7.01.14	Open and Thoracoscopic Approaches to Treat Atrial Fibrillation and Atrial Flutter (Maze and Related Procedures)		
Original Policy Date:	December 7, 2006	**Effective Date:**	July 1, 2023
Section:	7.0 Surgery	**Page:**	Page 1 of 36

Policy Statement

I. The maze or modified maze procedure, performed on a non-beating heart during cardiopulmonary bypass with concomitant cardiac surgery, may be considered **medically necessary** for the treatment of symptomatic atrial fibrillation or flutter.

II. Stand-alone minimally invasive, off-pump maze procedures (i.e., modified maze procedures), including those done via mini-thoracotomy, are considered **investigational** for the treatment of atrial fibrillation or flutter.

III. Hybrid ablation (defined as a combined percutaneous and thoracoscopic approach) is considered **investigational** for the treatment of atrial fibrillation or flutter.

IV. The use of an open maze or modified maze procedure performed on a non-beating heart during cardiopulmonary bypass without concomitant cardiac surgery is considered **investigational** for the treatment of atrial fibrillation or flutter.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Given the availability of less-invasive alternative approaches to treat atrial fibrillation (AF) (see Blue Shield of California Medical Policy: Catheter Ablation as Treatment for Atrial Fibrillation), performing the maze procedure without concomitant cardiac surgery should rarely be needed.

Per the 2017 Expert Consensus Statement by the Heart Rhythm Society, European Heart Rhythm Association, and European Cardiac Arrhythmia Society (Calkins et al, 2017, referenced in the Supplemental Information section), the indication for concomitant open or closed surgical ablation, stand-alone, and hybrid surgical ablation of atrial fibrillation is symptomatic disease refractory or intolerant to at least 1 Class I or III antiarrhythmic medication.

Coding

The following CPT codes are specific to the various open and endoscopic maze procedures:

- **33254**: Operative tissue ablation and reconstruction of atria, limited (e.g., modified maze procedure)
- **33255**: Operative tissue ablation and reconstruction of atria, extensive (e.g., maze procedure); without cardiopulmonary bypass
- **33256**: Operative tissue ablation and reconstruction of atria, extensive (e.g., maze procedure); with cardiopulmonary bypass
- **33265**: Endoscopy, surgical; operative tissue ablation and reconstruction of atria, limited (e.g., modified maze procedure), without cardiopulmonary bypass
- **33266**: Endoscopy, surgical; operative tissue ablation and reconstruction of atria, extensive (e.g., maze procedure), without cardiopulmonary bypass

There are CPT add-on codes for when the maze procedure is performed at the time of other cardiac procedures:

- **33257**: Operative tissue ablation and reconstruction of atria, performed at the time of other cardiac procedure(s), limited (e.g., 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 (e.g., 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 (e.g., maze procedure), with cardiopulmonary bypass (List separately in addition to code for primary procedure)

Description

There are various surgical approaches to treat atrial fibrillation (AF) that work by interrupting abnormal electrical activity in the atria. Open surgical procedures, such as the Cox maze procedure were first developed for this purpose and are now generally performed in conjunction with valvular or coronary artery bypass graft surgery. Surgical techniques have evolved to include minimally invasive approaches that use epicardial radiofrequency ablation, a thoracoscopic or mediastinal approach, and hybrid catheter ablations/open procedures.

Related Policies

- Catheter Ablation as Treatment for Atrial Fibrillation

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

Several radiofrequency ablation systems have been cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process for cardiac tissue ablation (product code OCL). Table 1 provides a select list.

Table 1. Radiofrequency Ablation Approved by the U.S. Food and Drug Administration

Device	Manufacturer	510(k)/Premarket Approval Date	510(k)/Premarket Approval Number
EPi-Sense Guided Coagulation System	Atricure	April 2021	P200002
Medtronic DiamondTemp™ System	Medtronic	Jan 2021	P200028
Cobra Fusion Ablation System	AtriCure	Feb 2019	K190151
Medtronic Cardioblate® System	Medtronic	Jan 2002	K013392
Cardima Ablation System	Cardima	Jan 2003	K022008
Epicor™ Medical Ablation System	Epicor Medical	Feb 2004	K022894
Isolator™ Transpolar™ Pen	AtriCure	Jun 2005	K050459

Device	Manufacturer	510(k)/Premarket Approval Date	510(k)/Premarket Approval Number
Estech COBRA® Cardiac Electrosurgical Unit	Endoscopic Technologies	Jan 2006	K053326
Coolrail™ Linear Pen	AtriCure	Mar 2008	K073605
Numeris® Guided Coagulation System with VisiTrax®	nContact Surgical	Feb 2009	K090202
EPi-Sense® Guided Coagulation System with VisiTrax®	nContact Surgical	Nov 2012	K120857

A number of cryoablation systems, which may be used during cardiac ablation procedures, have also been cleared for marketing, including those in Table 2.

