, and the use of emollients in preventing disease relapse.

## Methods

Data sources included electronic searching of MEDLINE, EMBASE, the Cochrane Controlled Clinical Trials Register, the Cochrane Skin Group specialized register of trials, handsearching of atopic eczema conference proceedings, followup of references in retrieved articles, contact with leading researchers, and requests to relevant pharmaceutical companies. Only RCTs of therapeutic agents used to prevent and treat atopic eczema in people of any age were considered for inclusion. Only studies where a physician diagnosed atopic eczema or atopic dermatitis were included. Two observers extracted data onto abstraction forms, with discrepancies resolved by discussion. In total, 1165 possible RCTs were retrieved in hard copy for further scrutiny. Of these, 893 were excluded from further analysis because appropriate data were missing. The 272 remaining RCTs of atopic eczema covered at least 47 different interventions which could be broadly categorized into ten main groups.

## Further research required

In addition to further primary research, this review also suggests the need for further secondary research by systematically reviewing some of the major treatment groups, eg, antihistamines and essential fatty acids (some of these are already underway within the Cochrane Skin Group). Methodological research is needed to increase the clinical relevance and reliability of outcome measures for atopic eczema. The RCT database in this report offers an opportunity for further general research into the relationship between study quality and treatment benefit. Reporting on atopic eczema can be improved by dermatology journals adopting rigorous checks on clinical trial reporting, and by registering ongoing trials with the Cochrane Skin Group.



<b>Title</b>	<b>Efficacy, Effectiveness, and Safety of Sacral Neuromodulation in the Treatment of Urinary Incontinence</b>
<b>Agency</b>	<b>CAHTA, Catalan Agency for Health Technology Assessment and Research</b> Travessera de les Corts, 131-159, 08028 Barcelona, Spain; tel: +34 93 55 66 469, fax:+34 93 227 2998, diraاتم@olimpia.scs.es, www.aatm.es
<b>Reference</b>	CAHTA HTA report May 2000, Pages: 47, References: 38. Available only in Spanish at <a href="http://es/cas/informes/i.html">es/cas/informes/i.html</a> (Report carried out on request of the Spanish Ministry of Health and Consumer Affairs under an agreement signed between the Instituto de Salud Carlos III and CAHTA)

## Aim

To assess the scientific state of the art on the efficacy, effectiveness, and clinical safety of sacral neuromodulation (SN) in treating urinary incontinence.

## Results and Conclusions

- The initial results of studies on the efficacy of SN are promising in the short term. After 6 months of followup, between 47% and 50% of the patients in the group treated with NS recovered continence completely (dry patients), and between 70% and 85% showed improvement equal to or exceeding 90% in terms of frequency of UI episodes and reduction in diaper consumption.
- This study also includes measurements on quality of life obtained from instruments such as the SF-36, with significant increases in certain dimensions detected, e.g. those that measure emotional and physical aspects, although quality of life overall remains unchanged. The average/low seriousness of complications (displacement of the electrode and/or wire, pain in the implant area or in other sites, infections, explantation) was around 40%. The failure of treatment, defined as less than 50% improvement in symptoms, was approximately 32% after 18 months. In the clinical series, improvement of the symptoms, particularly with regard to UI, was between 50% and 100% after 6 months, using a threshold improvement of 50% as reference.
- SN is costly (the approximate price of a stimulation system with implant is about 8132 Euros, including elements of the study prior to the permanent implant) and presents a substantial percentage of complications which, while not serious, require extra medical care. Therefore, and while data point to the benefits of SN, the reduced number of patients involved in the studies, the unequal followup periods, and the lack of homogeneity in measuring the results, leave questions about the long-term impact of SN, quality of life, prognostic factors, and its cost-effectiveness.
- The field of research on SN contains many uncertainties, and care should be taken in the introduction and dissemination of this treatment so that it is applied restrictively (in centers of excellence) favoring training and under multicenter research protocols to answer the above questions.

## Methods

Qualitative systematic review of scientific evidence and external peer review process.





**Title**      **Gamma Knife Radiosurgery, October 2000**

**Agency**    **MSAC, Medical Services Advisory Committee**

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
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**Reference** MSAC application 1028. Assessment report ISBN TBA.

ISSN 1443-720. <http://www.msac.gov.au>

### Aim

To assess the safety and effectiveness of the service and under what circumstances public funding should be supported for the service in relation to the treatment of arteriovenous malformation (AVM), cerebral metastases, and acoustic neuroma.

### Conclusions and Results

Methodological limitations of studies and patient heterogeneity preclude comprehensive assessment of the safety and effectiveness of gamma knife radiosurgery relative to alternative treatment.

