



Washington State
Health Care Authority

Health Technology Assessment Program

Health Technology Clinical Committee
November 2009 Meeting

Washington's Health Technology Assessment Program Background

- **Part of Governor's 2006 Five point health strategy for state to lead by example**
 - **Emphasize evidence-based health care**

<http://www.hca.wa.gov/conf/doc/GovGregoireHealthBrief.pdf>

- **Program Purpose: Achieve better health by paying for technologies that work**
 - Better health with better information: investigate what works and maintain a centralized website.
 - Open and transparent process: publish process, criteria, reports, and committee decisions in public meeting.
 - Eliminate Bias: contract for independent evidence report and independent clinical committee.
 - Promote consistency: state agencies rely on a single, scientifically based source.
 - Flexible: review evidence regularly to ensure update information is included.

- ❑ Overall Issue: WA citizens pay high cost for health care and receive poorer outcomes
- ❑ Government Issue: Public Programs have limited and/or shrinking resources and rising costs and needs.
- ❑ Common reaction: Reduce Eligibility, Rates or Benefits
 - “Thin the soup or cut the line”

Vision: Transform WA state from a passive payer to an active purchaser of higher quality, more efficient health care

- ❑ Action: Ensure WA pays for technologies that are proven safe, effective and cost-effective

“Better ingredients in the soup make it go farther”

Outcome: Pay for What Works

- Coverage decisions:
 - scientifically based
 - use transparent process, and
 - consistent across state health care purchasing agencies

- Formal, systematic process to identify, review, and cover appropriate health care technologies.
 - Is it safe?
 - Is it effective?
 - Does it provide value (improve health outcome)?

HTA Program – Ongoing Operations

Pay for What Works: Better Information is Better health

■ Coverage Decisions

- Cardiac Stents Finalization
- Bone Growth Stimulator Finalization
- Vagal Nerve Stimulator Finalization

■ Evidence Reports

- Calcium Scoring (CACs) - Complete
- Hip Resurfacing - Complete
- Electrical Neural Stimulation (ENS) - Complete
- Sleep Apnea Diagnosis and Treatment – AHRQ underway
- Glucose Monitoring – AHRQ underway

■ Staffing Changes

- Program Manager Hire – Margaret Dennis
- Clinical Consultant – contract refresh

HTA Program – Ongoing Operations

Pay for What Works: Better Information is Better health

- Topic Selection – 2010 Potential Topics Posted
 1. Kyphoplasty / Sacroplasty / Vertebroplasty
 2. Hyaluronic Acid Injections
 3. Spinal Injections
 4. MRI for Breast Cancer
 5. CT/MRI for abdomen/pelvis
 6. Spinal Cord Stimulation
 7. ABA Therapy for Autism
 8. Routine Ultrasound for Pregnancy
 9. Knee Replacement
 10. Prostate Specific Antigen Testing

1. HCA Administrator Selects Technology

Nominate, Review, Public Input, Prioritize



Semi-annual

2. Vendor Produce Technology Assessment Report

Key Questions and Work Plan, Draft, Comments, Finalize



2-8 Months

3. Clinical Committee Makes Coverage Determination

Review Report, Public Hearing

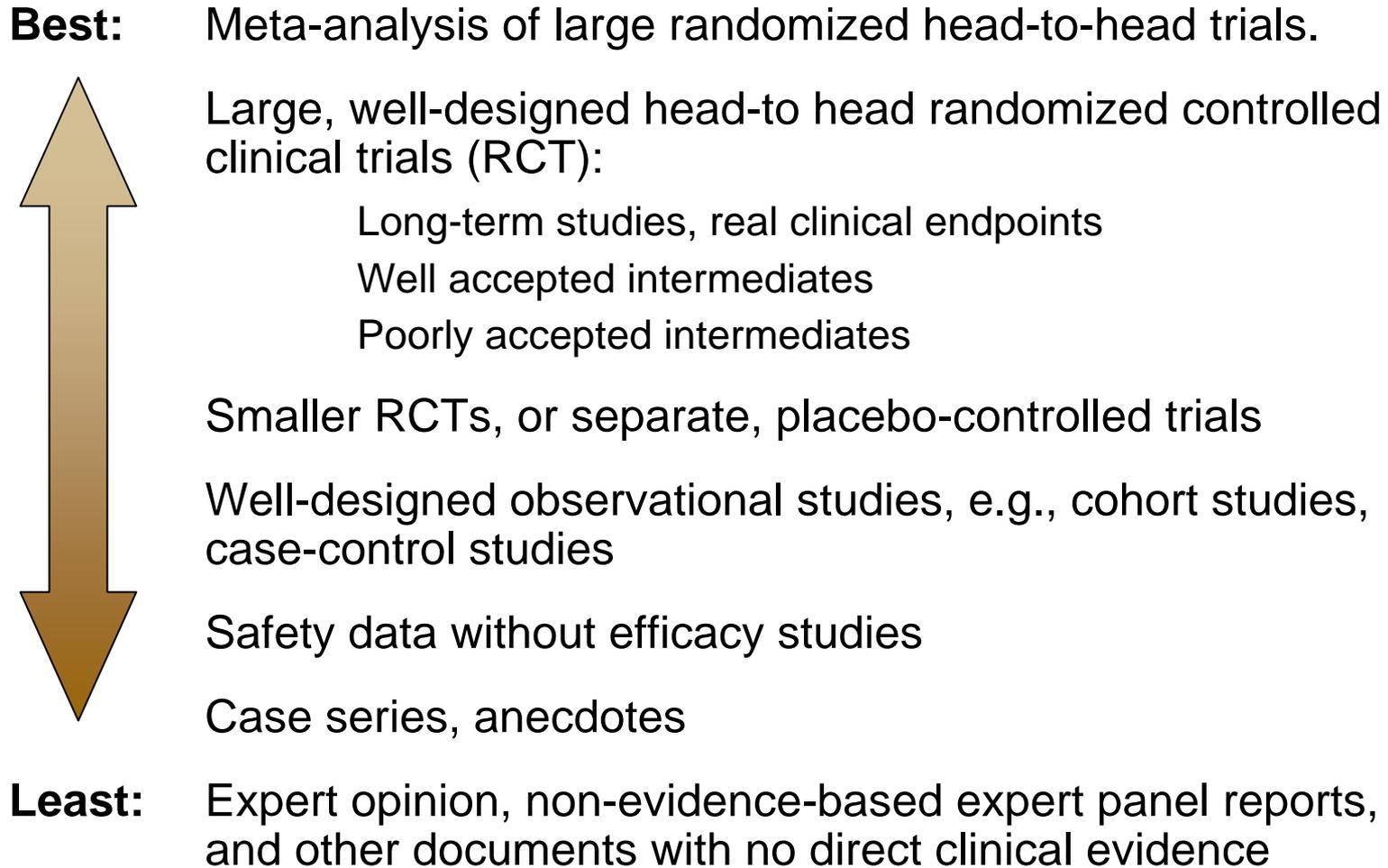


Meet Quarterly

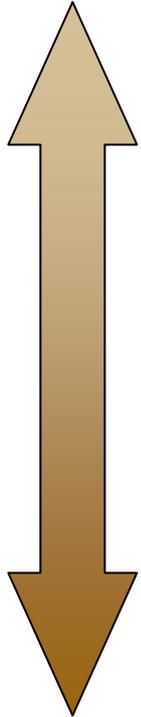
4. Agencies Implement Decision

Implements within current process unless statutory conflict

Hierarchy of Evidence



Evidence in Health Care Decision Making



- **Level 3:** *“What would I recommend to the state or nation?”*
 - **Must be based on rigorous assessment of the scientific evidence.**
 - **Affects hundreds of thousands, even millions of people.**

- **Level 2:** *“What would I recommend to my patient/client?”*
 - Influenced by prior experience, but the scientific evidence may play a greater role.
 - Affects possibly hundreds of people.

- **Level 1:** *“Would you have this done for yourself or for someone else in your immediate family?”*
 - Influenced by one’s personal experience with the disease and capacity to deal with risk.
 - Affects few people.

Used with Permission from Dr. Mark Helfand, OHSU

Different Data Sources

- Efficacy
 - How technology functions in “best environments”
 - Randomized trials-distinguish technology from other variables
 - Meta-analysis
- Effectiveness
 - How technology functions in “real world”
 - Population level analyses
 - Large, multicenter, rigorous observational cohorts (consecutive pts/objective observers)
- Safety
 - Variant of effectiveness
 - Population level analyses
 - Case reports/series, FDA reports
- Cost
 - Direct and modeled analysis
 - Administrative/billing data (charge vs cost)
- Context
 - Mix of historic trend, utilization data, beneficiary status, expert opinion

Topic Selection & Decision Process

Coronary Artery Calcium Scoring Topic

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

Heart Disease

- Heart disease is the leading cause of death and disability in US: with 700,00 deaths.
- The most common heart disease in the United States is coronary artery disease (CAD), which can lead to heart attack.
- CAD is a narrowing of one or more coronary arteries that results in an insufficient supply of oxygen to the heart muscle and is a leading cause of death in the US and developed countries.
- CAD may be asymptomatic or lead to chest pain (angina), heart attack- myocardial infarction (MI), or death

Diagnostic Tests

- Cardiac related diagnostic tests include both non-invasive and invasive tests.