Table 2. Cryoablation Systems Approved by the U.S. Food and Drug Administration

Device	Manufacturer	510(k)/Premarket Approval Date
Cryocare® Cardiac Surgery System	Endocare	Mar 2002
SeedNet™ System	Galil Medical	May 2005
SurgiFrost® XL Surgical CryoAblation System	CryoCath Technologies; now Medtronic	Jul 2006
Isis™ cryosurgical unit	Galil Medical	Mar 2007
Artic Front Advance™ and Arctic Front Advance Pro™ and the Freezer Max™ Cardiac Cryoablation Catheters	Medtronic	Jun 2020

Rationale

Background

Atrial Fibrillation

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterized by disorganized atrial activation with ineffective atrial ejection. The underlying mechanism of AF involves the interplay between electrical triggering events that initiate AF and the myocardial substrate that permits propagation and maintenance of the aberrant electrical circuit. The most common focal trigger of AF appears to be located within the cardiac muscle that extends into the pulmonary veins. The atria are frequently abnormal in patients with AF and demonstrate enlargement or increased conduction time. Atrial flutter is a variant of AF.

Treatment

The first-line treatment for AF usually includes medications to maintain sinus rhythm and/or control the ventricular rate. Antiarrhythmic medications are only partially effective; therefore, medical treatment is not sufficient for many patients. Percutaneous catheter ablation, using endocardial ablation, is an accepted second-line treatment for patients who are not adequately controlled on medications and may also be used as first-line treatment. Catheter ablation (CA) is successful in maintaining sinus rhythm for most patients, but long-term recurrences are common and increase over time. Performed either by open surgical techniques or thoracoscopy, surgical ablation is an alternative approach to percutaneous CA.

Open Surgical Techniques

The classic Cox maze III procedure is a complex surgical procedure for patients with AF. It involves sequential atriotomy incisions that interrupt the aberrant atrial conduction pathways in the heart. The procedure is also intended to preserve atrial pumping function. It is indicated for patients who do not respond to medical or other surgical antiarrhythmic therapies and is often performed in conjunction with the correction of structural cardiac conditions such as valve repair or replacement.

This procedure is considered the criterion standard for the surgical treatment of drug-resistant AF, with a success rate of approximately 90%.

The maze procedure entails making incisions in the heart that:

- direct an impulse from the sinoatrial node to the atrioventricular node;
- preserve activation of the entire atrium; and
- block re-entrant impulses responsible for AF or atrial flutter.

The classic Cox maze procedure is performed on a nonbeating heart during cardiopulmonary bypass. Simplification of the maze procedure has evolved with the use of different ablation tools such as microwave, cryotherapy, ultrasound, and radiofrequency energy sources to create the atrial lesions instead of employing the incisional technique used in the classic maze procedure. The Cox maze IV procedure involves the use of radiofrequency energy or cryoablation to create transmural lesions analogous to the lesions created by the "cut-and-sew" maze.

Minimally Invasive (Thoracoscopic) Techniques

Less invasive, transthoracic, endoscopic, and off-pump procedures to treat drug-resistant AF have been developed. The evolution of these procedures involves both different surgical approaches and different lesion sets. Alternative surgical approaches include mini-thoracotomy and total thoracoscopy with video assistance. Open thoracotomy and mini-thoracotomy employ cardiopulmonary bypass and open-heart surgery, while thoracoscopic approaches are performed on the beating heart. Thoracoscopic approaches do not enter the heart and use epicardial ablation lesion sets, whereas the open approaches use either the classic "cut-and-sew" approach or endocardial ablation.

Lesion sets may vary independent of the surgical approach, with a tendency toward less extensive lesion sets targeted to areas most likely to be triggers of AF. The most limited lesion sets involve pulmonary vein isolation and exclusion of the left atrial appendage. More extensive lesion sets include linear ablations of the left and/or right atrium and ablation of ganglionic plexi. Some surgeons perform left atrial reduction in cases of left atrial enlargement.

The type of energy used for ablation also varies; radiofrequency energy is most commonly applied. Other energy sources such as cryoablation and high-intensity ultrasound have been used. For our purposes, the variations on surgical procedures for AF will be combined under the heading of "modified maze" procedures.

