



Vagus Nerve Stimulators for Epilepsy and Depression Evidence Report Topic

Vagal Nerve Stimulators (VNS) Topic

- Brief Background Relevant to Policy Issues
 - Technology and Treatment
 - Disease
- Agency Prioritization Criteria and Concerns
- Medicare Coverage Decision
- Treatment Guidelines

- Vagus Nerve Stimulation
 - Clinical theory: physical stimulation impacts brain function and can be targeted to relieve neurologic and neuropsychiatric disorders
 - Exact mechanism of action by which VNS reduces clinical symptoms is not known, but imaging and clinical studies demonstrate brain function changes
 - One of several forms of therapeutic physical brain stimulation (both invasive and non-invasive):
 - electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), and deep brain stimulation (DBS)
 - Alternative treatments include:
 - pharmacotherapy and brain surgery

- Vagus Nerve Stimulation
 - VNS stimulates the left vagus nerve using electrical signals generated by an implanted pulse generator. The vagus nerve carries sensory information to the brain from the head, neck, thorax, and abdomen.
 - Evolving understanding continues on the neurobiological effects of VNS therapy as a function of the different use parameters (frequency, intensity, pulse width, duration, dose)
 - VNS first clinically applied as an anti-convulsant in 1980s and is now being explored for disease beyond epilepsy, including depression

Topic Background: Disease / Diagnosis

- This review focuses on the first clinical use for VNS (Epilepsy) and an expanded use (Depression)
- Epilepsy is a neurological condition impacting 2.3 million people in the US, with an estimated 600,000 experiencing complex partial seizures.
 - Epilepsy causes seizures that can involve loss of consciousness and may not be controlled by medication.
- Depression (major depressive disorder) is a mood disorder that affects approximately 18.8 million adults in the US annually.
 - Depression has a high recurrence rate and associated burden, interfering with ability to work, sleep, eat and function and with symptoms from persistent sadness or anxiety to suicide.

Topic Background: Treatments

- VNS has been used as an adjunct treatment for epilepsy (most continue with medication) in patients 12 years of age or older, who continue to suffer from partial-onset seizures, generally with:
 - a seizure frequency of at least six per month while on antiepileptic medication, and who have either failed surgical treatment or are not suitable surgical candidates.
- VNS was recently approved as an adjunct to treat major, treatment resistant depression in persons over 18
- Treatment expectation with VNS is a reduction in frequency and severity and length of seizures or depressive episodes.
- Not all patients respond to VNS treatment; and the treatment response can vary considerably among patients.

Topic Background: Selected Topic - Depression

- VNS can cause severe complications. Changing the stimulation parameters reverses many minor complications such as voice changes while others are permanent or may require device explantation.
- VNS may increase depression and suicide ideation and suicide attempts
- The etiology of depression is unclear, and it appears that a variety of genetic, environmental, and psychological factors may be involved in the onset of a depressive period.

Topic Background: Disease / Diagnosis

- 1997 - FDA approval to treat medically refractory, complex partial seizures in patients over age 12
- 2005 – FDA approval as adjunct to treat chronic or recurrent depression in patients over 18 experiencing major depressant episode without sufficient response to four or more adequate antidepressant treatments

■ **Safety concern: High**

- Primary safety concerns: VNS implantation and surgical risk; long term use unknowns; may increase suicide ideation
- The etiology of depression is unclear, and it appears that a variety of genetic, environmental, and psychological factors may be involved in the onset of a depressive period

■ **Efficacy concern: High**

- Primary concerns: adjunct treatment; patient selection and stimulation parameters still under study. Low evidence, but pressure to diffuse to uses other than anti-convulsant.

■ **Cost Concern: High**

- Cost concerns reflect mainly concern about over or mis-utilization and expansion to other treatment areas, and cost of additional (not replacement) treatment if no or little advantage

■ Key Question Function

- Sets parameters for research inquiry and policy decision

■ Key Question Components

- Legislatively, key questions are centered on a technology's evidence of safety, efficacy, effectiveness, and cost and application in any special population
- Methodologically, questions are refined to include a defined population, intervention, comparator(s), and outcome (PICO)

■ Vagus Nerve Stimulation

- The overall question related to VNS is what is the evidence of safety, efficacy, and effectiveness.
 - Is the use of VNS plus medication effective, compared with medication alone, in reducing the frequency or severity of clinical seizures or depressive episodes or in improving quality of life?
 - Are VNS safe?
 - Does effectiveness vary by age group, response to medication, or other patient characteristics?