Non-invasive tests include:

- Stress Echocardiograms -tests that compare blood flow with and without exercise and visualize the heart
- Single-photon emission computed tomography (SPECT), also known as nuclear stress testing or myocardial perfusion imaging
- CT angiography with or without calcium scoring uses 3D imaging of the to visualize the heart.

Invasive test includes:

- The “gold” standard is the conventional coronary angiography which involves placement of a catheter and injection of contrast material into a large artery or vein, followed by 2-dimensional visualization with x-rays.

Agency Prioritization

- ❑ Cardiac calcium scoring uses a CT to check for the buildup of calcium in plaque on the coronary arteries. This test identifies and quantifies a marker of coronary disease (plaque), believed to detect earlier stage of CAD.
- **Priority Concerns:**
 - ❑ **Safety–Medium; Efficacy-High; Cost-High**
- **Priority Concern Context CACS**
 - ❑ Concerns that CACS is rapidly diffusing, has a radiation risk (especially cumulative) and is costly, but with little evidence of connection between test result and treatment choices or better health outcomes.

- **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)

■ CACS Key Question Focus

- When used to diagnose persons with suspected coronary artery disease:
 - What are the test characteristics (PPV, NPV, sensitivity, specificity, reliability)
 - What is the evidence regarding safety?
 - What is the evidence that CACS influences clinical decision making and improves patient outcomes?
 - What is the evidence that CACS may perform differently in special populations?
 - What is the evidence about cost or cost effectiveness?

Medicare Coverage and Clinical Guidelines

- There is no National Medicare policy on CACS
- Clinical Guidelines:
 - American college of Cardiology Foundation (ACCF/AHA) 2007 expert consensus
 - Lack of evidence to determine if CAC measurement is superior or inferior
 - Additional statements related to specific issues/scenarios
 - American Heart Association (AHA 2006) and 2009 update:
 - Conflicting evidence and divergent opinion on use of CACS resulted in several scenarios where CACS may be considered and others where it should not be used.
 - American College of Radiology 2008 – for assessment of chest pain in low to medium risk patients
 - Appropriateness rating of 3 on scale of 0 to 9, and medium radiation level (1-10msv)

Questions?

Hip Resurfacing Topic

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



- Conservative management – primarily pain reduction
- Hip Surgery debate in AAOS
 - Total Hip Replacement is a proven, effective technique that results in excellent pain relief and function in most patients for many years.
 - Hip resurfacing has had its ups and downs—with implants that were introduced in the early 1990s, then withdrawn from the market, and reintroduced a decade later.
- “HR is not new...But direct-to-consumer advertising is driving patients to ask for the procedure without really understanding what is involved or even if they are suitable candidates.” 2008 AAOS Annual Meeting

<http://www.aaos.org/news/aaosnow/apr08/clinical4.asp>

Health Technology Clinical Committee Findings and Coverage Decision

Topic: Electrical Neural Stimulation (ENS)

Meeting Date: October 30th, 2009

Final Adoption:

Number and Coverage Topic

20091030A – Electrical Neural Stimulation

HTCC Coverage Determination

Electrical Neural Stimulation is a **non-covered benefit**. This decision applies to use of durable medical equipment ENS device and supplies outside of medically supervised facility settings (e.g. in home use).

HTCC Reimbursement Determination

❖ Limitations of Coverage

- Not Applicable

❖ Non-Covered Indicators

- The use of durable medical equipment ENS device and supplies outside of medically supervised facility settings (e.g., in home use).

❖ Agency Contact Information

Agency	Contact Phone Number
Labor and Industries	1-800-547-8367
Public Employees Health Plan	1-800-762-6004
Health and Recovery Services Administration	1-800-562-3022

Health Technology Background

The Electrical Neural Stimulation (ENS) topic was selected and published in December 2008 to undergo an evidence review process. Pain is a very prevalent and burdensome condition. Back pain is the most commonly reported of all types with more than 25% of adults reporting low back pain in the prior 3 months, with pain most commonly reported among adults 45 years of age and over. Many treatments, increasing in number, are available to manage acute and chronic pain including physical therapies, medications, surgical intervention, neural blocks, psychotherapy, and complementary and alternative practices.

Pain is one of the most common causes of disability in the United States. Low back pain, headache, and joint pain, aching, or stiffness are among the most common complaints. Types of acute pain: procedural pain, pre-and postoperative pain, post-traumatic pain, dental procedures, and labor pain. Conditions that can lead to chronic pain: arthritis, low back pain, and other musculoskeletal problems. Transcutaneous electrical stimulation (TENS) is a commonly prescribed treatment. Estimates of use are limited, but there were 275,000 reported TENS prescriptions in 1991. Proponents estimate 50% - 80% of chronic pain patients and 6% - 44% of acute pain patients benefit from TENS. Although TENS has been widely adopted, it is unclear that benefit has been established for pain relief in high quality studies.

Treatment with TENS involves the transmission of electrical energy from an external stimulator to the peripheral nerve system via cutaneously placed conductive gel pads (electrodes). Usually have a single channel (with two electrodes) or dual channels (with four electrodes). Manner in which the current is delivered can vary in frequency, intensity, pulse width, electrode placement and duration.

In September 2009, the HTA posted a draft and then followed with a final report from a contracted research organization that reviewed publicly submitted information; searched, summarized, and evaluated trials, articles, and other evidence about the topic. The comprehensive, public and peer reviewed, Electrical Neural Stimulation report is 102 pages, and identified a relatively large amount of literature.

An independent group of eleven clinicians who practice medicine locally meet in public to decide whether state agencies should pay for the health technology based on whether the evidence report and other presented information shows it is safe, effective and has value. The committee met on October 30th, reviewed the report, including peer and public feedback, and heard agency comments. Meeting minutes detailing the discussion are available through the HTA program or online at <http://www.hta.hca.wa.gov> under the committee section.

Committee Findings

Having considered the evidence based technology assessment report and the written and oral comments, the committee identified the following key factors and health outcomes, and evidence related to those health outcomes and key factors:

1. Evidence availability and technology features

The committee concludes that the best available evidence on electrical neural stimulation has been collected and summarized.

- ENS devices use electrical stimulation of nerves via pads on the skin. However, ENS topics is made difficult to assess by the wide variance in different devices, differing placement locations, and delivering varying pulse, and frequency of stimulation, and duration at each treatment and over time. Cochrane reviews included different modalities in their reports which were grouped by different clinical indications.
- Electrical neural stimulation (ENS) is a commonly prescribed treatment that has been in use for over 30 years, is widely used and adopted despite unclear benefit.
- Evidence from eight Cochrane reports reviewing 86 randomized controlled trials and six additional randomized, controlled trials, provides a relatively large evidence base consisting of randomized trials, but the evidence is mostly insufficient, low quality data providing mixed results on a generally narrow outcome of short term pain relief.
- Given the variety of device types and conditions, the committee sought to focus discussion and consideration. The data from agencies on cost was associated with durable medical equipment purchase or rental of ENS devices and supplies, and CMS' policy was similar. Agency comments indicated that charges for use in facility are included in overall charges, not generally separable and managed through daily or unit caps the apply to broad group of services. The committee decided to limit deliberation and decision(s) to ENS prescribed for take home or outside clinic setting and excluded further consideration of ENS used as part of a clinician's in facility services (e.g. use in labor or use in physical therapy facility).

2. Is the technology safe?

The committee concludes that the comprehensive evidence reviewed shows that the ENS technology is safe. Key factors to the committee's conclusion included:

- The committee agreed with the evidence report conclusions that indicated ENS is not associated with mortality.
- The evidence report concludes that most adverse effects were mild, most often associated with irritation at the electrode site or discomfort with the sensation of TENS current. No significant adverse outcomes identified, though studies may be underpowered for this event, the ENS devices are used to deliver small currents to the skin and no significant adverse complications would be expected.
- The devices have been in wide use for 30 years with no observed effects. A small issue for in home use and the possible unknown effect (long term) of over stimulation of nerve fibers was raised, but agreed unlikely.

3. Is the technology effective?

The committee concludes that the comprehensive evidence reviewed shows that TENS is not more effective for treatment of acute or chronic pain. Note: consistent with overall decision, this conclusion applies to use of durable medical equipment ENS device and supplies outside of medically supervised facility settings (e.g. in home use).