Hybrid Techniques

"Hybrid" ablation refers to the use of both thoracoscopic and percutaneous approaches in the same patient. Ablation is performed on the outer surface of the heart (epicardial) via the thoracoscopic approach, and on the inner surface of the heart (endocardial) via the percutaneous approach. The rationale for a hybrid procedure is that a combination of both techniques may result in a complete ablation. Thoracoscopic epicardial ablation is limited by the inability to perform all possible ablation lines because the posterior portions of the heart are not accessible via thoracoscopy. Percutaneous, endoscopic ablation is limited by incomplete ablation lines that often require repeat procedures. By combining both procedures, a full set of ablation lines can be performed, and incomplete ablation lines can be minimized.

The hybrid approach first involves thoracoscopy with epicardial ablation. Following this procedure, an electrophysiologic study is performed percutaneously followed by endocardial ablation as directed by the results of electrophysiology. Most commonly, the electrophysiology study and endocardial ablation are done immediately after the thoracoscopy as part of a single procedure. However, some hybrid approaches perform the electrophysiology study and endocardial ablation on separate days, as directed by the electrophysiology study.

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function, and include benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

Maze and Related Procedures as an Adjunct to Open Heart Surgery

Clinical Context and Therapy Purpose

The purpose of maze and related procedures in addition to on-bypass surgeries in individuals who have atrial fibrillation (AF) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review:

Populations

The relevant population of interest is individuals with symptomatic AF or flutter who are undergoing cardiac surgery with bypass.

Atrial fibrillation can be subdivided into 3 types: paroxysmal, persistent, and permanent. Paroxysmal AF episodes last <7 days and are self-terminating. Persistent AF episodes last for >7 days and are not self-terminating; long-standing persistent AF is persistent AF that lasts for more than a year. In permanent AF, normal rhythm cannot be restored. Individuals with paroxysmal AF may progress to persistent or permanent AF over time.

Interventions

The therapies being considered are Cox maze or modified maze procedures added to on-bypass surgeries.

The classic Cox maze III procedure is a complex surgical procedure for patients with AF. It involves sequential atriotomy incisions that interrupt the aberrant atrial conduction pathways in the heart. The procedure is also intended to preserve atrial pumping function. It is indicated for patients who do not respond to medical or other surgical antiarrhythmic therapies and is often performed in

conjunction with the correction of structural cardiac conditions such as valve repair or replacement. This procedure is considered the criterion standard for the surgical treatment of drug-resistant AF, with a success rate of approximately 90%.
The maze procedure entails making incisions in the heart that:

- direct an impulse from the sinoatrial node to the atrioventricular node;
- preserve activation of the entire atrium; and
- block re-entrant impulses responsible for AF or atrial flutter.

The classic Cox maze procedure is performed on a nonbeating heart during cardiopulmonary bypass. Simplification of the maze procedure has evolved with the use of different ablation tools such as microwave, cryotherapy, ultrasound, and radiofrequency energy sources to create the atrial lesions instead of employing the incisional technique used in the classic maze procedure. The Cox maze IV procedure involves the use of radiofrequency energy or cryoablation to create transmural lesions analogous to the lesions created by the "cut-and-sew" maze.

Comparators

The following practice is currently being used to treat individuals with symptomatic AF or flutter who are undergoing cardiac surgery with bypass: medical management or catheter ablation (CA). The success rate of CA remains low for long-standing persistent AF.

Outcomes

Relevant outcomes of interest are overall survival, medication use, and treatment-related morbidity. The 2017 joint expert consensus statement (including Heart Rhythm Society) on catheter and surgical ablation of AF affirmed that freedom from any atrial arrhythmia, defined as AF, atrial flutter, or atrial tachycardia, lasting for more than 30 seconds off antiarrhythmic drug therapy, is the gold standard for reporting the efficacy of ablation in AF trials. The statement also suggests that there should be a minimum of 12 months follow-up.[7,]

Many patients have asymptomatic AF episodes after ablation. Therefore, monitoring for symptoms alone is not sufficient to measure freedom from AF. AF monitoring can be performed with noncontinuous or continuous monitoring tools. Noncontinuous tools include electrocardiograms (ECGs), Holter devices, patient- and automatically activated devices, and external loop recorders. Continuous monitoring tools include implantable pacemakers or defibrillators and implantable loop recorders. [7,]

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

The evidence on the use of maze and related procedures in addition to on-bypass surgeries being done for other reasons (e.g., mitral valve replacements) consists of several RCTs evaluating AF ablation when performed as an add-on for patients undergoing open heart surgery, and systematic reviews of these trials.

