HEALTH EVIDENCE REVIEW COMMISSION (HERC)

COVERAGE GUIDANCE: ABLATION FOR ATRIAL FIBRILLATION

As posted for public comment 6/20/2014 to 7/21/2014

HERC COVERAGE GUIDANCE

AV node ablation is recommended for coverage only in persons with inadequate ventricular rate control resulting in symptoms, left ventricular systolic dysfunction or substantial risk of left ventricular systolic dysfunction. Coverage is recommended only when pharmacological therapy for rate control is ineffective or not tolerated *(weak recommendation)*

Transcatheter pulmonary vein isolation is recommended for coverage for those who are persistently symptomatic despite rate control medications and antiarrhythmic medications (*strong recommendation)*

Pulmonary vein isolation is recommended for coverage at the time of other cardiac surgery for patients who are persistently symptomatic despite rate control medications (*weak recommendation*).

The Maze procedure is recommended for coverage at the time of other cardiac surgery for patients with significant symptoms from atrial fibrillation *(weak recommendation)*

Note: Definitions for strength of recommendation are provided in Appendix A 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 Heath 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

Al-Khatib, S.M., Allen Lapointe, N., Chatterjee, R., Crowley, M.J., Dupre, M.E., Kong, D.F., et al. (2013). *Treatment of atrial fibrillation. Comparative Effectiveness Review 119*. (Prepared by the Duke Evidence-based Practice Center under

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Contract No. 290-2007-10066-I.) AHRQ Publication No.13-EHC095-EF. Rockville, MD: Agency for Healthcare Research and Quality. Retrieved from www.effectivehealthcare.ahrq.gov/reports/final.cfm

Chen, H.S., Wen, J.M., Wu, S.N., & Liu, J.P. (2012). Catheter ablation for paroxysmal and persistent atrial fibrillation. *Cochrane Database of Systematic Reviews, Issue 4*. Art. No.: CD007101. DOI: 10.1002/14651858.CD007101.pub2. Retrieved from

Hashimoto, R.E., Raich, A., Junge, M., & Skelly, A. (2013). Catheter ablation procedures for supraventricular tachyarrhythmia, including atrial flutter & atrial fibrillation. Olympia, WA: Washington State Health Care Authority Health Technology Assessment Program. Retrieved from http://www.hca.wa.gov/hta/Pages/Forms/HTA_Findings.aspx

January, C.T., Wann, L.S., Alpert, J.S., Calkins, H., Cleveland, Jr, J.C., Cigarroa, J.E., et al. (2014). 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *Circulation, 129.* doi:10.1161/CIR.0000000000000041. Retrieved from http://circ.ahajournals.org/content/early/2014/03/27/CIR.0000000000000041.citation

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

SUMMARY OF EVIDENCE

Clinical Background

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterized by uncoordinated atrial activation with consequent deterioration of mechanical function. Different systems have been proposed to classify AF. Although the type of AF can change over time, it is often helpful to characterize it at a given moment, as this may guide treatment. Types of AF include first-detected, paroxysmal (arrhythmia terminates spontaneously within 7 days), persistent (arrhythmia is sustained beyond 7 days), longstanding persistent (usually lasting for more than 1 year), and permanent AF (in which cardioversion has failed or has not been attempted).

It is estimated that more than 2.3 million Americans have AF. The prevalence of AF increases with age and approaches 8 percent in patients older than 80 years of age. AF is the most common sustained arrhythmia seen in clinical practice. The impact of AF is compounded by its known association with significant mortality, morbidity, and health care costs. Not only is the risk of death in patients with AF twice that of patients without

AF, but AF can result in myocardial ischemia or even infarction, heart failure exacerbation, and tachycardia-induced cardiomyopathy if the ventricular rate is not well controlled. The most dreaded complication of AF is thromboembolism, especially stroke. The risk of stroke in patients with AF is up to 8 percent per year, depending on the presence of stroke risk factors. Importantly, when ischemic stroke occurs in patients with AF, it is either fatal or of moderate to high severity in the majority of patients. The management of AF and its complications is responsible for almost $16 billion in costs to the U.S. health care system each year.

Treatment Strategies

Management of AF involves three distinct areas: rate control (treatments to slow the heart rate to a normal range), rhythm control (treatments to revert the heart rhythm back to normal), and prevention of thromboembolic events. Whether or not a rhythm-control strategy is adopted, current treatment guidelines suggest that adequate rate control should be achieved in all patients with AF to prevent myocardial infarction (if significant coronary artery disease is present), exacerbation of heart failure, and tachycardia-induced cardiomyopathy; to alleviate symptoms; and to improve exercise tolerance and quality of life.

