

# HEALTH EVIDENCE REVIEW COMMISSION (HERC)

## COVERAGE GUIDANCE: ADVANCED IMAGING FOR STAGING OF PROSTATE CANCER

Approved 1/8/2015

### HERC Coverage Guidance

To determine risk status and treatment options, prostate cancer clinical staging that includes PSA level and prostate biopsy with Gleason score is recommended for coverage. MRI is recommended for coverage for men with histologically proven prostate cancer if knowledge of the T or N stage could affect management. (*weak recommendation*)

CT of the pelvis is not recommended for coverage in men with low- to intermediate-risk prostate cancer (*strong recommendation*), unless MRI is contraindicated.

Radionuclide bone scanning is not recommended for routine coverage in men with low-risk prostate cancer. (*weak recommendation*)

Radionuclide bone scanning is recommended for coverage when hormone therapy is being deferred (through watchful waiting) in asymptomatic men who have high or intermediate risk prostate cancer. (*weak recommendation*) Risk levels are defined in Table 1.

PET imaging is not recommended for coverage in prostate cancer. (*strong recommendation*)

Note: Definitions for strength of recommendation are provided in Appendix B GRADE Element Description

### Rationale for guidance development

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. Coverage guidance may be based on an evidence-based guideline developed by the Evidence-based Guideline Subcommittee or a health technology assessment developed by the Health Technology Assessment Subcommittee. In addition, coverage guidance may utilize an existing evidence report produced by one of HERC's trusted sources, generally within the last three years.

## EVIDENCE SOURCES

### Trusted sources

National Institute for Health and Clinical Excellence. (2014). *Prostate Cancer: diagnosis and treatment*. London: National Institute for Health and Clinical Excellence. Retrieved from <http://guidance.nice.org.uk/CG175/Guidance>

### Additional sources

Medicare National Coverage Determinations Manual: Chapter 1, Part 4 (Sections 200-310.1). Retrieved from [http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/ncd103c1\\_Part4.pdf](http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/ncd103c1_Part4.pdf) on 11/11/14.

NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer. Version 1.2015. Retrieved from [http://www.nccn.org/professionals/physician\\_gls/PDF/prostate.pdf](http://www.nccn.org/professionals/physician_gls/PDF/prostate.pdf) on 11/11/14.

The summary of evidence in this document is derived directly from this evidence source, and portions are extracted verbatim.

## EVIDENCE OVERVIEW

### Clinical background

Prostate cancer is the most common cancer in men and makes up 26% of all male cancer diagnoses in the United Kingdom. It is predominantly a disease of older men (aged 65–79 years) but around 25% of cases occur in men younger than 65. There is also higher incidence of and mortality from prostate cancer in men of black African-Caribbean family origin compared with white Caucasian men.

Prostate cancer is usually diagnosed after a blood test in primary care has shown elevated prostate-specific antigen (PSA) levels. The introduction of PSA testing has significantly reduced the number of men presenting with metastatic cancer since the 1980s. Most prostate cancers are now either localized or locally advanced at diagnosis, with no evidence of spread beyond the pelvis.

A number of treatments are available for localized disease, including: active surveillance, radical prostatectomy, external beam radiotherapy and brachytherapy. Hormone therapy (androgen deprivation or anti-androgens) is the usual primary treatment for metastatic prostate cancer, but is also increasingly being used for men with locally advanced, non-metastatic disease.

The TNM classification is used to stage prostate cancer (see Appendix A). It describes the extent of the primary tumor (T stage), the absence or presence of spread to nearby lymph nodes (N stage) and the absence or presence of distant spread, or metastasis (M stage). The clinical stage is determined from information that is available without surgery. The pathologic stage is based on the surgical removal and histological examination of the entire prostate gland, the seminal vesicles and surrounding structures and, if relevant, pelvic lymph nodes. The management of prostate cancer will depend on the TNM stage of the disease as well as both

biochemical information (e.g. PSA) and pathological information (e.g. Gleason score), which have prognostic value. The optimum treatment for a man with prostate cancer requires an assessment of the risk of metastatic spread as well as the risk of local recurrence. For this, the results of imaging can be assessed in the light of information from clinical nomograms.

## EVIDENCE REVIEW

Men newly diagnosed with prostate cancer can initially be stratified into those for whom radical treatment is a possibility and those for whom it is not appropriate. The decision about treatment intent will be based on the man's life expectancy, his values, and the anticipated clinical course of the prostate cancer.

### Recommendations:

- Determine the provisional treatment intent (radical or non-radical) before decisions on imaging are made.
- Do not routinely offer imaging to men who are not candidates for radical treatment.

Qualifying statement: There was guideline development group (GDG) consensus, in the absence of any research evidence, that this will reduce the amount of inappropriate investigation. The cost effectiveness of routine magnetic resonance imaging MRI could not be concluded.

Both the clinical presentation and the treatment intent influence the decision about when and how to image the individual. The risk of recurrence of prostate cancer after definitive local treatment is the basis for the stratification of men with localized prostate cancer into risk groups: low, intermediate and high (see Table 1). The recommendations for imaging of localized disease are similarly based on these prognostic groups.