Systematic Reviews

A Cochrane review by Huffman et al (2016) evaluated the evidence on concomitant AF surgery for patients undergoing cardiac surgery.[8,] Included were 22 trials that compared the effect of AF surgery with no AF surgery in adults undergoing cardiac surgery for another indication. Three trials used a "cut-and-sew" technique, 3 trials used microwave ablation, 2 trials used cryoablation, and the remainder used radiofrequency ablation (RFA). All trials were considered at high-risk of bias. There was moderate-quality evidence that AF surgical interventions increased freedom from AF, atrial flutter, and atrial tachycardia when patients were off antiarrhythmic medications (51.0% vs 24.1%; relative risk [RR], 2.04; 95% confidence interval [CI] , 1.63 to 2.55), but the effect on all-cause mortality was uncertain, and these procedures increased the likelihood of permanent pacemaker implantation (6% vs 4.1%; RR, 1.69; 95% CI, 1.12 to 2.54).

Phan et al (2014) reported on the results of a systematic review and meta-analysis of RCTs comparing surgical ablation with no ablation among patients who had AF and were undergoing mitral valve surgery.[9,] Nine studies were selected and analyzed: 5 evaluated RFA, 2 evaluated Cox maze "cut-and-sew," 1 evaluated cryoablation, and 1 evaluated pulmonary vein isolation and Cox maze "cut-and-sew." In the pooled analysis, the risk of 30-day all-cause mortality did not differ significantly between the ablation (4.4%) and nonablation (2.7%) groups (odds ratio [OR], 1.45; 95% CI, 0.55 to 3.83; p=.46). The number of patients in sinus rhythm at discharge was significantly higher in the group that received mitral valve repair plus surgical ablation (67.9%) than in the group that received mitral valve repair only (17.0%; OR, 13.96; 95% CI, 6.29 to 30.99; p<.001); similarly, at 3-, 6-, 12-, and beyond 12-month follow-ups, a greater proportion of the surgical ablation group was in sinus rhythm.

In an earlier systematic review, Reston and Shuhaiber (2005) reviewed 4 RCTs and 6 comparative studies to determine whether a concurrent mitral valve surgery and maze procedure would reduce the risk of stroke or death in patients with chronic or paroxysmal AF.[10,] They found a reduction in stroke rates and a small increased risk in the need for pacemakers among patients receiving simultaneous maze procedures. Also, they noted that alternative energy sources (e.g., radiofrequency [RF]) might reduce the risk of postoperative bleeding associated with classic maze incisions.

Randomized Controlled Trials

Some of the larger RCTs evaluating AF ablation in conjunction with open surgery and included in the 2016 Cochrane review are described below.

Gillinov et al (2015) published results of a large controlled trial that randomized 260 patients with persistent or long-standing AF who required mitral valve surgery to ablation (either pulmonary vein isolation or ablation with a maze lesion set) during surgery (n=133) or to no ablation (n=127).[11,] Compared with controls, significantly more patients in the ablation group were free from AF at both 6 and 12 months (63.2% vs 29.4%, p<.001). The relative success ratio (ablation group vs control group) was 2.15 (95% CI, 1.54 to 3.00) on the basis of observed data. At 1 year, mortality rates did not differ significantly between the ablation group (6.8%) and the control group (8.7%; p=.57). A composite safety endpoint did not differ significantly between groups at 30 days, nor did serious adverse event rates at 1 year.

Budera et al (2012) reported on a RCT that randomized 224 patients from 3 clinical centers to cardiac surgery plus ablation or to cardiac surgery alone.[12,] Patients were eligible for inclusion if they had at least 2 documented episodes of AF in the last 6 months, as well as appropriate indications for cardiac surgery. Cardiac surgery procedures included coronary artery bypass graft (CABG), valve replacement/repair, or combined CABG and valve procedures. The primary efficacy outcome was sinus rhythm at 1 year following surgery, and the primary safety outcome was a composite outcome of death, myocardial infarction (MI), stroke, or new-onset renal failure requiring hemodialysis at 30 days postsurgery. Sinus rhythm at 1 year was documented in 60.2% (56/93) of patients in the surgery plus ablation group compared with 35.5% (27/76) of patients in the surgery alone group. Adverse

event rates were similar in both groups at 30 days and at 1-year follow-up. Secondary clinical outcomes, including mortality and New York Heart Association functional class, did not differ between groups at 1 year.