Indication	AVM	Cerebral metastases	Acoustic neuroma
Safety	There is insufficient information to assess the relative safety of gamma knife or linear accelerator (LINAC) radiosurgery and microsurgery. Studies contain methodological limitations, patient selection biases, and inconsistent adverse event definitions. Permanent neurological complications occurred in 1%-10% of radiosurgery patients and up to 15% of microsurgery patients (5% for small accessible lesions).	The only useful data are from case series: 10% incidence of radiation necrosis (1% fatal), 20% incidence of acute radiation-induced edema. One study suggests and whole radiosurgery brain radiotherapy (WBRT) incur similar complication rates.	Complication rates are similar for radiosurgery and microsurgery: facial nerve problems (20%) and hearing preservation (30%-90%). Few studies reported other complications.
Effectiveness	Two-year AVM obliteration rates are 26%-35% for gamma knife radiosurgery and 44%-68% for LINAC radiosurgery as a percentage of patients eligible for angiography. These are likely to be overestimates as only some of the patients eligible for angiography undertook the procedure and patient followup was inadequate. This compares to 85%-100% obliteration rates for microsurgery (higher for small accessible lesions).	One randomized trial, and some supportive case series data, suggest that radiosurgery in addition to WBRT shows no survival benefit, but may provide slightly improved local control when compared only to WBRT.	Microsurgical excision rates are close to 100% and tumor control rates with radiosurgery are measured at 80%-100%.
Cost effectiveness	Gamma knife was 1.7 to 2.9 times more expensive than LINAC radiosurgery. Uncertainties as to safety and effectiveness preclude an economic evaluation of gamma knife and comparators.		

### Recommendation

Public funding should not be supported for gamma knife radiosurgery at this time.

### Method

MSAC conducted a systematic review of medical literature using MEDLINE, PreMedline, EMBASE, the Cochrane Library, ISTAHC, Current Contents, HealthSTAR and NHS databases: (DARE, EED, HTA) from commencement until March 2000. Internet sites of certain health technology assessment groups were also included. The AANS and CNS Meeting Abstract Archive and the table of contents for *Radiosurgery* were also searched.





**Title**      **Hyperbaric Oxygen Therapy (HBOT), November 2000**

**Agency**      **MSAC, Medical Services Advisory Committee**

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
tel: +61 2 6289 6811, fax: +61 2 62 6289 8799, msac.secretariat@msac.gov.au, www.msac.gov.au

**Reference**      MSAC application 1018-1020. Assessment report ISSN 1443-7120.

<http://www.msac.gov.au>

### Aim

To assess the safety and effectiveness of HBOT and whether public funding should be supported.

### Conclusions and Results

*Safety:* HBOT carries some risk of myopia, barotrauma, claustrophobia, and oxygen toxicity, but most effects are self-limiting, and life-threatening events are rare.

<i>Effectiveness:</i>		Thermal burns	Little evidence of benefit and lack of well-conducted studies.
Diabetic wounds			More minor amputation risk, less major amputation risk with chronic ulceronecrotic lesions, better wound healing, reduced hospital stay.
Non-diabetic wounds			One study shows reduction in wound size.
Necrotizing soft tissue infections	general		Some indication that HBOT improved patient survival.
	necrotizing fasciitis		Inadequate information available.
	Fournier's gangrene		One study shows benefit.
Osteomyelitis			One negative study of an atypical HBOT regime.
Osteoradionecrosis	prevention		One representative study indicates HBOT is superior to penicillin.
	treatment		One positive study.
Skin graft survival			Possible benefit, but difficult to interpret.
Multiple sclerosis			Little supporting evidence.
Cardio-vasc. disease	acute myocardial infarction		No supporting evidence, possible benefit if used with thrombolytic therapy.
	cerebrovascular disease		Evidence conflicting.
	peripheral obstructive art. disease		No supporting evidence.
Soft tissue injuries	acute ankle sprains		No supporting evidence.
	crush injuries		Some supporting evidence that HBOT reduces surgical intervention.
Cluster headaches			Little supporting evidence
Migraine headaches			Some evidence of pain relief.
Facial paralysis			Some evidence of benefit.
Sudden deafness or acoustic trauma			Conflicting evidence.
Cancer	head and neck		Conflicting evidence.
	cervix		Little supporting evidence.
	bladder		Conflicting evidence.
	lymphomas		Some supporting evidence.
	lung		Little supporting evidence.
	neuroblastoma		Some positive evidence.
Carbon monoxide poisoning			A Cochrane Review found no reduction in neurologic sequelae.



**Title** Hyperbaric Oxygen Therapy (HBOT), November 2000

**Agency** MSAC, Medical Services Advisory Committee

Commonwealth Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601 Australia;  
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**Reference** MSAC application 1018-1020. Assessment report ISSN 1443-7120.  
<http://www.msac.gov.au>

*Cost-effectiveness:* HBOT is cost-effective for diabetic wounds and necrotizing soft-tissue infections, but may cost \$28,480 per case of osteoradionecrosis avoided.

## Recommendations

Public funding for HBOT in monoplace or multiplace chambers be supported for decompression illness, gas gangrene, air or gas embolism for which no alternative treatment exists, diabetic wounds (including gangrene and foot ulcers), necrotizing soft tissue infections (including necrotizing fasciitis), Fournier's gangrene, and prevention and treatment of osteoradionecrosis.

## Method

MSAC conducted a systematic review of the biomedical literature from 1966 to 1999 using biomedical electronic databases, the Internet and international health technology agency websites. Reference lists of publications and textbooks were consulted. Cost effectiveness is based on expert advice on HBOT costs and effectiveness evaluation in this report.

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