**Table 1**

Level of risk	PSA		Gleason Score		Clinical stage
<b>Low</b>	< 10 ng/ml	And	≤ 6	And	T1-T2a
<b>Intermediate</b>	10-20 ng/ml	Or	7	Or	T2b
<b>High</b>	>20 ng/ml	Or	8-10	Or	≥ T2c

Imaging may inform the choice between different radical treatments (for example by determining whether the cancer has extended beyond the prostatic capsule). It also assists in the identification of metastatic disease thereby leading to more appropriate treatment options.

### Imaging for T-staging and N-staging

The T-stage involves the assessment of the local extent of the primary tumor in the prostate and its relationship to surrounding structures. Using imaging to distinguish between T1 and T2 cancers does not usually affect treatment. But if radical treatment is being considered, it is important to decide whether a tumor is T2 (confined within the prostate) or T3/T4 (spread

outside the prostate). MRI is now the commonly used imaging technique for T-staging men with prostate cancer. Many of the original publications used now-outdated MRI technology, and the accuracy reported for MRI is improving. After transrectal prostate biopsy, intra-prostatic hematoma can affect image interpretation for at least four weeks. It is important to know the nodal status of men with localized disease, as the spread of cancer to the pelvic lymph nodes will affect the choice of treatment. Partin's Tables (Partin et al. 2001) are the most commonly used clinical nomograms for determining the risk of nodal spread. Currently, imaging is of some value for N-staging because computed tomography (CT) and conventional MRI rely on size criteria to assess the likelihood of metastatic spread to the lymph nodes. CT cannot characterize the internal architecture of an enlarged node and MRI is only able to provide partial information. Newer MRI contrast agents such as superparamagnetic iron oxide (SPIO) may improve the overall specificity of MRI for evaluating lymph nodes but are not yet routinely available.

***Recommendation:***

- Do not offer CT of the pelvis to men with low- or intermediate-risk localized prostate cancer (see Table 1).

Qualifying statement: There is not enough evidence to support the routine use of CT in men with intermediate-risk disease and it is considered inferior to MRI in this clinical situation.

No studies measuring the impact of diagnostic imaging on patient outcomes were found; instead most studies were of diagnostic test accuracy.

Two studies showed better staging accuracy with MRI than with CT. Other systematic reviews have considered the staging accuracy of MRI and CT separately. There was contradictory evidence, from small observational studies, about the benefit of adding of magnetic resonance spectroscopy (MRS) to MRI. There was consistent evidence, from observational studies, that MRI tumor stage was a prognostic factor for PSA relapse. One of the studies, however, concluded that MRI tumor staging only added clinically meaningful information for men at intermediate pre-treatment risk of PSA relapse. MRI tumor stage did not stratify PSA failure risk well enough to guide clinical decision making for other patients.

**Clinical question: Does staging with MRI improve outcomes in men with prostate cancer?**

***Biochemical recurrence-free survival***

One study provided very low quality evidence of no significant difference in the proportion of patients experiencing biochemical recurrence between those which had undergone imaging and those which had not ( $p=0.50$ ). However, the study was not limited only to those patients who underwent MRI (18%) and included patients who had received computerized tomography (81%) and bone scans (73%), with many patients receiving more than one type of imaging. [Very low strength of evidence (SOE).]

*Overall survival, treatment-related morbidity, and health-related quality of life*

No studies reported overall survival, treatment-related morbidity, or health-related quality of life.

*Clinical question: In which patients with prostate cancer will MRI staging alter treatment?*

Four studies reported change in management following MRI, 23 reported change in staging following MRI, and eight reported the diagnostic accuracy of both clinical and MRI staging, using radical prostatectomy as reference standard. All studies were of low to very low quality evidence, with most (96%) considered unrepresentative of the patients who would receive MRI in practice. Many (68%) of the studies also used MRI as the reference standard which may not have classified the target condition correctly. A number of pre-specified sub-groups were available for analyses.

*Change in management*

Two studies found a change in the management of radiotherapy strategy following MRI in 31% and 9% of patients. Two further studies found a change in surgical procedure in 44% and 30% of patients following MRI respectively. (Low SOE.)

*Change in stage*

All studies found reported MRI to result in up-staging of a proportion of their patients, ranging from at least 5% to 100% of all patients. Where reported, MRI also resulted in down-staging of between 5% and 19% of patients. This was found for low, intermediate and high risk patients. (Very low SOE.)

*Diagnostic accuracy*

Four studies found that MRI was not consistently more sensitive, specific or accurate than staging by DRE or TRUS. Six studies found MRI to be more sensitive than clinical staging in identifying patients with extracapsular extension (stage T3a), but not consistently more specific or accurate. MRI was not consistently more sensitive, specific or accurate than clinical staging in identifying patients with seminal vesicle invasion (stage T3b). Three studies of patients with clinically localized disease found MRI to be more sensitive than clinical staging when identifying extracapsular extension or seminal vesicle invasion, but not consistently more specific or accurate. One study found MRI to have higher sensitivity but lower specificity than DRE or TRUS for overall staging of prostate cancer, while another found MRI to have higher accuracy.