Van Breugel et al (2010) evaluated changes in quality of life in a related patient population.[13,] One hundred fifty patients with AF who were scheduled to undergo valve or CABG surgery were randomized to surgery alone or surgery plus a modified maze procedure. The primary endpoint was quality of life, as measured by the 36-Item Short-Form Health Survey, the EuroQoL-5D, and the Multidimensional Fatigue Inventory. A total of 132 patients had usable survey results. Both groups improved on all quality of life measures, but in general, there were no significant differences between groups. The only exception was on the EuroQoL-5D pain/discomfort subscale, which showed a greater degree of worsening in the control group than in the maze group.

Nonrandomized Comparative Studies

Saint et al (2013) attempted to quantify the incremental risk conferred by adding a Cox maze IV procedure to open mitral valve repair in a comparison of 213 patients with mitral valve disease and preoperative AF who underwent mitral valve surgery only (n=109) or mitral valve surgery with a Cox maze IV procedure (n=104).[14,] The operative mortality rate for the mitral valve procedure alone was predicted for each group based on the Society of Thoracic Surgeons Risk Calculator; the risk attributed to the addition of the Cox maze IV procedure was calculated by comparing the predicted mortality rate from the isolated mitral valve procedure with the actual mortality rate. At baseline, patients who had an isolated mitral valve procedure differed significantly from those who underwent the mitral valve procedure plus a Cox maze IV procedure regarding medical comorbidities and etiology of the mitral valve disease. The observed 30-day mortality rate for patients not offered a Cox maze IV procedure was 4.6% (expected, 5.5%), yielding an observed-expected 30-day mortality ratio of 0.84 (95% CI, 0.13 to 1.54). The observed 30-day mortality rate for patients who underwent a concomitant Cox maze IV procedure and mitral valve surgery was 2.9%. The Society of Thoracic Surgeons calculator predicted the score for isolated mitral valve surgery in this group was 2.5%, yielding an observed-expected 30-day mortality ratio of 1.16 (95% CI, 0.13 to 2.44). Interpretation of this study was limited because patients who received concomitant Cox maze IV procedures with mitral valve surgery were from a select low-risk population; however, findings did suggest that in the appropriate patient population, the Cox maze IV procedure can be added to mitral valve surgery with limited additional short-term mortality risk.

Noncomparative Studies

Since the publication of the RCTs previously described, several noncomparative studies have reported outcomes from surgical ("cut-and-sew") maze and modified RF maze procedures as an adjunct to planned cardiac surgery. Kim et al (2007) reported on long-term outcomes after 127 Cox maze cut-and-sew procedures in conjunction with mitral valve replacement.[15,] Patient disposition was well-documented in the analysis. Thirty percent of patients experienced late AF recurrence at a mean of 44 months. Freedom from AF was 93%, 82%, 71%, and 63% at 1, 3, 5, and 7 years, respectively, and pacemakers were implanted in 4.7% of patients. Other case series have reported success rates of the procedure in different populations, with rates of freedom from AF ranging from 53% to 79% at the latest follow-up.[16,17,18,19,20,]

Section Summary: Maze and Related Procedures as an Adjunct to Open Heart Surgery

Surgical treatment of AF can be performed in conjunction with valvular surgery or CABG with little additional risk. Evidence from RCTs assessing open heart surgery plus surgical treatment of AF versus surgery alone has established there is a high rate of success in maintaining sinus rhythm and avoiding the need for antiarrhythmic medications. Evidence for a benefit in other health outcomes, such as stroke rate or quality of life, is currently insufficient to form conclusions.

Maze and Related Procedures as a Stand-Alone Treatment for Atrial Fibrillation

Clinical Context and Therapy Purpose

The purpose of maze and related procedures as a stand-alone treatment in individuals who have AF is to provide a treatment option that is an alternative to or an improvement on existing therapies. The stand-alone procedures fall on a continuum of invasiveness, ranging from open repair with sternotomy to minimally invasive procedures done with video-assisted thoracoscopy. This section focuses on thoracoscopic maze procedures. Hybrid approaches include concomitant epicardial and endocardial procedures and are discussed separately.

The following PICO was used to select literature to inform this review:

Populations
The relevant population of interest is individuals with symptomatic drug-resistant AF or flutter not undergoing cardiac surgery with bypass.

Interventions
The therapies being considered are stand-alone minimally invasive, off-pump thoracoscopic maze procedures.

Less invasive, transthoracic, endoscopic, and off-pump procedures to treat drug-resistant AF have been developed. The evolution of these procedures involves both different surgical approaches and different lesion sets. Alternative surgical approaches include mini-thoracotomy and total thoracoscopy with video assistance. Open thoracotomy and mini-thoracotomy employ cardiopulmonary bypass and open-heart surgery, while thoracoscopic approaches are performed on the beating heart. Thoracoscopic approaches do not enter the heart and use epicardial ablation lesion sets, whereas the open approaches use either the classic "cut-and-sew" approach or endocardial ablation.