Rate Control

If pharmacological therapy is insufficient for rate control and symptom management or is associated with side effects, the 2006 ACC/AHA/ESC Guidelines recommend ablation of the atrioventricular node (AVN) in conjunction with permanent pacemaker implantation to control heart rate. As the latter involves implantation of an indwelling device that is not reversible, it is considered a treatment of last resort for patients for whom initial pharmacotherapy was ineffective.

Another clinical dilemma is whether patients with AF do better with strict or lenient rate control. In theory, strict control could reduce symptoms and prevent complications. However, stricter control requires more intensive use of medications, which carry their own side effects. The 2011 Focused Update on the Management of Patients With Atrial Fibrillation by the American College of Cardiology Foundation (ACCF), the AHA, and the Heart Rhythm Society (HRS) addressed the issue of strict versus lenient rate control in patients with AF. Specifically, these guidelines emphasized the following Class III recommendation (evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful): “Treatment to achieve strict rate control of heart rate (<80 bpm at rest or <110 bpm during a 6-minute walk) is not beneficial compared with achieving a resting heart rate <110 bpm in patients with persistent AF who have stable ventricular function (left ventricular ejection fraction >0.40) and no or acceptable symptoms related to the arrhythmia.”

Rhythm Control

If patients with AF continue to have significant symptoms despite adequate rate control through either pharmacological therapy or AVN ablation, then a rhythm-control strategy (either pharmacological or electrical) is currently recommended. For pharmacological cardioversion of AF, the 2014 ACC/AHA/ESC Guidelines recommend flecainide, dofetilide, propafenone, and ibutilide as Class I recommendations, and amiodarone as a Class IIa recommendation (weight of evidence/opinion is in favor of usefulness/efficacy). To enhance direct-current cardioversion, the 2014 ACC/AHA/ESC Guidelines recommend pretreatment with amiodarone, flecainide, ibutilide, propafenone, or sotalol. For maintenance of sinus rhythm after cardioversion, the 2014 ACC/AHA/ESC Guidelines list different antiarrhythmic medications for different clinical settings.

In addition to pharmacological and direct-current cardioversion, a number of surgical interventions are used for rhythm control. Catheter ablation for the treatment of AF, with pulmonary vein isolation (PVI) being the most commonly used ablation, has evolved rapidly from a highly experimental procedure to its current status as a commonly performed procedure that is widely regarded as a clinically useful treatment option for symptomatic patients with AF in whom medications are not effective or not tolerated.

Several other procedures for the treatment of AF have been investigated. One such procedure is the surgical Maze procedure, which appears to confer some benefit to selected patients with AF. Implantation of a cardiac resynchronization therapy (CRT) device is another procedure that may decrease the burden of AF in patients who are eligible for this device based on a left ventricular ejection fraction ≤35 percent, a wide QRS complex, and heart failure symptoms despite optimal medical therapy. Secondary analyses of major clinical trials have provided conflicting findings on the effect of CRT on AF burden.

Although several studies of rate- and rhythm-control strategies exist, to date no study has shown that maintaining patients with AF in sinus rhythm provides a long-term survival benefit. It is also unknown whether the risks and benefits of different therapies vary by AF type.

Evidence Review

<u>Rate-Control Procedures Versus Drugs or Versus Other Procedures in Patients for Whom Initial Pharmacotherapy Was Ineffective</u>

Al-Khatib 2013 reports on six RCTs (two good, three fair, and one poor quality) involving a total of 537 patients that compared the effectiveness of a procedural intervention versus a primarily pharmacological intervention for rate control of AF or comparing two primarily procedural interventions. Four studies recruited patients with only one specific type of AF, either permanent (three studies) or persistent (one study); one study

recruited patients with “resistant chronic” AF; and one study recruited patients with permanent or paroxysmal AF. These studies, however, evaluated and compared different types of treatments, preventing conclusions about whether effectiveness varied by type of AF. All studies included at least one treatment arm with radiofrequency ablation of either the AVN or His bundle, most often in conjunction with pacemaker placement. The comparison arms included a pharmacological intervention whose main purpose was to control ventricular heart rate rather than converting the underlying rhythm of AF; this was combined with a procedure in some studies.