Two studies only included patients with PSA < 10 ng/ml; one found the overall accuracy of staging to be the same between MRI and TRUS, while both found MRI to be more sensitive but less specific than TRUS when identifying extracapsular extension and less sensitive when identifying seminal vesicle invasion but not consistently more specific. Another study conducted a subgroup analysis by PSA level and found MRI to be more sensitive than TRUS in identifying both extracapsular extension and seminal vesicle invasion in patients with either PSA > 17 ng/ml or PSA < 10 ng/ml.

Two studies only included patients with Gleason  $\leq 6$ ; one found MRI to be more sensitive but less specific than TRUS when identifying extracapsular extension and less sensitive when identifying seminal vesicle invasion but of similar specificity. The other found MRI to have the same rate of false positives as clinical staging when identifying stage T3-T4 disease. Another study only included intermediate- and high-risk patients and found MRI to be more sensitive but less specific than clinical staging when identifying extracapsular extension, and to be more sensitive but have the same specificity when identifying seminal vesicle invasion.

### Recommendations:

Consider multiparametric MRI, or CT if MRI is contraindicated, for men with histologically proven prostate cancer if knowledge of the T or N stage could affect management.

### *Imaging for M-staging*

Isotope bone scans can be used to look for bone metastases at the time of presentation. The positivity rate for bone scans increases with PSA or Gleason score.

### Recommendation:

Do not routinely offer isotope bone scans to men with low-risk localized prostate cancer.

Qualifying statement: This recommendation is supported by case series evidence and will reduce unnecessary investigation.

Two systematic reviews looked at the role of radioisotope bone scans in the staging of men with newly diagnosed prostate cancer. One summarized bone scan results by serum PSA level in men with newly diagnosed prostate cancer. Serum PSA level and risk of a positive bone scan were strongly correlated. The other review concluded that PSA level was the best means of identifying those at risk of a positive bone scan and that men with PSA less than 10 ng/ml were unlikely to have a positive bone scan.

### Recommendation:

Offer isotope bone scans when hormonal therapy is being deferred through watchful waiting to asymptomatic men who are at high risk of developing bone complications.

Qualifying statement: In the absence of any evidence there was GDG consensus that making this recommendation would reduce the risk of patients developing spinal cord compression.

Searches found no direct evidence about the influence of imaging on the timing of systemic treatment or frequency of clinical follow-up in men for whom radical treatment is not intended. Small case series reported outcomes in men with positive bone scans at presentation. Two of these series found extensive disease on bone scan was an adverse prognostic factor for survival. There is observational evidence that extensive disease on bone scan is an independent risk factor for spinal cord compression in men without functional neurological impairment.

## Role of Positron-emission tomography (PET) in staging prostate cancer

Positron-emission tomography imaging using the radiopharmaceutical agent 18-FDG does not reliably show primary prostate cancer. This is because of the relatively low metabolic activity in tumors which are slow-growing and because the radiopharmaceutical agent accumulates in the bladder, obscuring the prostate. Newer positron-emitting tracers are under evaluation.

### Recommendation:

Do not offer PET imaging for prostate cancer in routine clinical practice.

Qualifying statement: There was a lack of evidence to support the use of PET imaging.

## Managing relapse after radical treatment

Magnetic resonance imaging (MRI) scanning may have some value in those with biochemical relapse being considered for further local therapy. It may detect significant extracapsular disease, seminal vesicle involvement or lymphadenopathy which might preclude radical salvage therapy. The chance of finding skeletal metastases in men with biochemical relapse is best predicted by the absolute PSA level and the rate of rise.

For men with evidence of biochemical relapse following radical treatment and who are considering radical salvage therapy:

- do not offer routine MRI scanning prior to salvage radiotherapy in men with prostate cancer
- offer an isotope bone scan if symptoms or PSA trends are suggestive of metastases.

Qualifying statement: These recommendations are based on case series evidence and GDG consensus.

The literature search found no studies reporting the impact of staging after biochemical recurrence on patient outcomes. Small case series report good sensitivity and specificity of MRI for the detection of local recurrence after radical prostatectomy. The rate of bone scans positive for malignancy in men with biochemical recurrence after radical prostatectomy was 4 to 14% in four case series. The rate of suspicious or indeterminate (but ultimately non-malignant) scans was almost as high at between 3 and 8%, raising questions about the specificity of the bone scan. Trigger PSA, PSA slope, and PSA velocity were all significant predictors of bone scan result. The risk of a positive bone scan for men with PSA less than 10ng/ml was between 1 and 3% in two series, compared with 75% for PSA greater than 10 ng/ml.

PET scanning was not discussed in the NICE guideline as an option for managing relapse after radical treatment, or in any other section other than diagnosis and staging (presented above).

## Evidence Summary

When determining when and how to image an individual, men with localized prostate cancer should be stratified into risk groups based on PSA level, Gleason score and clinical stage.

There is insufficient evidence to support the routine use of CT of the pelvis in men with low- or intermediate-risk localized prostate cancer, and it is considered inferior to MRI in this clinical situation. The evidence is insufficient to determine whether staging with MRI improve outcomes in men with prostate cancer. There is low SOE that staging with MRI can result in change in management, and a very low SOE that MRI results in up-staging or down-staging a highly variable proportion of patients. Most studies found staging with MRI more sensitive than staging with DRE or TRUS, but not consistently more specific or accurate. There is insufficient evidence to support the use of PET for any stage of prostate cancer.