Medicare Coverage and Clinical Guidelines

- There is a National Medicare policy on VNS for both epilepsy and depression:
 - VNS is reasonable and necessary for patients with medically refractory partial onset seizures for whom surgery is not recommended or for whom surgery has failed. (1999)
 - VNS is not reasonable and necessary for resistant depression. (2007)
 - VNS policy for Epilepsy did not cite evidence, but depression policy does.

Clinical Guidelines

- VNS for Epilepsy

- Three cited in report: two support FDA indicated use; one does not.
 - MSAC (Australia) 2008
 - British Medical Journal Review 2009
 - NICE (England) 2004

- VNS for Depression

- Three cited in report: all concluding insufficient evidence to recommend.
 - California Technology Assessment Forum/CTAF 2006
 - Institute for Clinical Systems Improvement/ICSI 2009
 - Kaiser Permanente Care Management Institute 2006

Questions?

Agency Medical Director Comments

Vagus Nerve Stimulation



**Washington State
Health Care Authority**



Vagus Nerve Stimulation

- Treatment for medically refractory epilepsy
- Adjunctive therapy for treatment resistant major depression and bipolar disorder



Clinical Overview Epilepsy

- 2.3 million people in US with epilepsy
- 600,000 with complex partial seizures
- 33% of people with inadequate control of epilepsy



Clinical Overview Depression

- 18.8 million people with depression
- 16.9% lifetime rates for major depressive disorder
- 1.5% lifetime rates for bipolar disorders



NeuroCybernetic Prosthesis(NCP)

- Marketed as VNS therapy
- Consists of implantable, programmable generator
- Controlled by patient with magnet
- Not affected by airport security or microwaves
- Potential concern with strong electromagnetic fields
- FDA approved



Challenges

- Plethora of clinical complications
- Close monitoring
- Difficulty in titrating stimulation dose
- Treatment effect delayed in epilepsy, unknown for depression

Implantation Procedures by Conditions

UMP & Medicaid Only | 2003-2008

Condition	Total
Epilepsy (345.41, 345.51, 780.39)	82
Epilepsy (345.xx, excluding above)	52
Depression (296.xx, 311)	4
Total	138



Total* Payments for Vagus Nerve Stimulators

UMP & Medicaid Only | 2003-2008

	2003	2004	2005	2006	2007	2008	Total
Epilepsy	\$74,053	\$312,322	\$276,473	\$371,855	\$510,892	\$407,164	\$1,952,758
Depression	\$12,514	\$0	\$0	\$7,426	\$1,020	\$1,240	\$22,200
Total	\$86,567	\$312,322	\$276,473	\$379,281	\$511,912	\$408,404	\$1,974,958

* Total includes inpatient, outpatient, implantations, revisions, removals, analysis, and medical devices

**Average expense of NCP $\$1,974,958/138=\$14,310$





Depression Studies in Progress

- Patient Registry Study-long term safety and effectiveness
- Randomized study comparing different stimulation settings (2010)
- Found at ClinicalTrials.gov (2009a)
 - * Long term safety & effectiveness
 - * Different stimulation settings



Recommendations

- Epilepsy
 - Complex Partial Seizures-with conditions
 - Other Seizure Disorders-no coverage
- Depression
 - Major Depressive Disorder-no coverage
 - Bipolar Disorder-no coverage

Consistent with CMS and other health plans evidenced-based coverage policy

Health Technology Assessment

Vagal Nerve Stimulators: Epilepsy

Public Comments and Responses

August 3rd, 2009

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Hayes Inc. RESPONSE TO PUBLIC COMMENTS

Hayes Inc. is an independent vendor contracted to produce evidence assessment reports for the WA HTA program on behalf of The MED Project at Oregon State Health Science University. For transparency, all comments received during the comments process are included. However, comments related to program decisions, process, or other matters not pertaining to the report are acknowledged through inclusion, but are not within the scope of response for report accuracy and completeness.