- Overall, the committee agreed with the evidence based report that concluded, despite identification a over 80 randomized trials, the evidence is insufficient for evidence based conclusions about efficacy or effectiveness of ENS due to mostly low or very low quality studies (small numbers, lack of blinding, intermediate or insufficient outcomes, variable devices, indications and settings used, inadequate descriptions and controls, and measurements, conflicting results), though some indications and devices have somewhat higher quality evidence.
- The committee reviewed findings primarily for the chronic pain, low back, and knee osteoarthritis indications as these were noted as primary uses by agencies and/or had relatively higher levels of evidence (either quantity or design).
- No reliable information was available on important outcomes of reduction in analgesic medication, improvement in functional status, or quality of life.
- Pain – the primary outcome measured generally focused on short term outcomes with no evidence on long term use or outcomes although primary state costs and usage are for longer term. Low quality is insufficient to conclude whether ENS treatment provides or does not provide benefit. If any benefit demonstrated, evidence is limited by short term trial duration/follow up.
- While there was broad agreement on lack of evidence of benefit, the clinical issue of the value of a placebo effect for some patients who may then not need treatment with medication (generally opioids) where there are known risks and costs was discussed. There is no current evidence that ENS usage eliminates or reduces medication use, but this was not evaluated and clinical experience indicates it may effect decision making. A related factor discussed was that the issue was payment, not ability to access (many items such as specialized mattresses or pillows available to try but not insured benefit), and the in clinic treatment is not under consideration.
- The committee discussed the issue of comparators, ultimately deciding on treatment with ENS versus treatment without ENS.

4. Is the technology cost-effective?

The committee concludes that the comprehensive evidence review shows no published good quality evidence on ENS treatment.

- Committee noted that where efficacy and effectiveness are not established, cost effectiveness is premature. No quality studies have been produced, and the one included cost savings estimate is based on assumptions of decreased medication and physical therapy use, neither of which have been studied, reported on or demonstrated.
- Committee acknowledged the state agency costs of nearly \$3million over last four years, generally increasing and reaching nearly 1 million last year (900,000) in the durable medical equipment (DMS) costs.

5. Medicare Decision and Expert Treatment Guidelines

Committee reviewed and discussed the Medicare coverage decision and expert guidelines as identified and reported in the technology assessment report.

- Centers for Medicare and Medicaid Services (2003) – CMS will cover the use of TENS for the relief of acute post-operative pain. TENS may be covered whether used as an adjunct to the use of drugs, or as an alternative to drugs. TENS devices, whether durable or disposable, may be used in furnishing this service. In cases where TENS is used for longer than 30 days, TENS may be covered as durable medical equipment (DME). PNT only covered if performed by a physician. No evidence cited for these decisions.
- Guidelines – a search of the National Guideline Clearinghouse (NGC) returned 8 potential guidelines on the use of TENS for pain management. Of those, 6 specifically described conditions for TENS use and provide specific recommendations. In general, very little information specific to the use of TENS with regard to chronic conditions like low back pain, rheumatoid arthritis, headache, and neuropathic pain were described. Two guidelines that described management of acute pain conditions, concluded that TENS therapy was generally not recommended. The following provides a summary of the guidelines that were most relevant:
 - (1) University of Iowa Gerontological Nursing Interventions Research Center, Research Translation and Dissemination Core – good evidence that TENS can be used as a non-pharmacological, physical method for the treatment of persistent pain in older adults; although, other therapies have been found to be useful, the evidence is still preliminary and inconclusive.
 - (2) American College of Occupational and Environmental Medicine (ACOEM) – the only recommendation was TENS therapy for low back pain; however, the evidence was described as limited and it was only recommended for select appropriate patients. All other ENS modalities were not recommended or described.
 - (3) Ottawa Panel evidence-based practice guidelines on electrotherapy for the management of rheumatoid arthritis – overall, only low frequency TENS applied to the hand and wrist showed a small clinical benefit.
 - (4) Institute for Clinical Systems Improvement (ICSI) – TENS units for migraine or muscle contraction headache have not been found to be more beneficial than placebo when evaluated in a controlled study.
 - (5) National Headache Foundation – Considering the inconvenience and the limited efficacy, this treatment was not recommended.
 - (6) European Federation of Neurological Societies (EFNS) – they concluded standard high-frequency TENS might be better than placebo.
 - (7) Stoke Rehabilitation Clinical Practice Guidelines – this guideline does not address the use of TENS for pain relief specifically, but describes TENS for decrease in spasticity, and increase in functional status (motor function, gait speed, passive shoulder range of motion, and sensation).
 - (8) American Pain Society – concluded there was insufficient evidence to accurately judge the efficacy of TENS versus other interventions for chronic low back pain or for acute low back pain. In a more recent guideline, TENS was not listed as an interventional therapy for patients with low back pain.

Committee Decision

Based on the deliberations of key health outcomes, the committee decided that it had the most complete information: a comprehensive and current evidence report, public comments, agency and state utilization information. The committee concluded that the current evidence on Electrical Neural Stimulation demonstrates that there is insufficient evidence to cover the use of Electrical Neural Stimulation. The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable. The committee found that Electrical Neural Stimulation didn't have a mortality rate; morbidity from ENS was unusual and generally mild, most often associated with irritation at the electrode site or discomfort with the sensation of ENS current; and ENS showed insignificant data to conclude it was effective in reducing pain relief, satisfaction and Analgesic Consumption.

Based on these findings, the committee voted 8 to 2 to not cover Electrical Neural Stimulation for durable medical equipment usage (buying or renting the equipment for home use).

Health Technology Clinical Committee Authority

Washington State's legislature believes it is important to use a scientific based, clinician centered approach for difficult and important health care benefit decisions. Pursuant to chapter 70.14 RCW, the legislature has directed the Washington State Health Care Authority, through its Health Technology Assessment program to engage in a process for evaluation process that gathers and assesses the quality of the latest medical evidence using a scientific research company and takes public input at all stages. Pursuant to RCW 70.14.110 a Health Technology Clinical Committee (HTCC) composed of eleven independent health care professionals reviews all the information and renders a decision at an open public meeting. The Washington State Health Technology Clinical Committee (HTCC), determines how selected health technologies are covered by several state agencies. RCW 70.14.080-140. These technologies may include medical or surgical devices and procedures, medical equipment, and diagnostic tests. HTCC bases their decisions on evidence of the technology's safety, efficacy, and cost effectiveness. Participating state agencies are required to comply with the decisions of the HTCC. HTCC decisions may be re-reviewed at the determination of the HCA Administrator.

WA Agency Data

Coronary Artery
Calcium scoring



Cardiac Artery Calcium Scoring (CACS)

- Cardiac calcium scoring uses CT to check for the buildup of calcium in the coronary arteries.
- Calcium is associated with atherosclerosis and is one marker of CAD.
- However, coronary calcium is not present in all atherosclerotic plaques and its relevance to risk and treatment is unclear.

Cardiac Artery Calcium Scoring (CACs)

- CACs scans the heart using CT by taking imaging “slices” of the heart.
- CACs is noninvasive. It offers a potentially less invasive alternative to detect CAD.
- Radiation exposure through this test is not insignificant.
- Issues: No clinically significant threshold of amount of calcium established; Unclear benefit of diagnosis with calcium score; and test can result in aggressive treatment with unknown health benefit.

Key Concerns for Prioritization

- Efficacy Concern: High
 - Test reliability unknown
 - Results of calcium scores not specific and do not correlate with cardiac event risk
- Safety Concern: Medium
 - CT radiation exposure- no system to validate low dose equipment or technique; incidental findings
- Cost Concern: High
 - The test is currently additive and not replacement
 - Testing can lead to more intensive and costly treatment without added health benefit
 - Prevalence of heart disease is very high

Key Concerns for Prioritization

- Efficacy Concern: High
 - Low specificity. Though very sensitive to the presence of calcium, not all atherosclerosis can be identified.
 - For symptomatic patients, unclear how this added test will change management.
 - Not demonstrated to improve health outcomes.
- Safety Concern: Medium
 - CT radiation exposure- no system to validate low dose equipment or technique; incidental findings
- Cost Concern: High
 - The test is currently additive and not replacement
 - Testing can lead to more intensive and costly treatment without added health benefit
 - Prevalence of heart disease is very high

Current Coverage Policy in State Agencies

- No Specific coverage policy established by UMP, L&I, or Medicaid
 - No utilization data from L&I as this is not typically related to workplace injury
 - Newer procedure code is being used and paid
- The agencies cover alternative and more accurate tests*
 - CT Angiography (inpatient only)
 - SPEC (i.e., nuclear medicine stress test)
 - STRESS ECHO
 - INVASIVE CORONARY ANGIOGRAPHY

*Coverage policies vary by agency

Utilization Trends in UMP, L&I, and Medicaid

Table 1.a. Procedure Code by Year (with payments)