## GRADE-INFORMED FRAMEWORK

The HERC develops recommendations by using the concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. GRADE is a transparent and structured process for developing and presenting evidence and for carrying out the steps involved in developing recommendations. There are four elements that determine the strength of a recommendation, as listed in the table below. The HERC reviews the evidence and makes an assessment of each element, which in turn is used to develop the recommendations presented in the coverage guidance box. Balance between desirable and undesirable effects, and quality of evidence, are derived from the evidence presented in this document, while estimated relative costs, values and preferences are assessments of the HERC members.

<b>Indication/ Intervention</b>	<b>Balance between desirable and undesirable effects</b>	<b>Quality of evidence*</b>	<b>Resource allocation</b>	<b>Variability in values and preferences</b>	<b>Coverage recommendation</b>	<b>Rationale</b>
CT of pelvis in low- to intermediate risk prostate cancer	Inferior to MRI	Low	Low	Moderate variability (many would prefer to avoid radiation exposure)	Do not recommend (strong), except when MRI is contraindicated.	Insufficient/mixed evidence, similar or more risk than available alternatives.
MRI staging of prostate cancer	MRI may result in change in management, and possibly change in stage; may be more sensitive than DRE and/or TRUS	Low to Very Low	Low, if other diagnostic testing can be limited	Low variability	Recommend (weak)	Sufficient evidence shows more effective, less risk and similar or less cost than alternatives.

Indication/ Intervention	Balance between desirable and undesirable effects	Quality of evidence*	Resource allocation	Variability in values and preferences	Coverage recommendation	Rationale
Bone scan in evaluation of newly diagnosed, low risk prostate cancer	Positive bone scan highly correlated with PSA level; those with PSA level < 10 unlikely to have positive bone scan..	Low	Low	Moderate variability (avoidance of multiple tests vs. perceived value from those tests)	Do not recommend (weak)	Sufficient evidence; similar risk and effectiveness to alternatives, but higher cost.
Bone scan in asymptomatic high-risk men	May result in earlier treatment of metastatic disease, resulting in prevention of spinal cord compression	Very Low	Low	Low variability (avoidance of spinal cord compression)	Recommend (weak)	Insufficient/mixed evidence, no alternatives available, similar or less risk than no treatment. Treatment is prevalent and research study is not reasonable.
PET for staging of prostate cancer	Unknown	Very Low	Moderate	Low variability	Do not recommend (strong)	Insufficient/mixed evidence; risk is similar or more than available alternative effective treatments

\*The Quality of Evidence rating was assigned by the primary evidence source, not the HERC Subcommittee

Note: GRADE framework elements are described in Appendix B

## POLICY LANDSCAPE

### Quality measures

One quality measure was identified when searching the National Quality Measures Clearinghouse that was pertinent to this coverage guidance. It was formulated by the American Urological Association, and is endorsed by the National Quality Forum. It states the following:

Prostate cancer: percentage of patients, regardless of age, with a diagnosis of prostate cancer, at low risk of recurrence, receiving interstitial prostate brachytherapy, OR external beam radiotherapy to the prostate, OR radical prostatectomy, OR cryotherapy who did not have a bone scan performed at any time since diagnosis of prostate cancer.

### Choosing Wisely®

Choosing Wisely® is part of a multi-year effort of the ABIM Foundation to help physicians be better stewards of finite health care resources. Originally conceived and piloted by the National Physicians Alliance through a Putting the Charter into Practice grant, more than 50 medical specialty organizations, along with Consumer Reports, have identified a number of tests or procedures commonly used in their field, whose necessity should be questioned and discussed. Each participating organization was free to determine how to create its own list, provided that it used a clear methodology and adhered to the following set of shared guidelines:

- Each item should be within the specialty's purview and control.
- The tests and/or interventions should be used frequently and/or carry a significant cost.
- Each recommendation should be supported by generally accepted evidence.
- The selection process should be thoroughly documented and publicly available on request.

One of the organizations that chose to participate in the Choosing Wisely® campaign is the American Society of Clinical Oncology. The first list created by this organization states the following:

Don't perform PET, CT, and radionuclide bone scans in the staging of early prostate cancer at low risk for metastasis.

- Imaging with PET, CT, or radionuclide bone scans can be useful in the staging of specific cancer types. However, these tests are often used in the staging evaluation of low-risk cancers, despite a lack of evidence suggesting they improve detection of metastatic disease or survival.
- Evidence does not support the use of these scans for staging of newly diagnosed low grade carcinoma of the prostate (Stage T1c/T2a, prostate-specific antigen (PSA) <10 ng/ml, Gleason score less than or equal to 6) with low risk of distant metastasis.

Unnecessary imaging can lead to harm through unnecessary invasive procedures, over-treatment, unnecessary radiation exposure, and misdiagnosis.

## Medicare National Coverage Determination

Effective September 4, 2014, Medicare makes the following coverage determination pertaining to PET scanning and prostate cancer:

### Initial Anti-Tumor Treatment Strategy Nationally Non-Covered Indications

- CMS continues to nationally non-cover initial anti-tumor treatment strategy in Medicare beneficiaries who have adenocarcinoma of the prostate.