Response to industry comments

Cyberonics

1. *Section of the letter entitled “Healthcare Utilization Reduced with VNS Therapy” (cited references included Bernstein et al., 2007 and Holmes et al., 2004)*

The Bernstein et al. (2007) article is described in the Economic Evaluations section of the report. We added additional information from this study to this section to address the manufacturer’s feedback.

Data from the Holmes et al. (2004) article are presented in Table 1. This article does not present data directly pertaining to healthcare utilization and thus does not meet criteria for inclusion in the Economic Evaluations section.

2. *Section of the letter entitled “Nonadherence to AEDs Increases Healthcare Costs” (cited references were Faught et al. 2008 and Faught et al. 2009)*

The references supplied by the manufacturer address how nonadherence to antiepileptic drugs increases healthcare costs. However, these references do not contain economic evaluation data directly pertaining to the use of VNS therapy for epilepsy and are thus not included in the Economic Evaluations section.

3. *Section of the letter entitled “Depression” (cited reference of Sperling et al. 2009)*

The data reported by Sperling et al. (2009) is discussed in the Economic Evaluations section of the VNS for Depression report.

PUBLIC COMMENTS

Cyberonics = 3 pages

July 24, 2009



Ms. Leah Hole-Curry, JD
Director – Health Technology Assessment
Health Care Authority
676 Woodland Square Loop SE
P.O. Box 42712
Olympia, WA 98504-2712

RE: HTA Draft Report – Vagus Nerve Stimulation (VNS Therapy™)

Dear Ms. Hole-Curry:

Cyberonics, Inc. appreciates this opportunity to comment on the Draft Report from the Washington HTA. We know that VNS Therapy offers cost-effective and unique therapeutic benefits to patients whose epilepsy or depression is not sufficiently controlled with drugs.

Epilepsy

Healthcare Utilization Reduced With VNS Therapy

We know that healthcare utilization of patients whose seizures were not controlled decreased when those patients received VNS Therapy.

As we previously submitted, Bernstein, et al (2006) demonstrated that patients implanted with VNS Therapy experienced significant decreases in healthcare utilization.¹

- A healthcare utilization study of 138 consecutive VNS patients from Kaiser Permanente compared the fourth quarter of year 4 after implantation with average utilization during the year before implantation and found
 - 91% decrease in outpatient visits
 - 99% decrease in emergency department (ED) visits
 - 67% decrease in the length of hospital stays
 - 70% decrease in hospital admissions

These decreases in healthcare utilization applied to the entire group, irrespective of changes in seizure frequency.

Many patients with uncontrolled seizures experience drop seizures that lead to injuries and result in healthcare utilization of ED visits and hospitalizations. VNS Therapy has been shown to decrease the number of drop seizures experienced by patients with epilepsy.²

¹ Bernstein AL et al. Vagus nerve stimulation therapy for pharmaco-resistant epilepsy: effect on health care utilization. *Epil Behav* 2007;10:134-137.

² Holmes MD et al. Effect of vagus nerve stimulation on adults with pharmaco-resistant generalized epilepsy syndromes. *Seizure* 2004;13:340-345.

- Holmes et al (2004) studied 16 patients with pharmaco-resistant generalized epilepsy syndromes who received VNS Therapy. The study concluded, “The benefits of reduced seizure frequency and reduced risk of injury merit consideration of VNS Therapy for patients with pharmaco-resistant generalized seizure syndromes.”
 - Patients experienced a statistically significant overall median seizure frequency reduction of 43.3%
 - Types of seizures that may involve a fall or collapse decreased with reductions in the frequency of
 - Myoclonic seizures: 60% reduction
 - Tonic seizures: 75% reduction
 - Atonic seizures: 99% reduction
 - Clonic seizures: 87%

Nonadherence to AEDs Increases Healthcare Costs

Medication nonadherence in patients with refractory epilepsy can result in major increase in morbidity and mortality. Serious health consequences can result from nonadherence with seizure medication, presenting additional challenges to clinicians treating patients with epilepsy.³