UMP & Medicaid

CPT CODE	2005	2006	2007	2008	Total
0144T (CT, heart, w/o contrast, with eval of coronary calcium)	0	1	3	23	27
0147T (CT angiography of coronary arteries with eval of coronary calcium)	0	8	20	11	39
0149T (Cardiac structure and morphology and CT angiography with eval of coronary calcium)	0	0	13	9	22
Total	0	9	36	43	88
Total Claims Submitted but not paid	0	25	69	83	177

Cost Trends in UMP, L&I, and Medicaid

Table 3. Average Payments* by Procedure by Year

UMP & Medicaid | 2005-2008

CPT Code	2005	2006	2007	2008	Total
0144T	\$0	\$149	\$391	\$132	\$161
0147T	\$0	\$206	\$202	\$418	\$264
0149T	\$0	\$0	\$564	\$516	\$577
Total	\$0	\$199	\$349	\$285	\$302

* includes facility and professional payments

Washington State Agencies Experience

SUMMARY AVERAGE PROCEDURE COSTS

Agencies 2006/2007	Patients	ICA	Stress ECHO	SPECT	CCTA
PEHP	27,293	\$1,163.20	\$152.57	\$409.49	\$722.22
DSHS	5,536	\$1,287.83	\$189.92	\$625.50	\$281.35
Totals	32,829	\$1,214.16	\$145.39	\$408.76	\$687.11

Fiscal Years 2006 and 2007.

Washington State Cardiac Tests

SUMMARY OVERALL COSTS

Agencies 2006/2007	Patients	ICA	Stress ECHO	SPECT	CCTA
PEHP	27,293	\$3,204,626	\$1,983,345	\$4,682,084	\$75,111
DSHS	5,536	\$2,454,604	\$297,421	\$1,285,400	\$2,535
Totals	32,829	\$5,659,230	\$2,280,766	\$5,967,484	\$77,646

Total costs in cardiac imaging ~ \$7.00 M per year

Fiscal Years 2006 and 2007.

Agency Conclusions

- **Cardiac Imaging in CAD is extensive**
 - Testing and Imaging options are available
 - CACS Technology use disseminating without demonstration of benefit
- **Safety**
 - Radiation Exposure
 - Dilemma of incidental findings (added studies/interventions)
- **Cost-effectiveness/value**
 - Unclear how this tests improves patient management/outcomes
 - Additive test to increasing Cardiac testing expense
 - theoretical use to rule out or reassure clinicians/patients not shown in real world to reduce further testing and may cause higher use of *aggressive tests/treatments*

Insufficient evidence of health benefit and evidence of harm and cost



Coronary Artery Calcium Scoring (CACs) as a Diagnostic Test for Detection of Coronary Artery Disease

Health Technology Clinical Committee Meeting
Washington State Health Technology Assessment Program

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November 20, 2009



Presentation Structure

- Scope, background and key questions
- Systematic review of published evidence
 - Evidence quality
 - Diagnostic test performance characteristics, patient outcomes
 - Potential harms
 - Economic implications
- Issues to consider



Scope of Report

This report critically summarizes relevant published research on the use of coronary artery calcium scoring (CACs) as a diagnostic test for identification of coronary artery disease in symptomatic persons.

The report focuses on the highest quality evidence available based on systematic review of the literature



Scope: Inclusion criteria

Population

- Symptomatic patients with suspected CAD
- Patients without prior revascularization

• Intervention

- CACS using computed tomography (EBCT, MDCT, Multi-slice, spiral or helical CT)

• Reference Standard

- Conventional coronary artery angiography (CCA)

• Study design

- Direct comparison, consecutive patients, prospective sought
- CACS and angiogram within 3 months of each other
- Formal, full economic analyses

• Publication

- Studies published in peer-reviewed journals in English

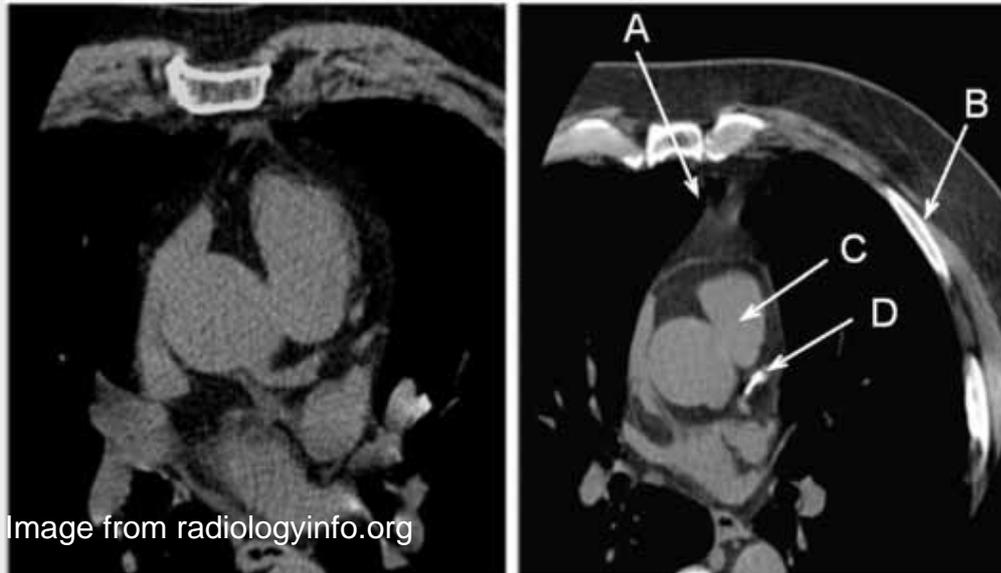


Scope: Primary Outcomes

- Diagnostic accuracy/validation
 - Sensitivity (% w/CAD who test +)
 - Specificity (% w/o CAD who test -)
 - Positive predictive value (% with + test who have CAD)
 - 1 - negative predictive value (% with – test who have CAD or % cases missed)
- Economic
 - Cost per correct diagnosis



Background: CACS



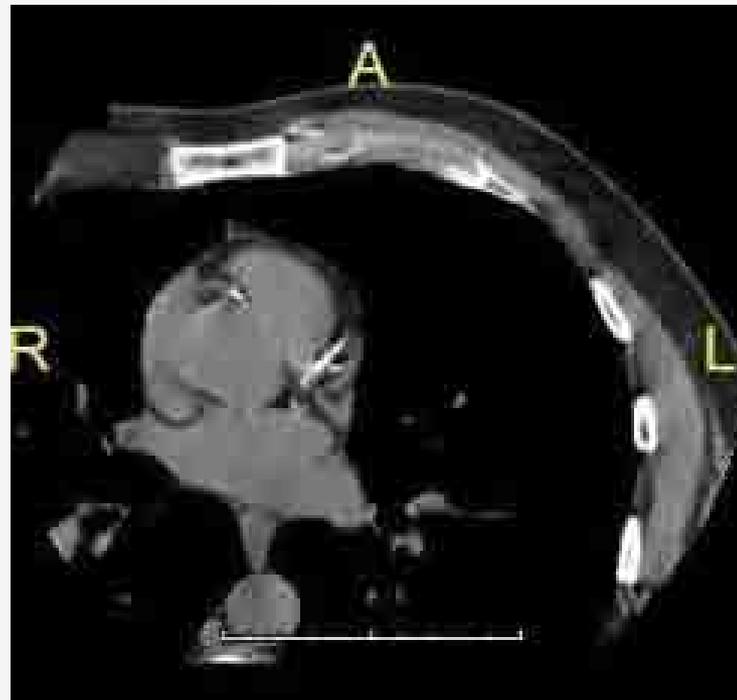
- Calcium deposition in arteries part of atherosclerotic process
- CAC is an indirect marker of atherosclerotic burden; correlation of amount with overall plaque on post-mortem
- Detection of CAC is not specific for obstructive lesion
- CAC increases with age particularly after 50 years in men, 60 years in women



Background: CT for CACS

Ultra-fast CT

- EBCT, MDCT, Multi-slice CT
- Requires 10-15 minutes
- No IV contrast, noninvasive
- Agatston Score
 - Lesion threshold: CT density of 130 Hounsfield units (HU), area $\geq 1\text{mm}^2$ to eliminate single pixels due to noise
 - For each focus of calcified plaque, area and maximum attenuation (HU) measured
 - CT number assigned to each plaque:
 - 1 = 130 – 199 HU
 - 2 = 200 – 299 HU
 - 3 = 300 – 399 HU
 - 4 = ≥ 400 HU
 - Score = Area x density determined for each calcified region; sum of all regions/slices for total score
 - Automated; continuous score produced



If calcium area = 5 pixels and 200 HU which is CT number of 2:

5 x 2 yields Agatston score of 10



Key Questions

When used to diagnose persons with suspected coronary artery disease (CAD):