### Subsequent Anti-Tumor Treatment Strategy Nationally Covered Indications (includes prostate cancer)

- Three FDG PET scans are nationally covered when used to guide subsequent management of anti-tumor treatment strategy after completion of initial anti-cancer therapy. Coverage of more than three FDG PET scans to guide subsequent management of anti-tumor treatment strategy after completion of initial anti-cancer therapy shall be determined by the local Medicare Administrative Contractors.

## National Comprehensive Cancer Network Guideline

This guideline states the following with regard to PET or PET/CT:

PET/CT using choline tracers may identify sites of metastatic disease in men with biochemical recurrence after primary treatment failure.

- Other choline radiotracers are under evaluation.
- Further study is needed to determine the best use of choline PET/CT imaging in men with prostate cancer.

Oncologic PET/CT is performed typically using [FDG]

- In certain clinical settings, the use of FDG-PET/CT may provide useful information, but FDG-PET/CT should not be used routinely since data on the utility of FDG-PET/CT in patients with prostate cancer is limited.

C-11 choline PET/CT has been used to detect and differentiate prostate cancer from benign tissue. The sensitivity and specificity of the technique in restaging patients with biochemical failure are 85% and 88%, respectively. C-11 choline PET/CT may be useful to detect distant metastases in these patients.

Newer technology using 18F-NaF as the tracer for a PET scan can be used as a diagnostic staging study. This test appears to have greater sensitivity than 99-technetium bone scan. However, there is controversy about how the results of 18F-NaF PET bone scan would be acted upon since all phase 3 clinical trials to date have based

progression criteria on the 99-technetium bone scans. PET and hybrid imaging bone scans appear more sensitive than conventional 99-technetium bone scans.

Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

## APPENDIX A. TNM STAGING FOR PROSTATE CANCER

Stage	Sub-Stage	Definition
<b><u>Tumor (T)</u></b>		<b>Primary Tumor</b>
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1		<b>Clinically inapparent tumor, neither palpable nor visible by imaging</b>
	T1a	Tumor incidental histological finding in 5% or less of tissue resected
	T1b	Tumor incidental histological finding in more than 5% of tissue resected
	T1c	Tumor identified by needle biopsy, e.g., because of elevated prostate-specific antigen (PSA)
T2		<b>Tumor confined within prostate</b>
	T2a	Tumor involves one-half of one lobe or less
	T2b	Tumor involves more than one-half of one lobe, but not both lobes
	T2c	Tumor involves both lobes
T3		<b>Tumor extends through the prostatic capsule</b>
	T3a	Extracapsular extension (unilateral or bilateral) including microscopic bladder neck involvement
	T3b	Tumor invades seminal vesicle(s)
T4		<b>Tumor is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall</b>
<b><u>Node (N)</u></b>		<b>Regional lymph nodes</b>
	NX	Regional lymph nodes cannot be assessed
	N0	No regional lymph nodes metastasis
	N1	Regional lymph node metastasis
<b><u>Metastasis (M)</u></b>		<b>Distant metastasis</b>
	M0	No distant metastasis
	M1	Distant metastasis
	M1a	Non-regional lymph node(s)
	M1b	Bone (s)
	M1c	Metastasis at other site(s)

## APPENDIX B. GRADE ELEMENT DESCRIPTIONS

Element	Description
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Resource allocation	The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted

### Strong recommendation

**In Favor:** The subcommittee is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences.

**Against:** The subcommittee is confident that the undesirable effects of adherence to a recommendation outweigh the desirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences.

### Weak recommendation

**In Favor:** The subcommittee concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences, but is not confident.

**Against:** The subcommittee concludes that the undesirable effects of adherence to a recommendation probably outweigh the desirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences, but is not confident.

### Quality or strength of evidence rating across studies for the treatment/outcome<sup>1</sup>

**High:** The subcommittee is very confident that the true effect lies close to that of the estimate of the effect. Typical sets of studies are RCTs with few or no limitations and the estimate of effect is likely stable.

**Moderate:** The subcommittee is moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Typical sets of studies are RCTs with some limitations or well-performed nonrandomized studies with additional strengths that guard against potential bias and have large estimates of effects.

**Low:** The subcommittee's confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Typical sets of studies are RCTs with serious limitations or nonrandomized studies without special strengths.

**Very low:** The subcommittee has very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect. Typical sets of studies are nonrandomized studies with serious limitations or inconsistent results across studies.