Based on three studies reported in Al-Khatib 2013 (one good, two poor quality) involving 175 patients, patients undergoing a procedural intervention had a significantly lower heart rate at 12 months than those receiving a primarily pharmacological intervention. This was measured differently in all three studies. In one, the mean heart rate in the intervention group was 71 ±6 bpm compared to 83 ± 8 bpm in the medication group ($p<0.01$). In this study, maximum heart rate did not differ between groups. In the second study, those in the ablation group had higher minimum (70±9 vs. 39±9 bpm; $p<0.05$) and mean (76±7 vs. 71±11 bpm; $p<0.05$) heart rates than the medication group, but lower maximum heart rates (117 ± 16 bpm vs. 152 ± 37 bpm; $p<0.05$). The third study reported the percent of each group who had either a normal or uncontrolled ventricular rate; in the ablation group, 100% had a normal ventricular rate (50-90 bpm) compared to 58% in the medication group. Similarly, none of the ablation group had an uncontrolled heart rate (>90 bpm at rest or > 130 bpm on exertion), while 42% of the medication group did. There was no difference by treatment arm in all-cause mortality (two studies [one good, one fair quality], 201 patients); cardiovascular mortality (one study [good quality], 102 patients); or exercise capacity (two studies [one good, one fair quality], 135 patients) (all low strength of evidence). There was insufficient strength of evidence to support findings for other outcomes, including quality of life.

<u>Rhythm-Control Procedures and Drugs for Maintenance of Sinus Rhythm</u>

Al-Khatib 2013 included 65 studies enrolling 6,739 patients that evaluated procedures for rhythm control. Of those that specified type of AF, eleven included only patients with longstanding persistent AF, 17 studies included only patients with paroxysmal AF, and 4 studies included only patients with persistent AF.

Transcatheter PVI versus antiarrhythmic drugs

Al-Khatib 2013 concluded, based on eight RCTs (five good, three fair quality) involving 921 patients, that transcatheter PVI is superior to antiarrhythmic drugs for **maintenance of sinus rhythm** over 12 months of follow up in patients with AF (one RCT reported 48 months of follow up). All trials had statistically significant results, as did meta-analysis of all eight trials (OR 6.51, 95% CI 3.22 to 13.16). This evidence is strongest in younger

patients with little to no structural heart disease and with mild or no enlargement of the left atrium. Only one trial was limited to patients receiving ablation as first line therapy (Wazni 2005), while five specifically required failure of at least one AAD to be included in the study. The Wazni trial included 70 patients who experienced monthly episodes of symptomatic AF for at least three months, and found that at one year follow up, 63% of those treated with AADs had at least one recurrence of AF, compared to 13% of those who received PVI. Another trial included only in Hashimoto 2013 included only patients with persistent AF (MacDonald 2011), and reported that at final follow up (6 months), 50% of patients in the PVI group were in sinus rhythm while none of the control group were (no statistical testing done). This latter trial was limited to patients with advanced heart failure. (Note: This outcome is reported as freedom from recurrence in Hashimoto 2013, but results are similar.)

Al-Khatib 2013 concluded, based on two RCTs (Pappone 2006, Forleo 2009, both good quality) involving 268 patients, that transcatheter PVI is superior to antiarrhythmic medications in **reducing cardiovascular hospitalizations** (moderate strength of evidence). Both of these trials were also included in Hashimoto 2013. A third study, Stabile 2006, reported only in Hashimoto 2013, found a lower number of hospitalizations in the PVI group which did not reach statistical significance. A fourth RCT, Wazni 2005, reported only in Al-Khatib 2013, found the rate of hospitalization specifically for AF was higher in the AAD arm (15 of 35) than the PVI arm (3 of 32, $p< 0.001$) in the first 12 months of follow up.

Chen 2012 reported that only one trial (Stabile 2006) reported all-cause **mortality**. There were no statistically significant differences between groups for this outcome. In this trial, the one death that occurred in the PVI group was from a stroke that occurred during the procedure and was followed by a brain hemorrhage 9 months later. There were two deaths in the AAD group (diagnosis not specified).

Al-Khatib 2013 also reported only one study for the outcome of all-cause mortality, however, it was a different study than was reported by Chen. This study (Oral 2006) reported one death in the PVI arm at 12 months compared to none in the AAD arm; no statistical testing was done.

Hashimoto 2013 reported that four RCTs (Jais 2008, Wilbur 2010, Stabile 2006, Oral 2006) reported overall mortality rates (not procedure related) at 9 to 12 months of follow up. Mortality rate in the PVI arm ranged from 1% to 3%, while in the AAD arm a rate of 3% was reported in two studies. According to Hashimoto, Stabile 2006 was the only RCT to report mortality in both arms. Two cohort studies included in Hashimoto 2013 did report an increased risk of death in the AAD group at follow up times ranging from 1 to 3 years (Pappone 2003: 6.5% in the PVI group vs. 14.3% in the AAD group, p<

0.001) or at a mean follow up of 69 months (Sonne 2009: 2.1% in the PVI group vs. 16.5% in the AAD group, p = 0.001).

Eight studies evaluated **quality of life (QOL) or functional status**, three RCTs reported in all three source reports, two additional RCTs reported in both Hashimoto 2013 and Al-Khatib 2013, two additional RCTs in Hashimoto 2013 only and one cohort study reported in Al-Khatib 2013 only. In general, there was greater improvement from baseline in these scores in patients randomized to the PVI arm, compared to the AAD arm, and in most of these studies, results were statistically significant for at least some measures.