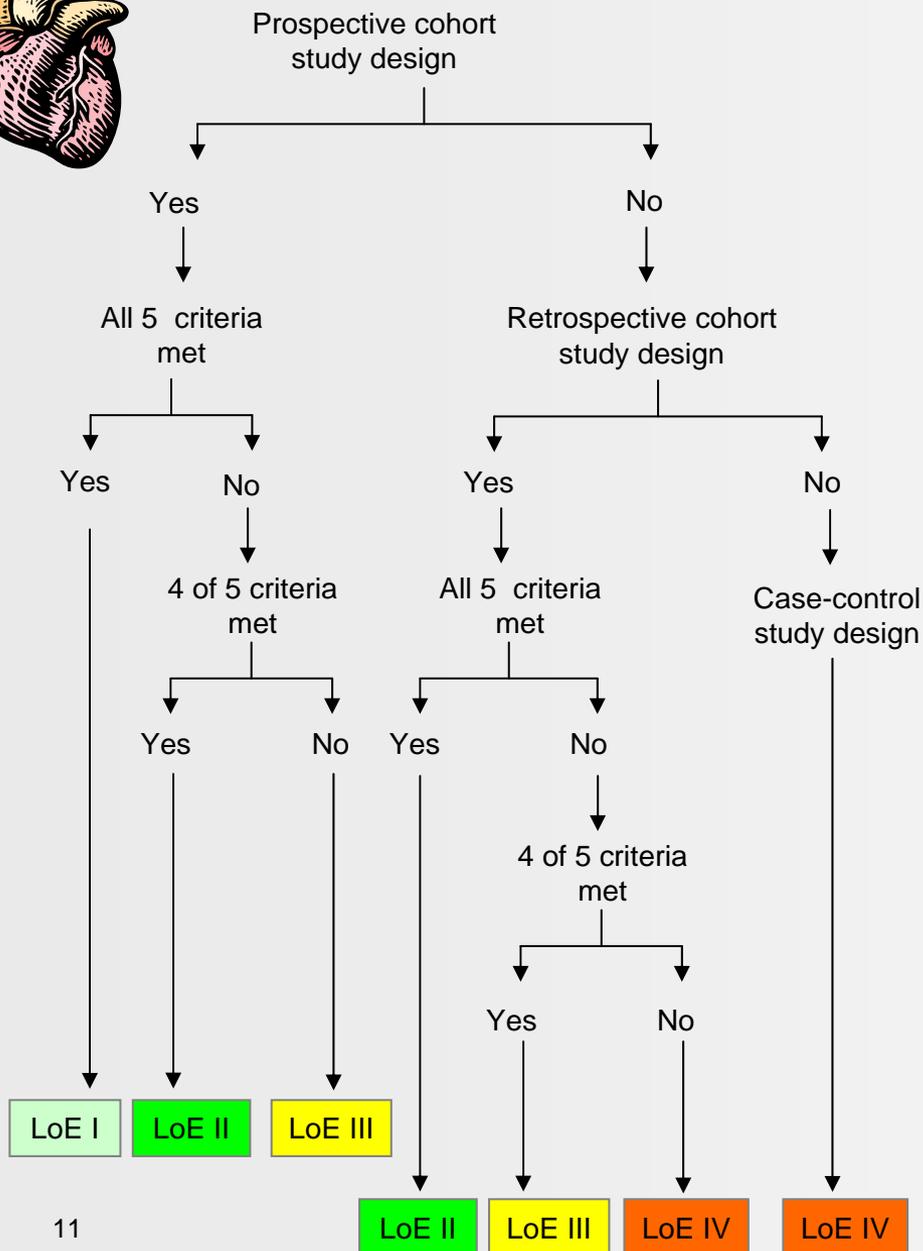
1. What are the test characteristics (PPV, NPV, sensitivity, specificity) of CACS compared with CCA? What is the reliability of CACS?
2. What is the evidence regarding safety?
3. What is the evidence that CACS influences clinical decision making and improves patient outcomes?
4. What is the evidence that CACS may perform differently in special populations?
5. What is the evidence of cost implications and cost-effectiveness for CACS compared with other tests?



Literature search and included studies

186 potentially relevant studies identified, 55 retained, some with information relevant to multiple key questions

- 30 primary accuracy/validity studies identified
- 3 reliability studies in symptomatic persons; 2 accuracy studies had reliability information
- 7 studies contributed safety information
- 10 studies related to decision making and patient outcomes
- 5 studies described special populations
- 2 full economic analyses, 1 costing study



Criteria – Accuracy Studies

1. Broad spectrum of persons with expected condition
2. Appropriate reference standard used
3. Adequate description of test and referent for replication
4. Blinded comparison of tests
5. Reference standard performed independently of diagnostic test



Test: CACS by CT

Referent: Conventional Coronary Angiography

- Studies comparing CACS with $\geq 50\%$ vessel narrowing (obstructive CAD) by CCA used in meta-analyses
- Both are anatomic (versus physiologic) tests
- CCA has limitations
- Presence of calcification implies atherosclerosis but not necessarily stenosis
 - Plaque formation “remodels” vessel, creates outward expansion with little \downarrow in lumen size initially
 - CAC may not predict angiographic stenosis (i.e. $>50\%$ lumen narrowing); Calcium part of plaque, lumen may not be narrowed



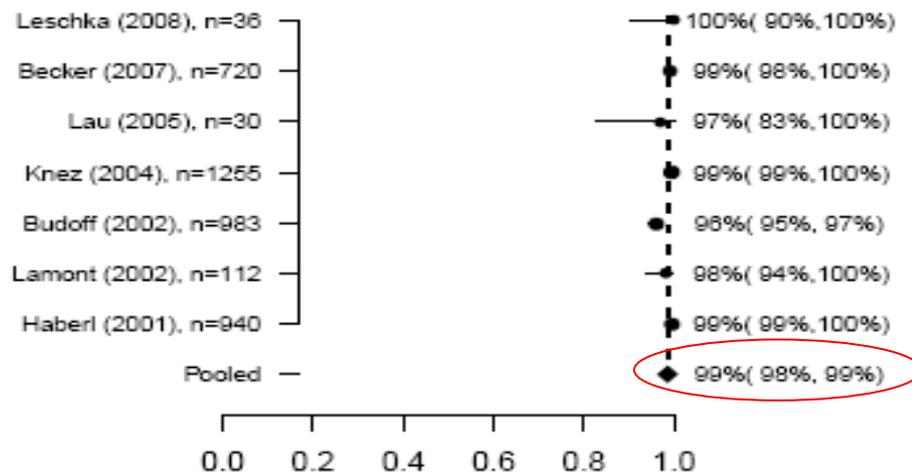
Meta-analysis of accuracy studies

- Of 30 accuracy studies, 11 were LoE I or II, 8 were LoE III and 11 were LoE IV
- Primary meta-analysis of LoE I/II studies – documentation of independent performance and blinded comparison of CACS and CCA
 - Study populations included symptomatic patients with typical and atypical chest pain, referral for elective angiography or after positive exercise testing (report page 42)
 - CAD prevalence ranged from 48.6% to 76.2% based on angiography
- CACS thresholds: > 0 (any), ≥ 100 and ≥ 400