Faught et al (2008) evaluated claims data from over 33,000 patients comprising 388,564 quarters from 3 state Medicaid programs. They reported that patients did not adhere to their AED regimens during 26% of those quarters. The study also showed that Nonadherence to AED's:

- Contributes significantly to mortality and other serious clinical events
- Increases the risk of death by more than a 3-fold
- Is associated with a higher incidence of fractures and injuries due to motor vehicle accidents
- Increases significantly healthcare utilization
 - 16% increase in ED visits
 - 39% increase in hospitalizations
 - 76% increase in inpatient days

“In the interest of both patient well being and costs, state Medicaid programs should have a vested interest in strategies aiming to reduce AED nonadherence.”⁴ Clinicians, payers, and drug innovators should promote treatment strategies for epilepsy that offer an increased likelihood of adherence.³

³ Faught E, et al. Nonadherence to antiepileptic drugs and increased mortality: Findings from the RANSOM study. *Neurology* 2008; 71 (20): 1572-1578.

⁴ Faught E, Weiner J, Guerin A. Impact of nonadherence to antiepileptic drugs on health care utilization and costs: Findings from the RANSOM study. *Epilepsia*. 2009;50(3):501-509.

As a proven adjunctive treatment for patients with refractory epilepsy, VNS Therapy's automatic delivery ensures adherence for patients whose seizures are not controlled by anti-epileptic medications only.

Depression

- Sperling W et al (2009) studied 9 patients with treatment-resistant depression who received VNS Therapy
 - Average length of hospitalization of 65 days per year, averaged over the 5 years before implantation, was significantly reduced in the first post-implantation year to an average of 44 days, a savings of 7350€.
 - Average number of outpatient consultations was reduced from 33 to 14 per year, a savings of 570€.
 - Average number of medications was reduced from 4.1 to 2.7 per year, a savings of 600€
 - Average savings for the year after VNS implantation was 1905€, roughly \$2,700

I hope you find these materials helpful with the technology evaluation of VNS Therapy. If you have any questions or require any additional information on the treatment of VNS Therapy of either refractory epilepsy or treatment-resistant depression, please feel free to e-mail Stan Jackson, National Director of Reimbursement at Stanley.Jackson@cyberonics.com.

With best regards,



Daniel J. Moore
President & Chief Executive Officer

HTCC Coverage and Reimbursement Determination Analytic Tool

HTA's goal is to achieve *better health care outcomes* for enrollees and beneficiaries of state programs by paying for proven health *technologies that work*.

To find best outcomes and value for the state and the patient, the HTA program focuses on these questions:

1. Is it safe?
2. Is it effective?
3. Does it provide value (improve health outcome)?

The principles HTCC uses to review evidence and make determinations are:

Principle One: Determinations are Evidence based

HTCC requires scientific evidence that a health technology is safe, effective and cost-effective¹ as expressed by the following standards.²

- Persons will experience better health outcomes than if the health technology was not covered and that the benefits outweigh the harms.
- The HTCC emphasizes evidence that directly links the technology with health outcomes. Indirect evidence may be sufficient if it supports the principal links in the analytic framework.
- Although the HTCC acknowledges that subjective judgments do enter into the evaluation of evidence and the weighing of benefits and harms, its recommendations are not based largely on opinion.
- The HTCC is explicit about the scientific evidence relied upon for its determinations.

Principle Two: Determinations result in health benefit

The outcomes critical to HTCC in making coverage and reimbursement determinations are health benefits and harms.³

- In considering potential benefits, the HTCC focuses on absolute reductions in the risk of outcomes that people can feel or care about.
- In considering potential harms, the HTCC examines harms of all types, including physical, psychological, and non-medical harms that may occur sooner or later as a result of the use of the technology.
- Where possible, the HTCC considers the feasibility of future widespread implementation of the technology in making recommendations.
- The HTCC generally takes a population perspective in weighing the magnitude of benefits against the magnitude of harms. In some situations, it may make a determination for a technology with a large potential benefit for a small proportion of the population.
- In assessing net benefits, the HTCC subjectively estimates the indicated population's value for each benefit and harm. When the HTCC judges that the balance of benefits and harms is likely to vary substantially within the population, coverage or reimbursement determinations may be more selective based on the variation.
- The HTCC considers the economic costs of the health technology in making determinations, but costs are the lowest priority.