Harms were reported in eight RCTs, but for the most part, were not statistically analyzed. Complications reported in each study are summarized in the Table below:

Author	N	PVI Arm	AAD Arm
Krittayaphong	30	1 stroke, 1 groin hematoma	AE in 7 patients (47%): GI AE in 6 pts, corneal deposits in 2 pts, hypothyroidism in 2 pts, abnormal LFTs in 2 pts, hyperthyroidism in 1 pt, sinus node dysfunction in 1 pt
Wazni	70	No TE events, no bradycardia, 1 asymptomatic PV stenosis	No TE events, 8.6% bradycardia
Pappone	198	No serious AE	Sig AE leading to drug withdrawal in 23 pts,
Oral	146	None	None
Stabile	137	4.4% major complications (stroke, phrenic paralysis, pericardial effusion)	1 TIA, 2 cancer, 1 sudden death
Jais	112	2 cardiac tamponade, 2 groin hematomas, 1 PV stenosis requiring stent	1 hyperthyroidism, 2 deaths (unrelated)
Forleo	70	1 groin hematoma	17% sig drug AE (bradycardia, atrial flutter, sinus node dysfunction
Wilber	167	5 major AE (pericardial effusion, pulmonary edema, pneumonia, vascular complication, heart failure)	5 major AE (2 life-threatening arrhythmias, 3 disabling drug intolerance requiring discontinuation)

TE = thromboembolic; PV = pulmonary vein

Cryoablation PVI vs. AAD

One RCT reported in Hashimoto 2013 found that patients randomized to receive cryoablation had significantly greater freedom from recurrence compared with those

patients randomized to receive AADs alone (69.9% versus 7%, respectively; P < .001). There was one death (0.6%) in the cryoablation PVI group and none in the AAD group at 12 months, which was not statistically significant.

Surgical Maze versus standard of care (mitral valve surgery)

Al-Khatib 2013 included seven RCTs (one good, six fair quality) involving 361 patients for this comparison. Surgical Maze at the time of other cardiac surgery (specifically mitral valve surgery) is superior to mitral valve surgery alone for **maintenance of sinus rhythm** over at least 12 months of followup in patients with persistent AF (OR 5.80, 95% CI 1.79 to 18.81). Six studies reported on all cause mortality; meta-analysis found an OR of 1.97 (95% CI 0.81 to 4.80) suggesting an increased risk of death with the Maze procedure, but this did not reach statistical significance.

PVI done at the time of cardiac surgery versus cardiac surgery alone or cardiac surgery in combination with antiarrhythmic drugs (AADs) or catheter ablation

Al-Khatib 2013 included eight RCTs (five good, three fair quality) involving 532 patients for this comparison. Pulmonary vein isolation done at the time of cardiac surgery is superior to cardiac surgery alone or cardiac surgery in combination with AADs or catheter ablation for **maintenance of sinus rhythm** over 12 months of followup in patients with persistent AF (OR 3.91, 95% CI 1.54 to 9.91). Two studies reported no difference between groups in all-cause mortality or stroke.

There are insufficient data on the effect of rhythm control with PVI or surgical Maze on final outcomes, such as all-cause mortality, stroke, heart failure, and left ventricular ejection fraction, and on the safety and durability of the effectiveness of these procedures beyond 12 months.

Other comparisons

There are a variety of other comparisons included in Al-Khatib 2013 and Chen 2012, most of which had a limited number of studies and were considered outside the scope of this guidance document. These include the following:

- Circumferential PVI versus Segmental PVI
- Transcatheter PVI with complex fractionated atrial electrogram (CFAE) ablation versus transcatheter PVI without CFAE ablation
- Transcatheter PVI using different types of ablation catheters
- Transcatheter PVI with Cavotricuspid isthmus (CTI) ablation vs. transcatheter PVI without CTI ablation

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- Transcatheter PVI vs transcatheter PVI with ablation sites other than CTI and CFAE and transcatheter PVI involving all four PVs vs transcatheter PVI involving arrhythmogenic PVs only
- Transcatheter PVI Alone vs transcatheter PVI plus postablation antiarrhythmic drugs
- Left atrial ablation vs. bi-atrial ablation
- PVI, circumferential PVI or left atrium ablation vs. ablation plus additional linear ablation
- PV-left atrium junction ablation vs. PV-left atrium junction ablation combined with CTI ablation
- Circumferential PV ablation vs. circumferential PV ablation plus PVI
- Superior PV ablation vs. four-PV ablation
- Small area isolation vs. large area isolation around PVs in circumferential PV ablation
- CFAE plus PV atrum isolation vs. PV atrum isolation alone
- Circumferential PV ablation vs. modified circumferential PV ablation
- Arrhythmogenic PVI vs all PVI