<sup>1</sup> Includes risk of bias, precision, directness, consistency and publication bias

## APPENDIX C. APPLICABLE CODES

<b>CODES</b>	<b>DESCRIPTION</b>
<b>ICD-9 Diagnosis Codes</b>	
185	Malignant neoplasm of prostate
233.4	Carcinoma in situ of prostate
<b>ICD-10 Diagnosis Codes</b>	
C61	Malignant neoplasm of prostate
D07.5	Carcinoma in situ of prostate
<b>ICD-9 Volume 3 (Procedure Codes)</b>	
88.38	Other computerized axial tomography
88.95	Magnetic resonance imaging of pelvis, prostate, and bladder
92.14	Bone scan
92.19	Scan of other sites
<b>CPT Codes</b>	
72192	Computed tomographic, pelvis; without contrast material
72193	Computed tomographic, pelvis; with contrast material(s)
72194	Computed tomographic, pelvis; without contrast material, followed by contrast material(s) and further sections
72195	Magnetic resonance, pelvis; without contrast material
72196	Magnetic resonance, pelvis; with contrast material(s)
72197	Magnetic resonance , pelvis; without contrast material, followed by contrast material(s) and further sequences
78300	Bone and/or joint imaging; limited area
78305	Bone and/or joint imaging; multiple areas
78306	Bone and/or joint imaging; whole body
78315	Bone and/or joint imaging; 3 phase study
78320	Bone and/or joint imaging; tomographic (SPECT)
78811	Positron emission tomography (PET) imaging; limited area
78812	Positron emission tomography (PET) imaging; skull base to mid-thigh
78813	Positron emission tomography (PET) imaging; whole body
78814	Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; limited area
78815	Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; skull base to mid-thigh
78816	Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; whole body
<b>HCPCS Level II Codes</b>	
	None

Note: Inclusion on this list does not guarantee coverage

## APPENDIX C. HERC GUIDANCE DEVELOPMENT FRAMEWORK

### HERC Guidance Development Framework Principles

This framework was developed to assist with the decision making process for the Oregon policy-making body, the HERC and its subcommittees. It is a general guide, and must be used in the context of clinical judgment. It is not possible to include all possible scenarios and factors that may influence a policy decision in a graphic format. While this framework provides a general structure, factors that may influence decisions that are not captured on the framework include but are not limited to the following:

- Estimate of the level of risk associated with the treatment, or any alternatives;
- Which alternatives the treatment should most appropriately be compared to;
- Whether there is a discrete and clear diagnosis;
- The definition of clinical significance for a particular treatment, and the expected margin of benefit compared to alternatives;
- The relative balance of benefit compared to harm;
- The degree of benefit compared to cost; e.g., if the benefit is small and the cost is large, the committee may make a decision different than the algorithm suggests;
- Specific indications and contraindications that may determine appropriateness;
- Expected values and preferences of patients.