¹ Based on Legislative mandate: See RCW 70.14.100(2).

² The principles and standards are based on USPSTF Principles at: <http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm>

³ The principles and standards are based on USPSTF Principles at: <http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm>

Using Evidence as the basis for a Coverage Decision

Arrive at the coverage decision by identifying for Safety, Effectiveness, and Cost whether (1) evidence is available, (2) the confidence in the evidence, and (3) applicability to decision.

1. **Availability of Evidence:**

Committee members identify the factors, often referred to as outcomes of interest, that are at issue around safety, effectiveness, and cost. Those deemed key factors are ones that impact the question of whether the particular technology improves health outcomes. Committee members then identify whether and what evidence is available related to each of the key factors.

2. **Sufficiency of the Evidence:**

Committee members discuss and assess the evidence available and its relevance to the key factors by discussion of the type, quality, and relevance of the evidence⁴ using characteristics such as:

- Type of evidence as reported in the technology assessment or other evidence presented to committee (randomized trials, observational studies, case series, expert opinion);
- the amount of evidence (sparse to many number of evidence or events or individuals studied);
- consistency of evidence (results vary or largely similar);
- recency (timeliness of information);
- directness of evidence (link between technology and outcome);
- relevance of evidence (applicability to agency program and clients);
- bias (likelihood of conflict of interest or lack of safeguards).

Sufficiency or insufficiency of the evidence is a judgment of each clinical committee member and correlates closely to the GRADE confidence decision.

Not Confident	Confident
Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence.	Very certain of evidentiary support. Further information is unlikely to change confidence

3. **Factors for Consideration - Importance**

At the end of discussion at vote is taken on whether sufficient evidence exists regarding the technology's safety, effectiveness, and cost. The committee must weigh the degree of importance that each particular key factor and the evidence that supports it has to the policy and coverage decision. Valuing the level of importance is factor or outcome specific but most often include, for areas of safety, effectiveness, and cost:

- risk of event occurring;
- the degree of harm associated with risk;
- the number of risks; the burden of the condition;
- burden untreated or treated with alternatives;
- the importance of the outcome (e.g. treatment prevents death vs. relief of symptom);
- the degree of effect (e.g. relief of all, none, or some symptom, duration, etc.);
- value variation based on patient preference.

⁴ Based on GRADE recommendation: <http://www.gradeworkinggroup.org/FAQ/index.htm>

Medicare Coverage and Guidelines

Organization	Date	Outcome	Evidence Cited?	Grade / Rating
Medicare Pub. 100-03, Manual Section 160.18	NR	<p>There is a National Coverage decision for VNS for epilepsy and depression:</p> <p>VNS is reasonable and necessary for patients with medically refractory partial onset seizures for whom surgery is not recommended or for whom surgery has failed.</p> <p>VNS is not reasonable and necessary for resistant depression (not covered).</p>	<p>No</p> <p>Yes</p>	<p>N/A</p> <p>Good RCT showed no benefit</p>
Guidelines – WA HTA p. 48 and p.110	NA	<p><u>Epilepsy</u> MSAC (Australia) VNS is reasonably safe in context of the condition being treated but insufficient evidence of effectiveness and net benefit of VNS for patients with medically refractory epilepsy.</p> <p>Clinical Evidence/BMJ report high level VNS may reduce seizure frequency in people with partial seizures that are refractory to medication; complications and long term effect unknown.</p> <p>NICE: VNS indicated for use as an adjunctive therapy in reducing the frequency of seizures in children and adults who are refractory to antiepileptic medication and who are not suitable candidates for resective surgery. VNS is indicated for patients with epileptic disorder with predominantly partial seizures, with or without secondary generalized epilepsy, and generalized epilepsy.</p> <p><u>Depression</u> CTAF concluded that VNS for depression does not meet criteria four and five for effectiveness and improvement of health outcomes in treatment resistant depression.</p> <p>ISCI concluded that quality of evidence currently does not meet ICSI's threshold for recommendation.</p> <p>Kaiser Permanente Care Management concluded insufficient evidence to recommend VNS.</p>	<p>Yes</p> <p>Yes</p>	

HEALTH TECHNOLOGY EVIDENCE IDENTIFICATION

Discussion Document: What are the key factors and health outcomes and what evidence is there?