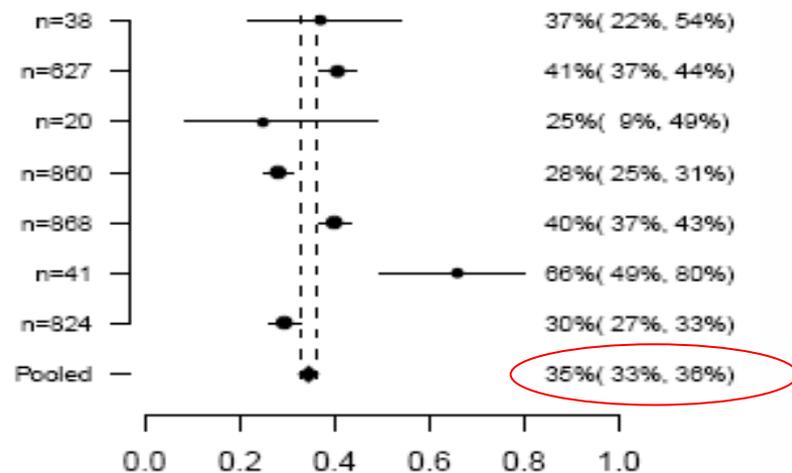


Meta-analysis: 7 LoE I/II studies CACS > 0

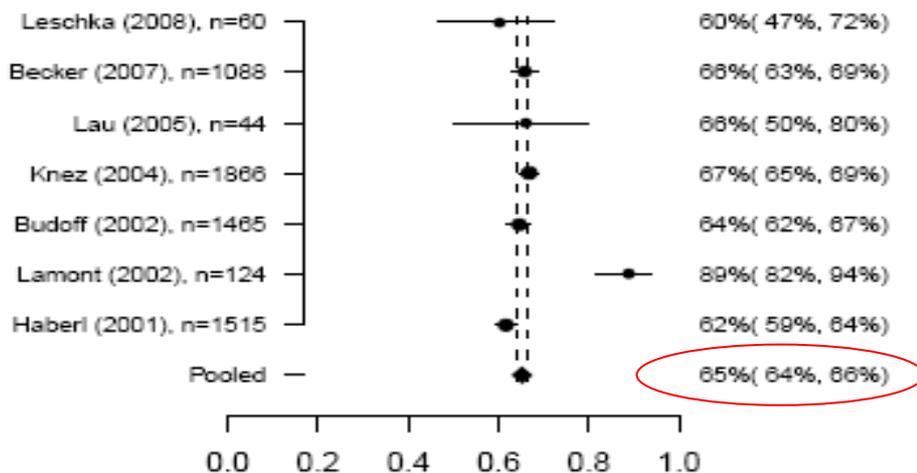
% Positive Test among CAD



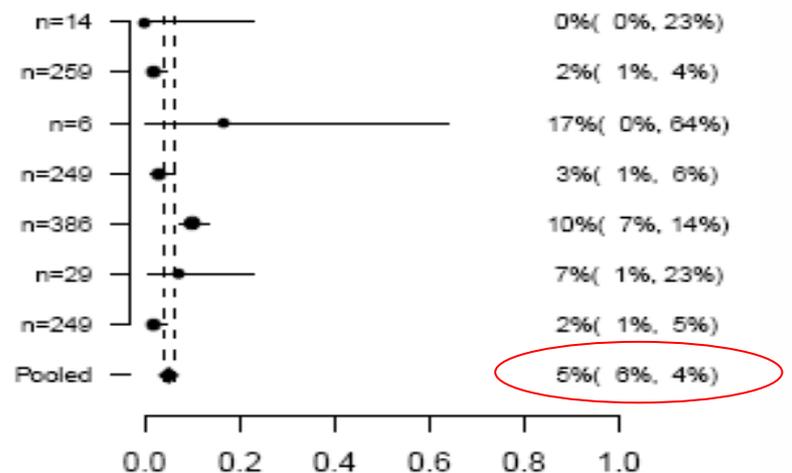
% Negative Test among non-CAD



% CAD among Positive Tests



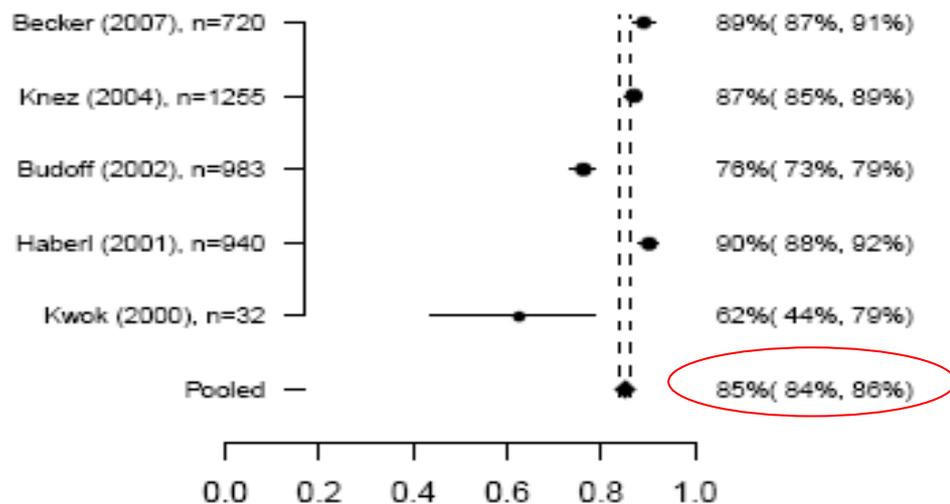
% CAD among Negative Tests



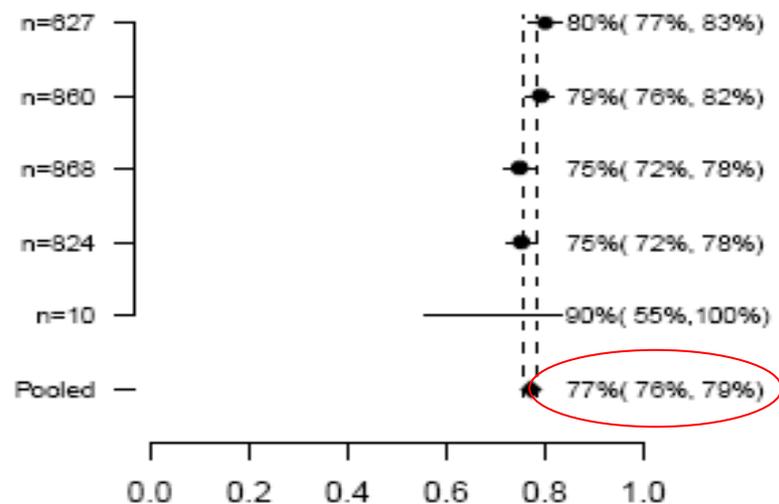


Meta-analysis: 4 LoE III studies CACS ≥ 100

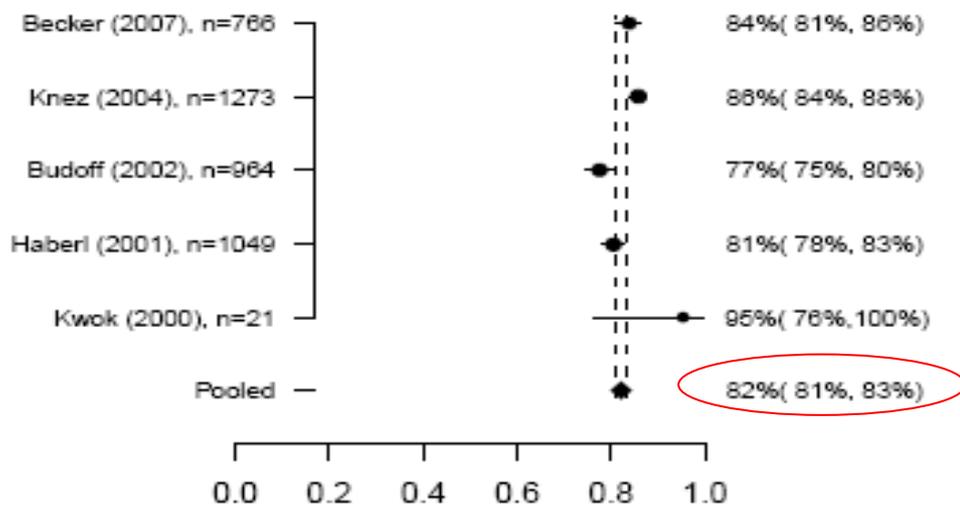
% Positive Test among CAD



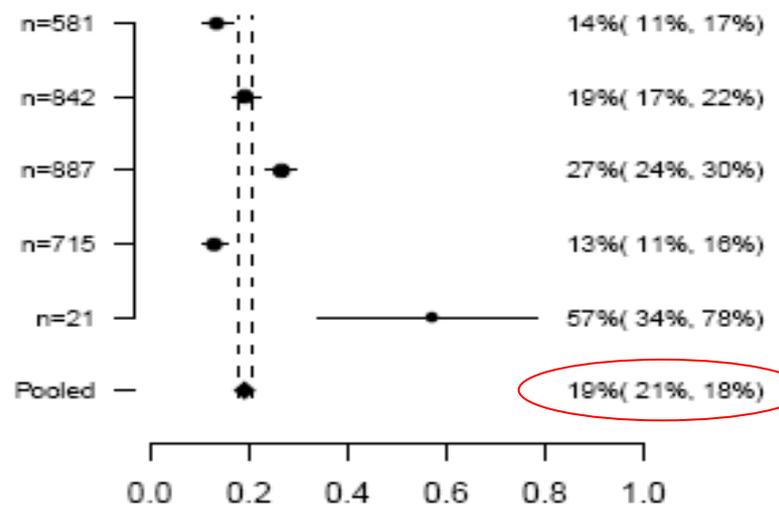
% Negative Test among non-CAD

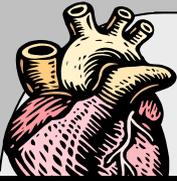


% CAD among Positive Tests



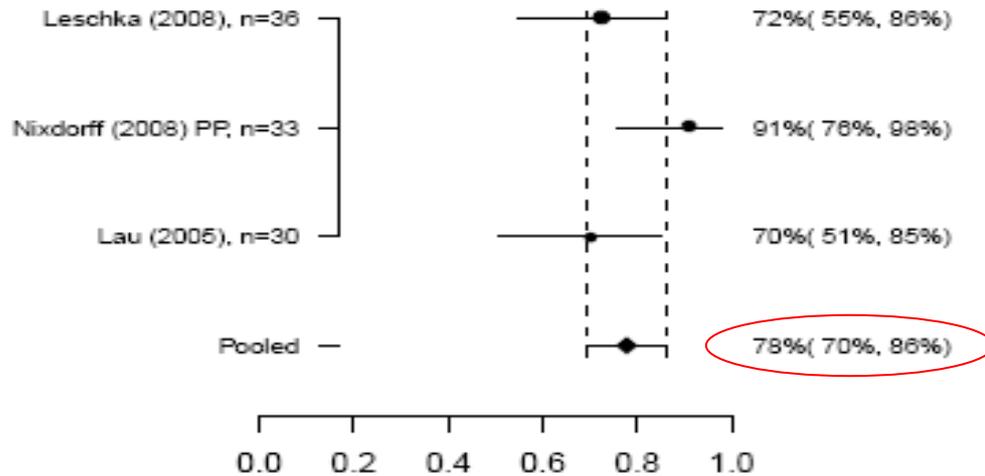
% CAD among Negative Tests



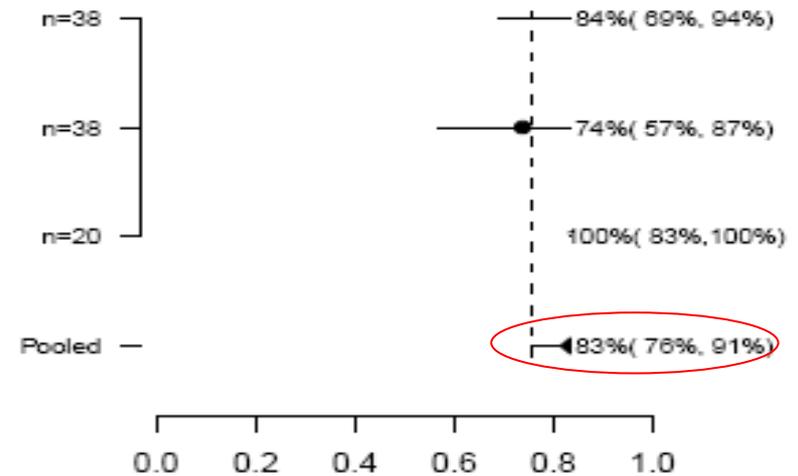


Meta-analysis: 3 LoE III studies CACS ≥ 400

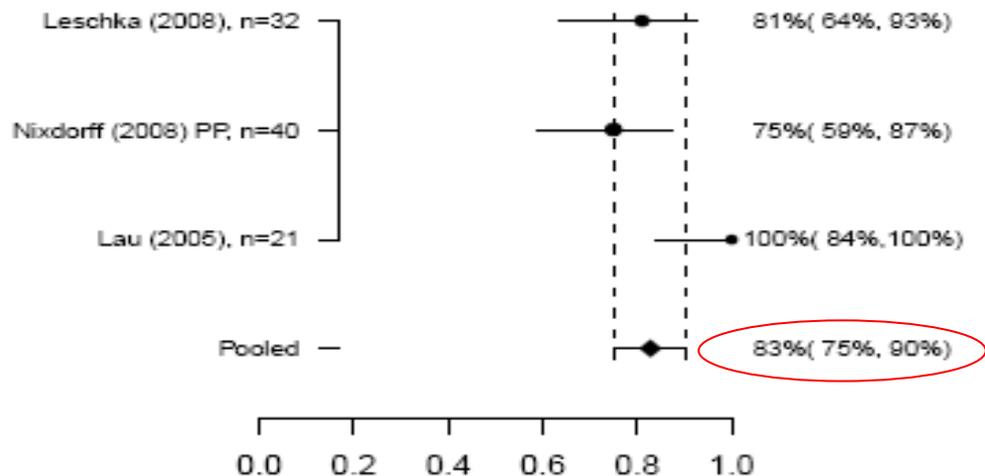
% Positive Test among CAD



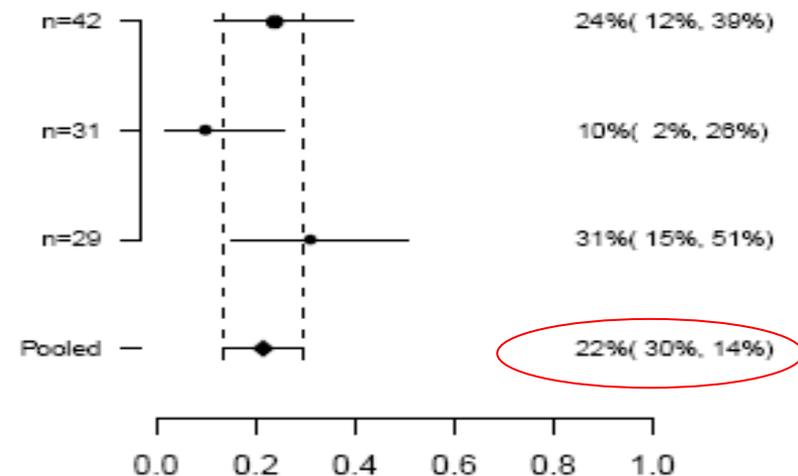
% Negative Test among non-CAD



% CAD among Positive Tests



% CAD among Negative Tests





Meta-analysis: Comparison of higher (LoE I/II) and lower quality (LoE III) studies CACS >0

LoE III studies

- Most stated blinded interpretation; unclear that CACS/CCA were performed independently, creating potential bias
- Angiographic CAD prevalence higher for most LoE III studies vs. LoE I/II studies and ranged from 47% - 88%

CACS >0	LoE III studies (6 studies)	LoE I or II studies (7 studies)
Sensitivity	93% (92, 95%)	99 % (98%, 99%)
Specificity	44% (40, 48%)	35% (33%, 36%)
Positive predictive value	71% (69%, 74%)	65% (63%, 66%)
1 – negative predictive value	19% (15%, 23%)	5% (4%, 6%)



Comparative Test Performance

Study	Noninvasive test	Sensitivity	Specificity
Gianrossi (N = 24,074 patients; 141 studies)	Exercise ECG	68% (range 23% - 100%)	77% (range 17% - 100%)
Fleischmann (N = 2637; 24 articles*)	Exercise Echo	85% (95% CI 83%, 87%)	77% (95% CI 74%, 80%)
Fleischmann (N = 2637 patients; 27 articles*)	Exercise SPECT	87% (95% CI 86, 88)	64% (95% CI 60%, 68%)