CT of pelvis; PET for staging of prostate cancer

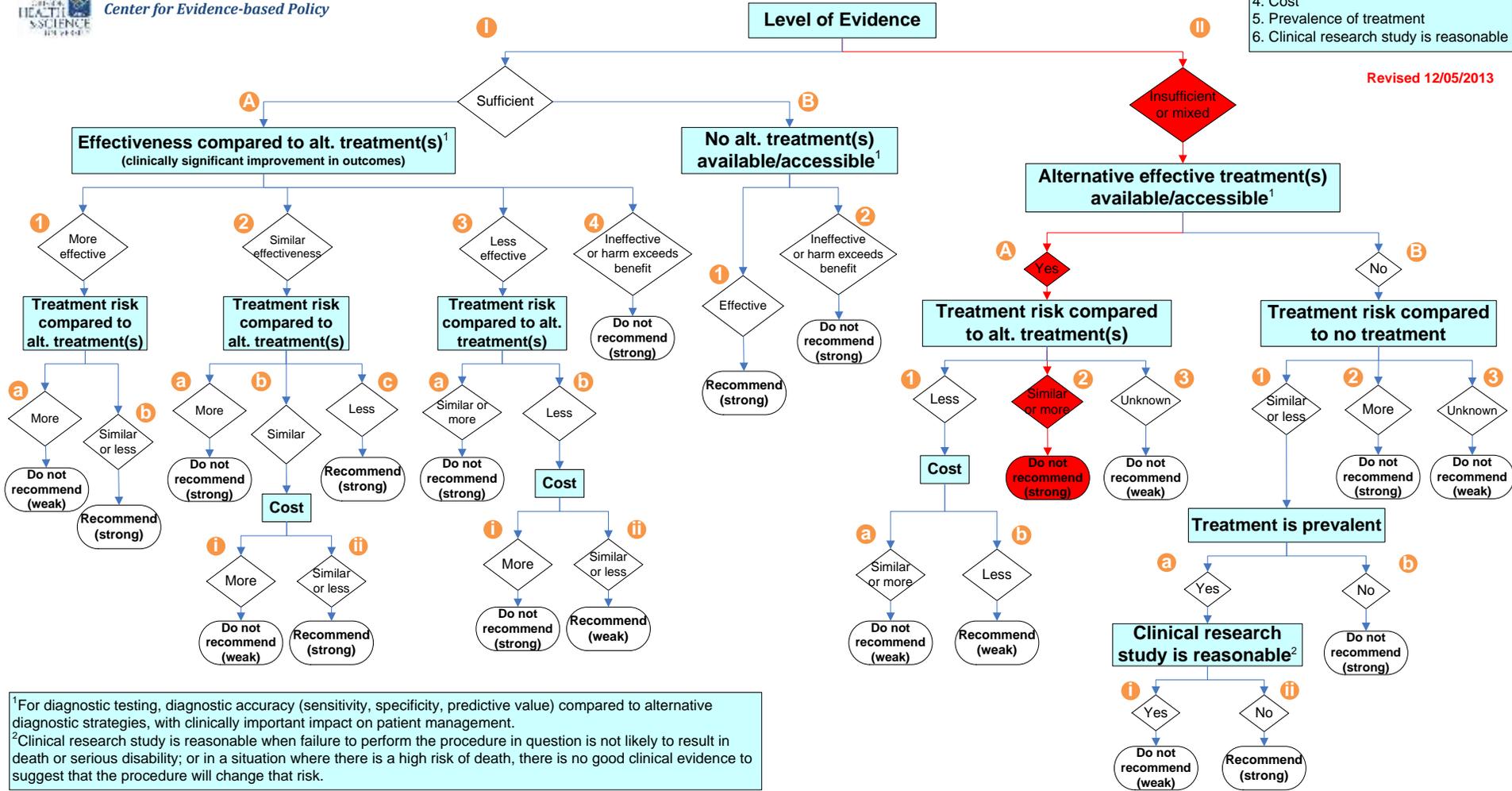


Center for Evidence-based Policy

HERC Guidance Development Framework
Refer to HERC Guidance Development Framework Principles for additional considerations

- Decision Point Priorities
1. Level of evidence
2. Effectiveness & alternative treatments
3. Harms and risk
4. Cost
5. Prevalence of treatment
6. Clinical research study is reasonable

Revised 12/05/2013



1 For diagnostic testing, diagnostic accuracy (sensitivity, specificity, predictive value) compared to alternative diagnostic strategies, with clinically important impact on patient management.
2 Clinical research study is reasonable when failure to perform the procedure in question is not likely to result in death or serious disability; or in a situation where there is a high risk of death, there is no good clinical evidence to suggest that the procedure will change that risk.

# MRI staging of prostate cancer



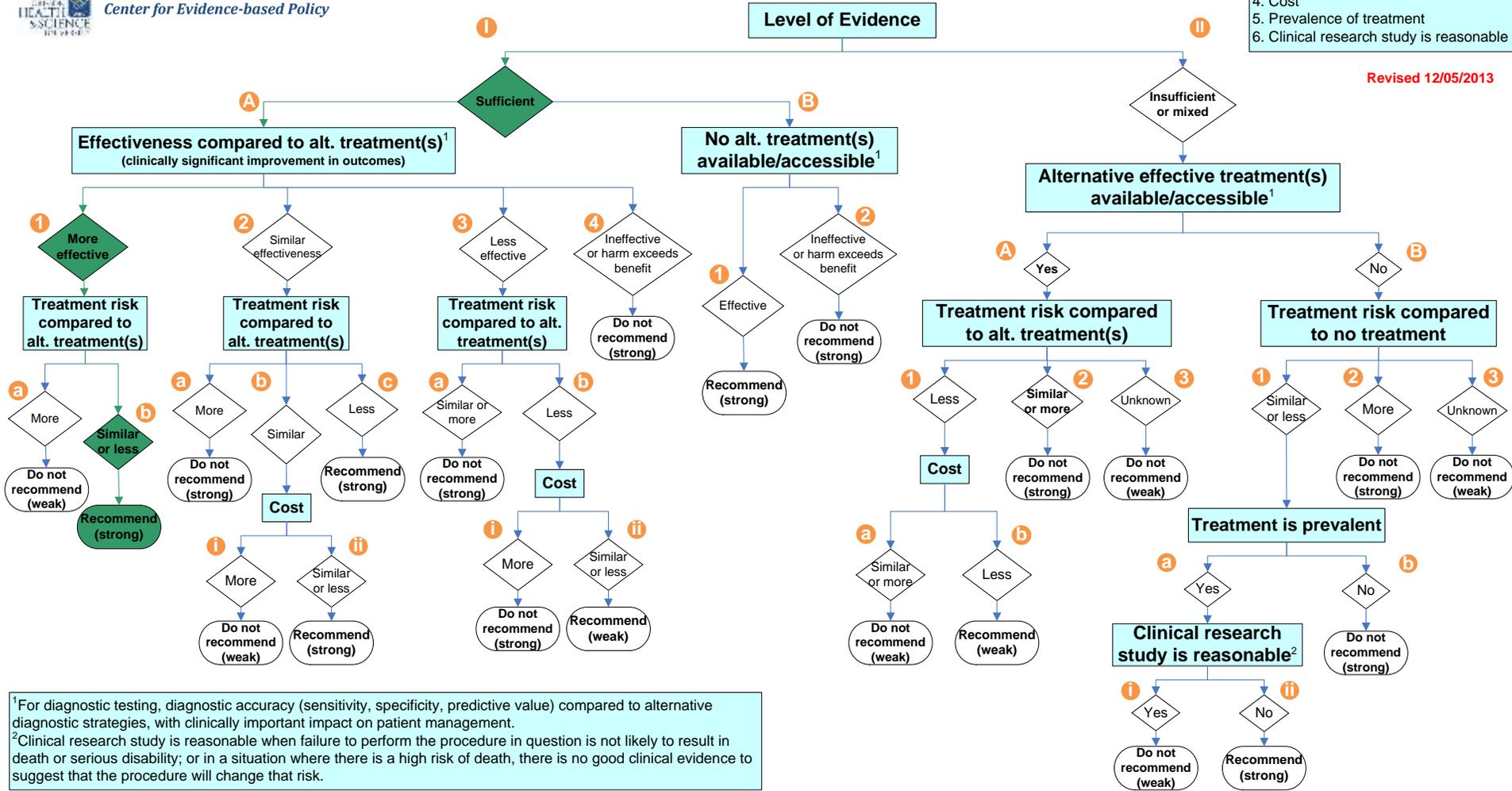
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## HERC Guidance Development Framework