Lesion sets may vary independent of the surgical approach, with a tendency toward less extensive lesion sets targeted to areas most likely to be triggers of AF. The most limited lesion sets involve pulmonary vein isolation and exclusion of the left atrial appendage. More extensive lesion sets include linear ablations of the left and/or right atrium and ablation of ganglionic plexi. Some surgeons perform left atrial reduction in cases of left atrial enlargement.

The type of energy used for ablation also varies; radiofrequency energy is most commonly applied. Other energy sources such as cryoablation and high-intensity ultrasound have been used. For our purposes, the variations on surgical procedures for AF will be combined under the heading of "modified maze" procedures.

Comparators
The following practice is currently being used to treat individuals with symptomatic drug-resistant AF or flutter not undergoing cardiac surgery with bypass: medical management or CA. The success rate of CA remains low for long-standing persistent AF.

Outcomes
Relevant outcomes of interest are overall survival, medication use, and treatment-related morbidity. The 2017 joint expert consensus statement (including Heart Rhythm Society) on catheter and surgical ablation of AF affirmed that freedom from any atrial arrhythmia, defined as AF, atrial flutter, or atrial tachycardia, lasting for more than 30 seconds off antiarrhythmic drug therapy, is the gold standard for reporting the efficacy of ablation in AF trials. The statement also suggests that there should be a minimum of 12 months follow-up.[7,]

Although freedom from AF is an important outcome following AF treatment procedures, the evaluation of stand-alone maze and related procedures also requires assessment of surgery-related complications.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

The evidence on the use of maze and related procedures as stand-alone treatments for AF includes evaluations of open surgical ablation, minimally invasive surgical ablation, and "hybrid" approaches.

Review of Evidence

Systematic Reviews

Van Laar et al (2017) reported on a meta-analysis of stand-alone thoracoscopic maze procedures for the treatment of AF.[21,] Reviewers included 14 studies (3 RCTs, 7 prospective cohort studies, 11 observational studies; N =1171 patients). All studies used RFA and included bilateral pulmonary vein isolation and left atrial appendage exclusion or removal. The pooled drug-free success rate at 1 year was 77% (95% CI, 72% to 83%), with a similar success rate at 2 years. Subgroup analysis of the type of AF showed the highest success rate for paroxysmal AF at 81% (95% CI, 73% to 86%). The in-hospital complication rate was 2.9% and included conversion to sternotomy, rethoracotomy due to excess bleeding, pulmonary problems, stroke, pacemaker implantation, pneumonia, and reintubation for hypoxia.

Yi et al (2020) conducted a systematic review of 6 RCTs (N=466) comparing thoracoscopic surgical ablation with CA with regard to clinical outcomes in patients with AF.[22,] For the review's primary efficacy outcome of freedom from atrial tachyarrhythmia without antiarrhythmic drug use, treatment success was significantly higher in the surgical ablation group as compared to the CA group (75% vs. 57.1%; OR, 0.41; 95% CI, 0.2 to 0.85; p=.02). However, a significantly increased number of serious adverse events were seen in the surgical versus CA group (OR, 0.16; 95% CI, 0.006 to 0.46; p=.0006).

Phan et al (2016) conducted a systematic review of studies comparing thoracoscopic surgical ablation with CA, including the Atrial Fibrillation Catheter Ablation Versus Surgical Ablation Treatment (FAST) trial.[23,] Eight comparative studies, with a total of 321 video-assisted thoracoscopic surgical ablation patients and 378 CA patients, met inclusion criteria. For the review's primary efficacy endpoint of freedom from AF without the use of antiarrhythmic drugs, the treatment success was significantly higher in the surgical ablation group (81%) than in the CA group (64.3%) at 6 months postprocedure (RR, 1.23; 95% CI, 1.02 to 1.49; p=.03). This difference was maintained at 12 months postprocedure. Patients treated with surgical ablation had significantly higher rates of major complications (including death, stroke, transient ischemic attack, major bleeding, pericardial effusion, cardiac tamponade, pulmonary vein stenosis, pneumothorax, hemothorax, pneumonia, MI, conversion to complete thoracotomy) compared with CA -treated patients (28.2% vs 7.8%; RR, 3.30; 95% CI, 1.73 to 6.29; p<.001).