Present Spectrum Research HTA (N = 7354 patients; 7 studies) (N = 7119 patients; 5 studies) (N = 195 patients ; 3 studies)	CT CACS score > 0	99% (95% CI 98%, 99%)	35% (95% CI 33%, 36%)
	score ≥ 100	85% (95% CI 84%, 86%)	77% (95% CI 76%, 78%)
	score ≥ 400	78% (95% CI 86%, 70%)	83% (95% CI 76%, 91%)

*not unique patient data sets



Reliability

- Three studies in symptomatic patients suggest moderate to high inter-observer agreement between raters of calcium scores
- Test-retest reliability in symptomatic patients was overall moderate to good across 3 studies

Author (year)	Study	Measure of reliability	LoE
Broderick (1996) N = 101	Test-retest Inter-rater	Intraclass correlation coefficient 0.90 (test-retest), (N = 17) 0.99 (inter-rater)	II
Möhlenkamp (2001) N = 50	Test-retest	Variability of Agatston score 21.8% (mean), 19.2% (median)	II
Serafin (2009) N = 50	Test-retest	Variability of Agatston score 3.9% (median)	II
Leschka (2008)	Inter-rater	kappa = 0.84	*
Lau (2005)	Inter-rater	Intraclass correlation coefficient = 1.00	*

* Leschka, Lau were validation studies; specifics on reliability evaluation not provided



Key Question 2: Potential Harms – Radiation

Exposure type	Typical effective dose (millisieverts)
Environmental Exposures	
Natural source (average US per year)	3
Round trip cross-country air flight	0.02-0.05
Nuclear power plant worker	3
Exposures from diagnostic radiology	
Dental X-ray	0.005
Chest Xray (PA and lateral)	0.1
Cervical spine X-ray	0.2
Mammogram	0.4
Lumbar spine X-ray	1.5
Head CT	2
CT calcium scoring	3
Range found in validation studies in this report*	(1.2 —10)
Range found in literature 1980-2007 [Mettler]	(1—12)
Range reported in 2006 AHA Statement [Budoff]	(0.7 – 1.9)
Interventional coronary angiography	7
Barium enema with fluoroscopy	8
Virtual colonoscopy	10
Chest CT for pulmonary embolism	15
CT coronary angiography	16