[Evidence Source]

Evidence Summary

Ablation of the AV node or bundle of His in patients with AF results in lower heart rate at 12 months than pharmacologic treatment (moderate SOE), although there is no difference in mortality or exercise capacity (low SOE). Pulmonary vein isolation (PVI) results in a greater likelihood of maintaining sinus rhythm at 12 months than pharmacologic treatment (high SOE); most of the evidence for this finding is in patients with AF who have failed at least one AAD. This procedure (PVI) also results in lower risk of hospitalization over 12 months (moderate SOE) and improved QOL (moderate SOE), but the evidence is insufficient to assess the impact of PVI on mortality.

The surgical Maze procedure, when done at the time of other cardiac surgery, results in a higher likelihood of maintaining sinus rhythm than not performing the Maze (moderate SOE). Similarly, PVI done at the time of other cardiac surgery results in a higher likelihood of maintaining sinus rhythm than not performing PVI (high SOE), and no apparent difference in all-cause mortality or stroke (low SOE).

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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.

Indication/ Intervention	Balance between desirable and undesirable effects	Quality of evidence*	Resource allocation	Variability in values and preferences	Coverage recommendation	Rationale
Ablation of AV node/bundle of His compared to rate control medications in patients for whom initial pharmacotherapy was ineffective	Lower heart rate, no difference in mortality/exercise capacity	Moderate/Low based on 1 to 3 poor to good quality studies, depending on the outcome	High	High	AV node ablation is recommended for coverage only in symptomatic persons when pharmacological therapy for rate control is ineffective or not tolerated. *(weak recommendation)*	Studies show mixed clinical significance of a lower heart rate. In those with persistently uncontrolled heart rate despite AADs, AV node ablation is a reasonable alternative to prevent the negative consequences of an uncontrolled rate such as MI, exacerbation of CHF or cardiomyopathy.
Transcatheter PVI vs. AAD	Better maintenance of SR, fewer	High/Moderate, based on 1 to	High	Moderate	Transcatheter PVI is recommended for	Transcatheter PVI produces

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Indication/ Intervention	Balance between desirable and undesirable effects	Quality of evidence*	Resource allocation	Variability in values and preferences	Coverage recommendation	Rationale
	hospitalizations, better QOL, possibly lower mortality	8 fair to good quality studies, depending on the outcome			coverage when a rhythm control strategy is desired *(strong recommendation)*	superior clinical outcomes to antiarrhythmic drugs alone when a rhythm control strategy is pursued
Maze procedure	Better maintenance of SR; possible (nonsignificant) increase in mortality	Moderate based on 1 good and six fair quality studies	Moderate (concurrent with other cardiac surgery)	Moderate	The Maze procedure is recommended for coverage at the time of other cardiac surgery if the benefits of maintenance of sinus rhythm are thought to outweigh the potential risk of increased mortality *(weak recommendation)*	Maze may help maintain sinus rhythm but concerning nonsignificant increased risk of mortality
PVI done with other cardiac surgery	Better maintenance of SR	High based on 5 good and 3 fair quality studies	Moderate (concurrent with other cardiac surgery)	Low	PVI is recommended for coverage *(weak recommendation)*	PVI may help maintain sinus rhythm without significant additional risks

SR = sinus rhythm PVI = pulmonary vein isolation AAD = anti-arrhythmic drugs

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

Note: GRADE framework elements are described in Appendix A

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POLICY LANDSCAPE

Nine quality measures pertaining to atrial fibrillation were identified when searching the National Quality Measures Clearinghouse; however, none of them referenced ablation.

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 Heart Rhythm Society. The most recent list created by this organization states the following:

> **"Don't ablate the atrioventricular node in patients with atrial fibrillation when both symptoms and heart rate are acceptably controlled by well-tolerated medical therapy.**
>
> Atrioventricular node ablation and pacemaker implantation may provide benefit in some patients when rate and related symptoms cannot be controlled by medication therapy,(Class IIa, indicated) or when there is concern for possible tachycardia-induced cardiomyopathy (Class IIb, may be considered). However, according to current professional society clinical guidelines, the risks of AV node ablation outweigh the benefits among patients with no symptoms and who have appropriate rate control with well-tolerated medical therapy."