Randomized Controlled Trials

Tables 3 and 4 outline characteristics and results of key RCTs; tables 5 and 6 outline limitations related to their relevance, design, and conduct. The Atrial Fibrillation Catheter Ablation Versus Surgical Ablation Treatment (FAST) RCT, reported by Boersma et al (2012) provides most of the direct evidence comparing surgical AF ablation to CA (Table 3). FAST compared stand-alone surgical ablation with percutaneous ablation.[24,] This trial enrolled 124 patients from 2 clinical centers in Europe, who had symptomatic AF for at least 1 year and had failed at least 1 antiarrhythmic medication. Patients were randomized to surgical ablation using video-assisted thoracoscopy under

general anesthesia or to percutaneous CA. Both techniques used RF energy. All patients in the surgical ablation group also had their left atrial appendage removed. The primary outcome was freedom from AF while off all antiarrhythmic medications during 12 months of follow-up. Secondary outcomes were freedom from AF, including patients still on medications and adverse events. Prior unsuccessful CA had been performed in 67% of patients.

At 1 year, (Table 4) freedom from AF while off all antiarrhythmic drugs was achieved by 65.6% (40/61) of the surgical ablation group compared with 36.5% (23/63) of the CA group (p=.002). Freedom from AF, on or off medications, was achieved by 78.7% (48/61) of the surgical ablation group compared with 42.9% (27/63) of the CA group (p<.001). Serious adverse events were more common in the surgical group (23.0% [14/61]) than the CA group (3.2% [2/63]; p=.001). In each group, there was 1 episode of tamponade and stroke. Additional complications in the surgical group included 6 patients with pneumothorax, 2 who required pacemaker insertion, and 1 patient each who had hemothorax, rib fracture, pneumonia, or required sternotomy for bleeding. In 2019, Castella et al (2019) reported extended follow-up of patients randomized in the FAST trial.[25,] After a mean follow-up of 7.0 years from randomization, recurrence of atrial arrhythmias was significantly lower in the thoracoscopic ablation group compared to the CA group (56% [34/61] versus 87% [55/63]; adjusted hazard ratio [HR] , 0.40; 95% CI, 0.25 to 0.64; p<.001). Additional ablation procedures were more common in the CA group (49% versus 13%; p<.001). Rates of the composite outcome of death, MI, or cerebrovascular event (transient ischemic attack, ischemic or hemorrhagic stroke) were similar between groups (15% following thoracoscopy [9/61] and 16% following CA [10/63]; adjusted HR for time to first event, 1.11; 95% CI, 0.40 to 3.10). Although encouraging, due to important study conduct limitations including inadequate control for selection bias (i.e., fewer patients with persistent AF patients in the thoracoscopic ablation group), insufficient power to detect a difference in clinical outcomes, and lack of data on type of arrhythmia recurrence, further RCT data are required to verify these findings
In a subsequent smaller RCT, Pokushalov et al (2013) randomized patients with a prior failed first CA procedure for AF to repeat CA (n=32) or to surgical ablation with video-assisted thoracoscopy (n=32).[26,] After 12 months, a higher proportion of patients who underwent surgical ablation were free of AF and atrial tachycardia without antiarrhythmic drugs (81% vs 47%, p=.004). Although the total number of adverse events did not differ significantly between groups, the number of serious adverse events was higher in the surgical ablation group (7 vs 1, p=.02).

Additionally, Adiyaman et al (2018) published results of a small, single-center RCT that compared minimally invasive thoracoscopic pulmonary vein isolation with left atrial appendage ligation (surgical MIPI) to percutaneous CA in 52 patients with symptomatic paroxysmal or early persistent AF (continuous AF duration, <3 months) with failure of at least 1 class 1 or 3 antiarrhythmic drugs, but no previous CA.[27,] An implantable loop recorder was used for follow-up continuous rhythm monitoring for 2 years. In contrast to the previously discussed RCTs, such as FAST, that found better efficacy with surgical ablation, this RCT found no difference in arrhythmia-free survival between the CA and MIPI groups (56% vs 29.2%; HR, 0.56; 95% CI, 0.26 to 1.20) and major complications were greater in the MIPI group (20.8% in MIPI v s 0% in CA; difference, 20.8%; 95% CI, 4.8% to 36.9%; p=.029).

The Catheter Ablation Versus Thoracoscopic Surgical Ablation in Long Standing Persistent Atrial Fibrillation (CASA-AF) trial, reported by Haldar et al (2020), is the first RCT that evaluated the efficacy and safety of thoracoscopic surgical ablation versus CA as the index procedure in 120 patients with long-standing persistent AF.[28,] Tables 3 and 4 summarize the key characteristics and results of the CASA-AF trial. Beyond the tabular results, a reduction in AF burden of ≥75% was seen in 67% in the surgical ablation group versus 77% in the CA group (OR, 1.13; 95% CI, 0.67 to 4.08; p=.3). Improvements in AF symptoms were increased following CA; surgical ablation was more expensive and was associated with fewer quality-adjusted life years (p=.02) compared with CA.