Safety Outcomes	Safety Evidence
Mortality - Overall Mortality	
Morbidity -	
Efficacy/Effectiveness Outcomes	Efficacy/Effectiveness Evidence
Reduction in severity or frequency of seizure	
Reduction in severity or frequency of depressive episode	
Quality of life improvement	
Cost Outcomes	Cost Evidence
Other Factors	Evidence
Special Populations, patient characteristics, adjunct treatments	

Clinical Committee Evidence Votes

First voting question

The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

Is there sufficient evidence under some or all situations that the technology is:

	Unproven (no)	Equivalent (yes)	Less (yes)	More (yes)
Effective				
Safe				
Cost-effective				

Discussion

Based on the evidence vote, the committee may be ready to take a vote on coverage or further discussion may be warranted to understand the differences of opinions or to discuss the implications of the vote on a final coverage decision.

- Evidence is insufficient to make a conclusion about whether the health technology is safe, efficacious, and cost-effective;
- Evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions;
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for some conditions or in some situations

A straw vote may be taken to determine whether, and in what area, further discussion is necessary.

Second vote

Based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, it is

_____ Not Covered. _____ Covered Unconditionally. _____ Covered Under Certain Conditions.

Discussion Item

Is the determination consistent with identified Medicare decisions and expert guidelines, and if not, what evidence is relied upon.

Clinical Committee Findings and Decisions

Next Step: Cover or No Cover

If not covered, or covered unconditionally, the Chair will instruct staff to write a proposed findings and decision document for review and final adoption at the following meeting.

Next Step: Cover with Conditions

If covered with conditions, the Committee will continue discussion.

- 1) Does the committee have enough information to identify conditions or criteria?
 - Refer to evidence identification document and discussion.
 - Chair will facilitate discussion, and if enough members agree, conditions and/or criteria will be identified and listed.
 - Chair will instruct staff to write a proposed findings and decision document for review and final adoption at next meeting.
- 2) If not enough or appropriate information, then Chair will facilitate a discussion on the following:
 - What are the known conditions/criteria and evidence state
 - What issues need to be addressed and evidence state

The chair will delegate investigation and return to group based on information and issues identified. Information known but not available or assembled can be gathered by staff ; additional clinical questions may need further research by evidence center or may need ad hoc advisory group; information on agency utilization, similar coverage decisions may need agency or other health plan input; information on current practice in community or beneficiary preference may need further public input. Delegation should include specific instructions on the task, assignment or issue; include a time frame; provide direction on membership or input if a group is to be convened.

Efficacy Considerations:

- What is the evidence that use of the technology results in more beneficial, important health outcomes? Consider:
 - Direct outcome or surrogate measure
 - Short term or long term effect
 - Magnitude of effect
 - Impact on pain, functional restoration, quality of life
 - Disease management
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to no treatment or placebo treatment?
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to alternative treatment?
- What is the evidence of the magnitude of the benefit or the incremental value
- Does the scientific evidence confirm that use of the technology can effectively replace other technologies or is this additive?
- For diagnostic tests, what is the evidence of a diagnostic tests' accuracy
 - Does the use of the technology more accurately identify both those with the condition being evaluated and those without the condition being evaluated?
- Does the use of the technology result in better sensitivity and better specificity?
- Is there a tradeoff in sensitivity and specificity that on balance the diagnostic technology is thought to be more accurate than current diagnostic testing?
- Does use of the test change treatment choices

Safety

- What is the evidence of the effect of using the technology on significant morbidity?
 - Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or;
 - Adverse effect on health that can result in lasting harm or can be life-threatening.
- Other morbidity concerns
- Short term or direct complication versus long term complications
- What is the evidence of using the technology on mortality – does it result in fewer adverse non-fatal outcomes?

Cost Impact

- Do the cost analyses show that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?

Overall

- What is the evidence about alternatives and comparisons to the alternatives
- Does scientific evidence confirm that use of the technology results in better health outcomes than management without use of the technology?