They cite the 2011 publication of the ACCF/AGA guidelines on the management of patient with AF as supporting evidence. These guidelines were recently updated (2014), and are rated fair quality using the MED standard criteria,

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primarily because study selection criteria was not specified and the quality of included studies was not assessed. These guidelines state the following with regard to AV node ablation for rate control in AF:

Class IIa
3. AV nodal ablation with permanent ventricular pacing is reasonable to control the heart rate when pharmacological therapy is inadequate and rhythm control is not achievable. *(Level of Evidence: B)*

Class III: Harm
1. AV nodal ablation with permanent ventricular pacing should not be performed to improve rate control without prior attempts to achieve rate control with medications. *(Level of Evidence: C)*

For catheter ablation for rhythm control (e.g. PVI), the guidelines state the following:

Class I
1. AF catheter ablation is useful for symptomatic paroxysmal AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication when a rhythm control strategy is desired. *(Level of Evidence: A)*

2. Prior to consideration of AF catheter ablation, assessment of the procedural risks and outcomes relevant to the individual patient is recommended. *(Level of Evidence: C)*

Class IIa
1. AF catheter ablation is reasonable for selected patients with symptomatic persistent AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication. *(Level of Evidence: A)*

2. In patients with recurrent symptomatic paroxysmal AF, catheter ablation is a reasonable initial rhythm control strategy prior to therapeutic trials of antiarrhythmic drug therapy, after weighing risks and outcomes of drug and ablation therapy. *(Level of Evidence: B)*

Class IIb
1. AF catheter ablation may be considered for symptomatic long-standing (>12 months) persistent AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication, when a rhythm control strategy is desired. *(Level of Evidence: B)*

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2. AF catheter ablation may be considered prior to initiation of antiarrhythmic drug therapy with a class I or III antiarrhythmic medication for symptomatic persistent AF, when a rhythm control strategy is desired. *(Level of Evidence: C)*

Class III: Harm

1. AF catheter ablation should not be performed in patients who cannot be treated with anticoagulant therapy during and following the procedure. *(Level of Evidence: C)*

2. AF catheter ablation to restore sinus rhythm should not be performed with the sole intent of obviating the need for anticoagulation. *(Level of Evidence: C)*

COMMITTEE DELIBERATIONS – VALUE-BASED BENEFITS SUBCOMMITTEE

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.

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Appendix A. 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[1]

***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.

[1] Includes risk of bias, precision, directness, consistency and publication bias

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***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.

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Appendix B. Applicable Codes

CODES	DESCRIPTION
ICD-9 Diagnosis Codes	
427.31	Atrial fibrillation
ICD-10 Diagnosis Codes	
I48.0	Paroxysmal atrial fibrillation
I48.1	Persistent atrial fibrillation
I48.2	Chronic atrial fibrillation
I48.91	Unspecified atrial fibrillation
ICD-9 Volume 3 (Procedure Codes)	
None	
CPT Codes	
33250	Operative ablation of supraventricular arrhythmogenic focus or pathway (eg, Wolff-Parkinson-White, atrioventricular node re-entry), tract(s) and/or focus (foci); without cardiopulmonary bypass (For intraoperative pacing and mapping by a separate provider, use 93631) Codes 33254-33256 are only to be reported when there is no concurrently performed procedure that requires median sternotomy or cardiopulmonary bypass.
33251	…with cardiopulmonary bypass
33254	Operative tissue ablation and reconstruction of atria, limited (eg, modified maze procedure)
33255	Operative tissue ablation and reconstruction of atria, extensive (eg, maze procedure); without cardiopulmonary bypass
33256	…with cardiopulmonary bypass
33257	Operative tissue ablation and reconstruction of atria, performed at the time of other cardiac procedure(s), limited (eg, modified maze procedure) (List separately in addition to code for primary procedure)
33258	Operative tissue ablation and reconstruction of atria, performed at the time of other cardiac procedure(s), extensive (eg, maze procedure), without cardiopulmonary bypass (List separately in addition to code for primary procedure)
33259	Operative tissue ablation and reconstruction of atria, performed at the time of other cardiac procedure(s), extensive (eg, maze procedure), with cardiopulmonary bypass (List separately in addition to code for primary procedure)
33261	Operative ablation of ventricular arrhythmogenic focus with cardiopulmonary bypass