Refer to *HERC Guidance Development Framework Principles* for additional considerations

- Decision Point Priorities**
1. Level of evidence
  2. Effectiveness & alternative treatments
  3. Harms and risk
  4. Cost
  5. Prevalence of treatment
  6. Clinical research study is reasonable

Revised 12/05/2013



# Bone scan in evaluation of newly diagnosed, low-risk prostate cancer



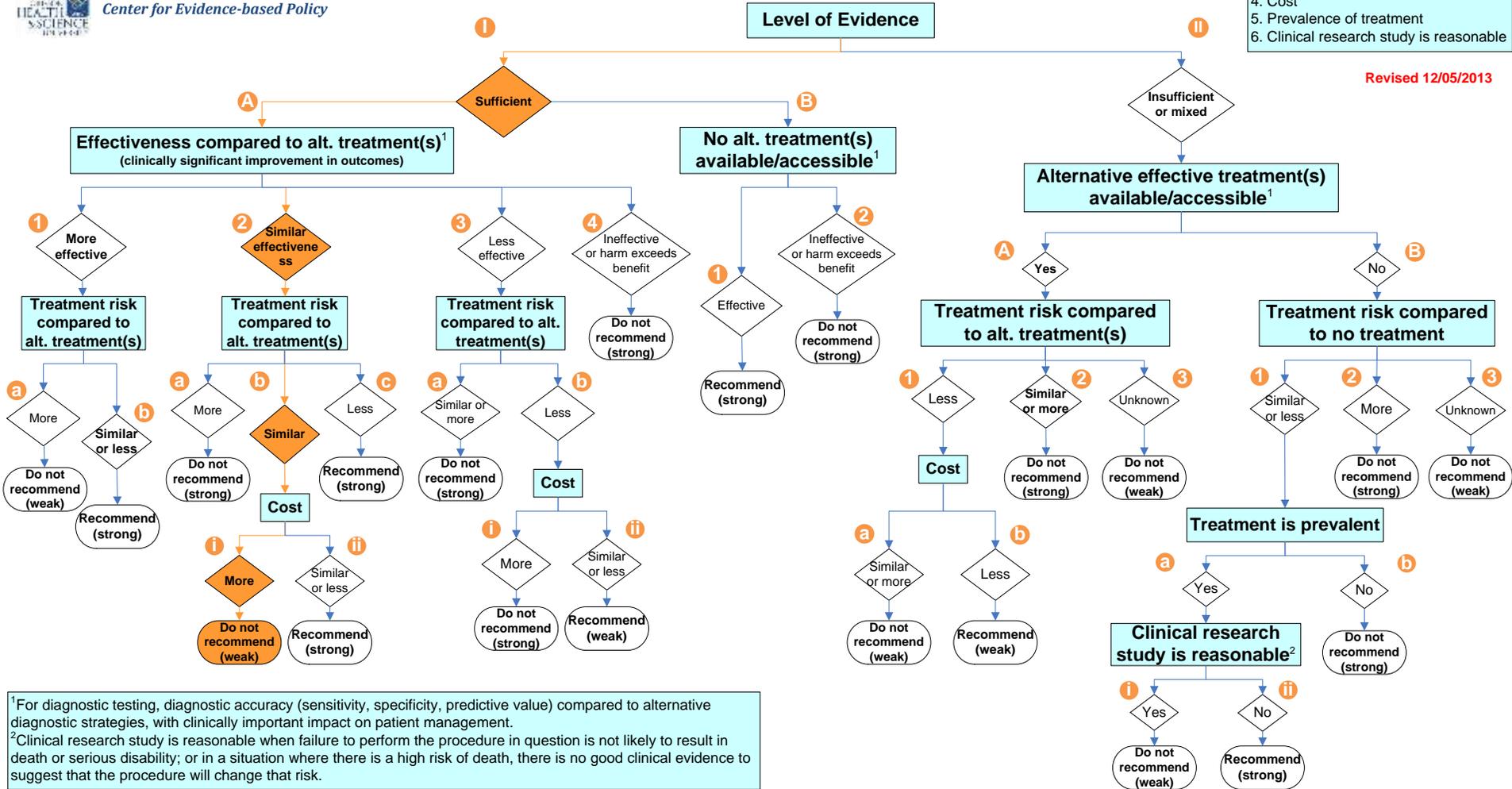
Center for Evidence-based Policy

## HERC Guidance Development Framework

Refer to HERC Guidance Development Framework Principles for additional considerations

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Revised 12/05/2013



# Bone scan in asymptomatic high-risk men



Center for Evidence-based Policy

## HERC Guidance Development Framework

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Revised 12/05/2013