Potential Harms – Radiation

- No large-scale epidemiologic studies evaluating CT- associated cancer risk yet published
- A recent simulation suggests that a single CACS in asymptomatic persons at
 - age 40 may increase life-time cancer risk by 9/100,000 for men, 28/100,000 for women
 - age 55 may increase life-time lung cancer risk by 6/100,000 for men, 14/100,000 for women
- Individual risk cannot be quantified



Potential Harms – Radiation

Factors to consider

- Actual risk associated with low dose radiation is unknown - there are different theories (linear quadratic approach vs. linear, no-threshold hypothesis) and competing risks
- ALARA – AHA guidelines suggest prospective gating, 2.5 – 3.0 mm slices, adjust for body size; newer equipment/protocols may reduce exposure
- Total radiation exposure: To the extent that CACS
 - avoids need for CCA or other tests, total reduced
 - currently is an additional test, total increased
 - leads to additional testing, total increased



Key Question 2: Potential harms (benefits) – Incidental findings

- Incidental findings requiring further testing: 7.8% to 10.5% (2 studies); 1.2% required therapeutic intervention (1 study) in symptomatic patients
 - Majority of extra cardiac findings: Pulmonary nodules
 - Mitral or aortic valve calcification most common cardiac findings requiring additional testing
- Potential benefits: Early detection (may or may not improve outcomes)
- Potential harms: Additional testing (associated costs, risks), patient anxiety



Key Question 3: Clinical decision making and outcomes

- The role of CACS as a diagnostic test and threshold for decision making are not clear
- Studies did not include comparison groups (LoE IV)
- As triage test (low-intermediate risk patients)
 - 5 studies suggest that $CACS = 0$ or <10 may allow discharge of patients with suspected CAD from ED.
 - Extent to which actual decision for discharge was based on algorithms described and the independent influence of CACS in decision making are unclear
 - 1 study suggests increased referral for CCA with increasing CACS



Key Question 3: Prediction of future outcomes

- No randomized studies were found
- 3 prognostic (LoE III) studies reported CACS predicted future cardiac events; confidence intervals are wide
- None evaluated the role of therapies that may have influenced outcomes, definitions of outcomes varied

Comparison of CACS ≥ 100 vs. < 100

Study	Total events	RR (95% CI)
Keelan (2001) N = 317	n = 22	3.2 (1.2, 8.7) unadjusted
Schmermund (2004) N = 300	n = 40	12.0 (4.7, 30.6) unadjusted 4.4 (1.4, 12.6) age, score adjusted
Kennedy (1998) N = 368	n = 13	NR



Key Question 4: Special Populations

Diabetic patients

Author	N	Sens	Spec	PPV	NPV	1-NPV	% CAD	LoE
Cut-off >0								
Khaleeli (2001)	168	98%	39%	82%	89%	11%	74%	II
Hosoi (2002)	100	99%	25%	91%	75%	25%	88%	III
Cut-off >100								
Khaleeli (2001)	168	77%	77%	90%	54%	46%	74%	II
Hosoi (2002)	100	67%	75%	95%	24%	76%	88%	III
Cut-off >400								
Hosoi (2001)	100	49%	92%	98%	20%	80%	88%	III



Key Question 4: Special Populations Sex

	Author	N	Sens	Spec	PPV	NPV	1- NPV	% CAD	LoE	
CACs > 0	Female									
	Budoff (2002)	387	96%	57%	61%	96%	4%	41%	II	
	Rumberger (1995)	50	100%	66%	62%	100%	0%	36%	III	
	Haberl (2001)	539	100%	41%	60%	100%	0%	47%	II	
	Male									
	Budoff (2002)	733	96%	46%	NR	89%	11%	70%	II	
CACs < 100	Rumberger (1995)	89	98%	57%	72%	95%	5%	53%	III	
	Haberl (2001)	1225	99%	24%	62%	96%	4%	56%	II	
	Female									
CACs < 100	Haberl (2001)	539	82%	76%	75%	82%	18%	47%	II	
	Male									
	Haberl (2001)	1225	93%	75%	83%	89%	11%	56%	II	

* Similar ages for men and women in Budoff, Haberl (56-60 yrs); Rumberger –women 10 years older (56 yrs) vs. men (47 yrs)



Key Question 4: Special Populations Sex and Age

- **Sex**
 - Women present ~10 years later
 - Specificity of 65% in premenopausal women vs. 42% post-menopausal women (1 study)
- **Age (7 studies)**
 - ↑ CACS score with increasing age regardless of gender, presence or absence of significant stenosis
 - Some suggest that sensitivity and predictive values go up with increasing age, others suggest that the best sensitivity and specificity may be in middle aged patients (40 – 60 years)



Key Question 5: Economic impact

- Two moderate-quality full economic studies- CACS as a stand alone test, triage for CCA
- At CAD prevalence up to 70%, CACS may be more cost-effective than CCA, but incremental cost-effectiveness not described
- Cost of CCA > CACS, however CCA may still be required as a second test and other tests may be done (e.g. functional tests)
- Modeling of FP and FN consequences, use of additional testing and impact of incidental findings not explicit



Key Question 5: Economic impact Influences on cost per correct diagnosis

- CAD prevalence:
 - Pre-test CAD likelihood increase from 30%-40% had decrease cost from €2345 to €1897 in one study [Dewey], modified societal perspective
 - Using CACS > 0 in another study [Rumberger], based on short-term direct costs, cpcd were
 - \$24,703 USD at 10% prevalence
 - \$6,329 USD at 50% prevalence
 - \$4,957 USD at 70% prevalence



Key Question 5: Economic impact Influences on cost per correct diagnosis

- CACS accuracy and threshold:
 - Rumberger (1999) –total direct costs for testing pathway

CACS	TP Rate	CPCD
> 0	96%	\$6,329
37	90%	\$5,410
80	84%	\$5,290
168	72%	\$5,186

* CAD prevalence of 50%

- Dewey (2006) – sensitivity analysis
 - At lowest accuracy, CACS only cost effective at 40% pre-test likelihood vs. traditional approaches
 - At highest accuracy, more cost-effective vs. traditional approaches at pre-test likelihoods of 20%-50%
 - Concluded CACS cannot be recommended from economic perspective



Overall Strength of Evidence

Test accuracy – SoE is high

- CACS role as diagnostic test in symptomatic patients is unclear; some suggest a triage role with CACS > 0
- Highly sensitive, 99%, for identifying obstructive CAD (based on CCA lumen decrease $\geq 50\%$)
- Has very low specificity (35%)
- 5% of persons with negative test would have obstructive CAD on CCA (1 – negative predictive value)

• Safety – Radiation exposure - SoE very low

- Hypothetical increase in life-time cancer risk based on simulation; true attributable risks cannot be determined
- Reduced if CACS results in fewer CCA, however if CACS is an additional test or leads to additional testing, may be increased

• Safety – Incidental findings - SoE very low

- 7.8%-10.5% require additional testing, 1.2 % needed tx



Overall Strength of Evidence

- **Clinical decision making and outcomes**
 - ED triage – SoE is low
 - Proponents suggest CACS = 0 may allow patient discharge; Decision making does not appear to be explicitly evaluated
 - Studies of variable quality, no comparison
 - Other settings SoE is very low (1 study)
 - Referral for CCA increased with higher CACS; explicit evaluation of decision making (or impact) not described
 - Prediction of outcomes – SoE is low
 - 3 prognostic studies suggest higher CACS is associated with higher risk of future events, but role of therapeutic interventions not evaluated



Overall Strength of Evidence

Special populations

- Diabetic populations – SoE is very low
 - Sensitivity, specificity for any calcium similar to general population. Higher prevalence of CAD; higher % (4%-11%) of missed cases based on 2 moderate quality studies
- Male/female – SoE is low
 - Sensitivity similar; specificity ~ lower in men
 - Lower CAD prevalence in women vs. men and higher % missed (men) – possibly age related
- Age – SoE is moderate
 - CAC increases with age; mixed results



Overall Strength of Evidence

Economic – SoE is very low

- Two moderate quality studies suggest that at CAD prevalence of up to 70%, CACS may be more cost-effective than CCA, but incremental cost effectiveness not described.
- Insufficient evidence for conclusions on long-term cost-utility of CACS compared with CCA alone or in conjunction with other non-invasive tests



Remaining Questions

- What is the role of CACS as a diagnostic test?
 - Unclear from the literature; no consensus on thresholds
- Could CACS be used to triage patients? What threshold?
 - Is the accuracy for CACS > 0 acceptable for decision making?
 - What % of missed cases is acceptable? What FP rate is acceptable?
- Does CACS improve upon current triage practices?
- How does CACS (as diagnostic test) fit in current clinical practice? What is the effect of CACS on total radiation exposure in clinical practice?
- What is the clinical pathway for evaluation of patients with a positive CACS? How is cost-effectiveness impacted?
- Does CACS increase or decrease use of CCA or other tests? How/where does it fit with other non-invasive tests?
- How does it influence decision making for further testing and/or treatment?