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CODES	DESCRIPTION
33265	Endoscopy, surgical; operative tissue ablation and reconstruction of atria, limited (eg, modified maze procedure), without cardiopulmonary bypass
33266	…operative tissue ablation and reconstruction of atria, extensive (eg, modified maze procedure), without cardiopulmonary bypass
93613	Intracardiac electrophysicologic 3-dimensional mapping (List separately in addition to code for primary procedure)
93650	Intracardiac catheter ablation of atrioventricular node function, atrioventricular conduction for creation of complete heart block, with or without temporary pacemaker placement
93653	Comprehensive electrophysiologic evaluation including insertion and repositioning of multiple electrode catheters with induction or attempted induction of an arrhythmia with right atrial pacing and recording, right ventricular pacing and recording, His recording with intracardiac catheter ablation of arrhythmogenic focus; with treatment of supraventricular tachycardia by ablation of fast or slow atrioventricular pathway, accessory atrioventricular connection, cavo-tricuspid isthmus or other single atrial focus or source of atrial re-entry (Do not report 93653 in conjunction with 93600-93603, 93610, 93612, 93618-93620, 93642, 93654)
93655	Intracardiac catheter ablation of a discrete mechanism of arrhythmia which is distinct from the primary ablated mechanism, including repeat diagnostic maneuvers, to treat a spontaneous or induced arrhythmia (List separately in addition to code for primary procedure) (Use 93655 in conjunction with 93653, 93654, 93656)
93656	Comprehensive electrophysiologic evaluation including transseptal catheterizations, insertion and repositioning of multiple electrode catheters with induction or attempted induction of an arrhythmia with atrial recording and pacing, when possible, right ventricular pacing and recording, His bundle recording with intracardiac catheter ablation of arrhythmogenic focus, with treatment of atrial fibrillation by ablation by pulmonary vein isolation
93657	Additional linear or focal intracardiac catheter ablation of the left or right atrium for treatment of atrial fibrillation remaining after completion of pulmonary vein isolation (List separately in addition to code for primary procedure)
93799	Unlisted cardiovascular service or procedure

DRAFT

CODES	DESCRIPTION
HCPCS Level II Codes	
None	

Note: Inclusion on this list does not guarantee coverage

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Appendix C. HERC Guidance Development Framework

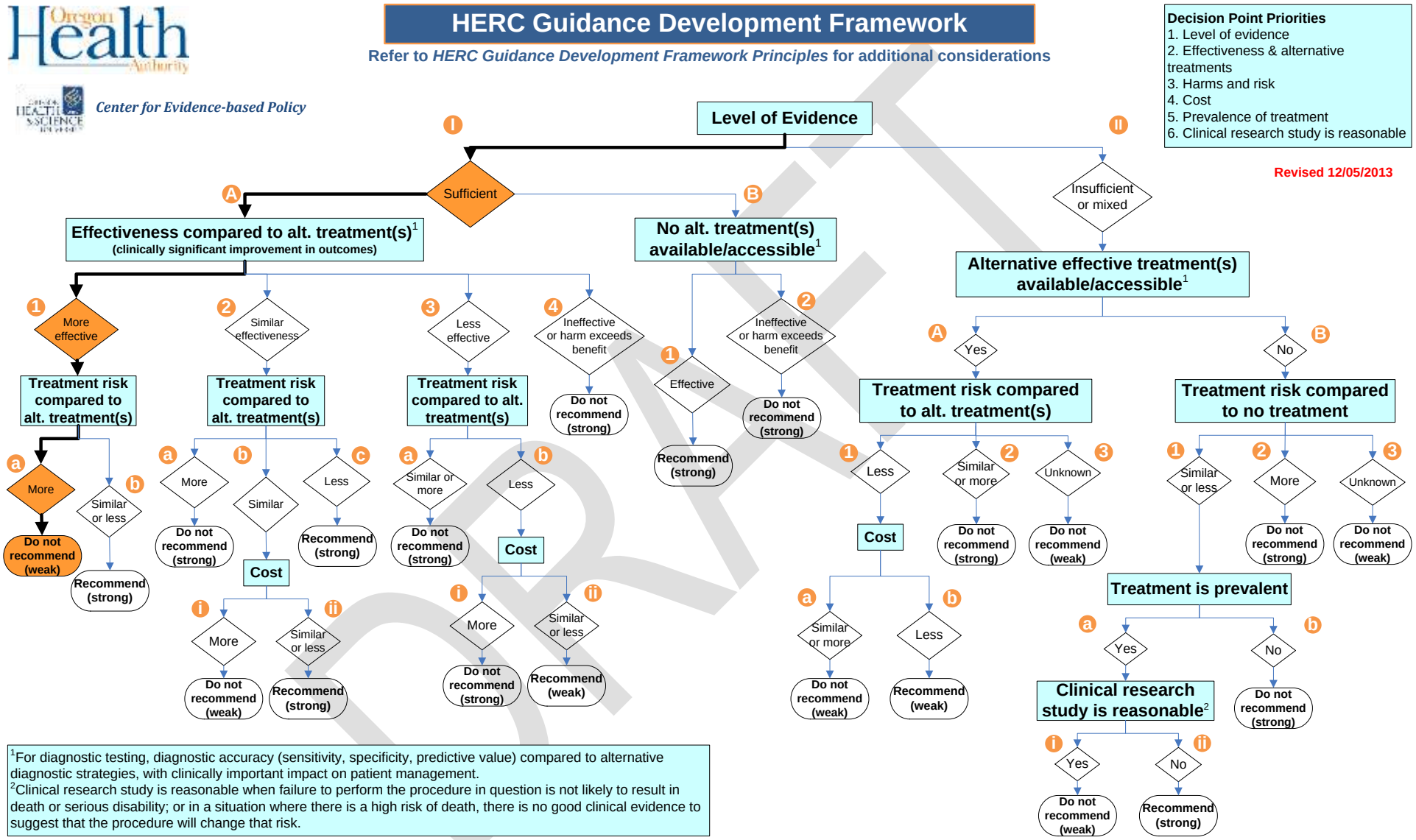
HERC Guidance Development Framework Principles

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.

DRAFT

Ablation of AV node/bundle of His vs. rate control medications



[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.

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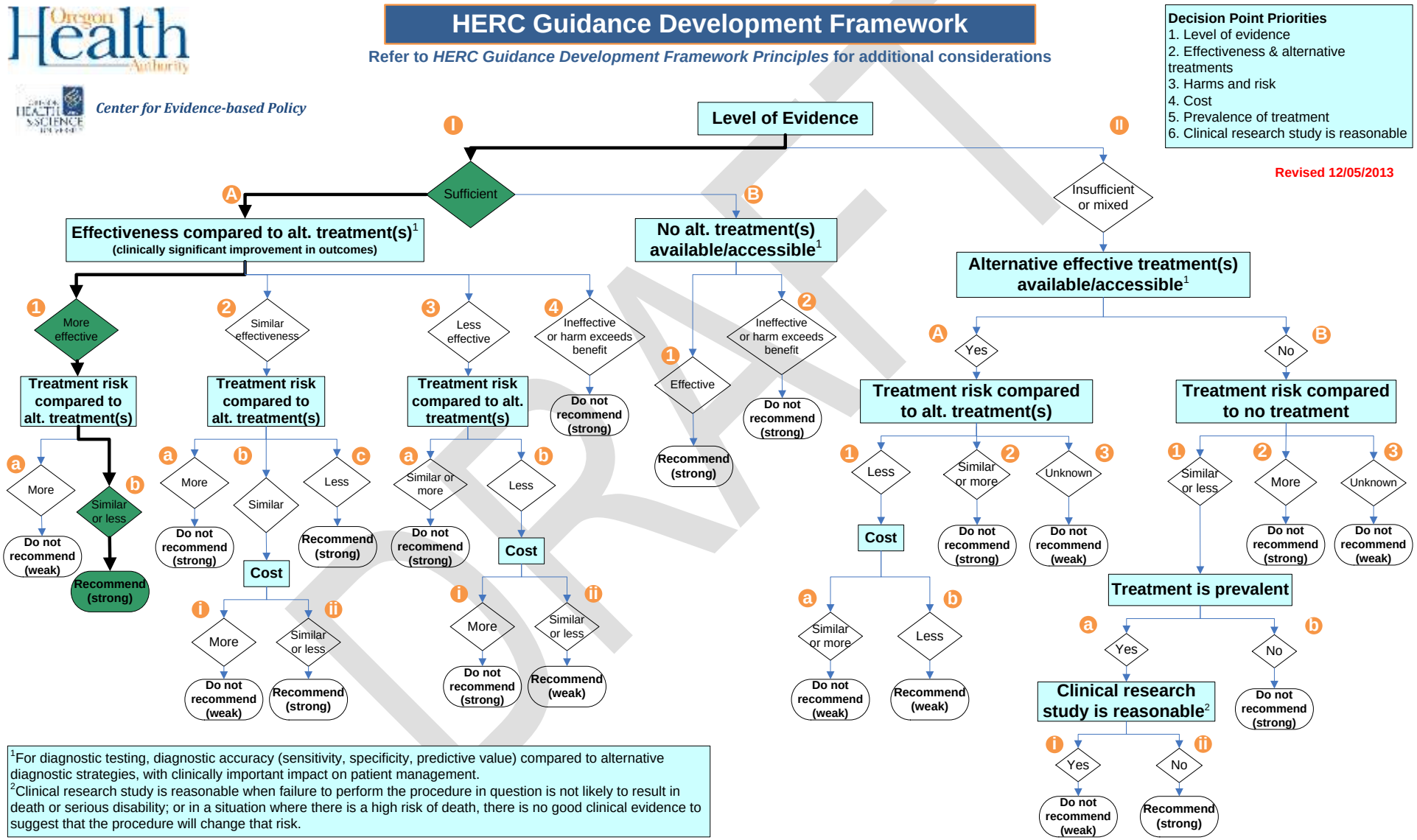
Transcatheter pulmonary vein isolation (PVI) vs. antiarrhythmic drugs (AAD); Maze procedure; PVI done with other cardiac surgery



[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.