Table 3. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator

Study	Countries	Sites	Dates	Participants	Interventions	
Haldar (2020); CASA-AF[28],	UK	4	2015-2018	Individuals with long-standing PersAF, EHRA symptom score >2, and left ventricular ejection fraction ≥40%	Stand-alone surgical ablation, N=60	CA, N=60
Boersma (2012); FAST[24],	EU	2	2007-2010	Individuals with symptomatic AF for at least 1 year and had failed at least 1 antiarrhythmic medication; 67% prior failed CA	Stand-alone surgical ablation, N=63	CA, N=63
Pokushalov (2013)[26],	Russia	1	2011-2013	Individuals with a history of symptomatic PAF/PersAF after a previous failed first RF ablation procedure	Stand-alone surgical ablation, N=32	CA, N=32
Adiyaman (2018)[27],	The Netherlands	1	NR	Individuals with symptomatic PAF or early PersAF (continuous AF duration, <3 months) with failure of at least 1 class 1 or 3 antiarrhythmic drugs, but no previous CA	Stand-alone surgical ablation, N=26	CA, N=26

AF: atrial fibrillation; CA: catheter ablation; EHRA: European Heart Rhythm Association; EU: Europe; NR: not reported; PAF: paroxysmal atrial fibrillation; PersAF: persistent atrial fibrillation; RCT: randomized controlled trial; RF: radiofrequency; UK: United Kingdom.

Table 4. Summary of Key RCT Results

Study	Freedom from AF while off all antiarrhythmic drugs	Mortality	Serious Adverse Events	Recurrence of atrial arrhythmias
Haldar (2020); CASA-AF[28],	1-year		1-year	
Surgical ablation	26% (14/54)	1	18% (10/55)	NR
CA	28% (17/60)	0	15% (9/60)	NR
Relative measure	OR, 1.128; 95% CI, 0.46 to 2.82, p=.84	NR	p=.65	NR
Boersma (2012); FAST[24],	1-year	1-year	1-year	7-years
Surgical ablation	65.6% (40/61)	0	23.0% (14/61)	56% (34/61)
CA	36.5% (23/63)	1.6% (1/63)	3.2% (2/63)	87% (55/63)
Relative measure	p=.002	NR	p=.001	HR, 0.40; 95% CI, 0.25 to 0.64; p<.001
Pokushalov (2013)[26],	1-year	1-year	1-year	1-year
Surgical ablation	81% (26/32)	0	7[1]	3% (1/32)
CA	47% (15/32)	0	1[1]	9% (3/32)
Relative measure	p=.004	N/A	p=.02	NR
Adiyaman (2018)[27],	2 years	2 years	2 years	2 years
Surgical ablation	29.2%	0	NR	20.8%
CA	56%	0	NR	0%
Relative measure	HR, 0.56; 95% CI, 0.26 to 1.20	N/A	NR	Difference, 20.8%; 95% CI, 4.8% to 36.9%

AF: atrial fibrillation; CA: catheter ablation; CI: confidence interval; HR: hazard ratio; N/A: not applicable; NR: not reported; OR: odds ratio; RCT: randomized controlled trial.
[1]Number of events

Table 5. Study Relevance Limitations of Key RCTs

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Haldar 2020; CASA-AF[28,]	4. Study population included patients at 4 highly specialized centers, which may have an impact on generalizability				
Boersma (2012); FAST[24,]	4. Most patients had undergone a prior unsuccessful CA and had paroxysmal AF				
Pokushalov (2013)[26,]				4. Used implantable loop recorder to measure AF, which "may detect more episodes than many centers routinely capture using external ECG methods and does not exactly conform to HRS guidelines"	
Adiyaman (2018)[27,]					

AF: atrial fibrillation;CA: catheter ablation; ECG: Electrocardiography; HRS: Heart Rhythm Society; RCT: randomized controlled trial.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 6. Study Design and Conduct Limitations of Key RCTs

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Haldar (2020); CASA-AF[28,]		1. Not blinded to treatment assignment; 2. Not blinded outcome assessment				

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Boersma (2012); FAST[24,]	4. Surgical patients had more paroxysmal AF (74% vs 59%), both as the initial diagnosis and in the preprocedural Holter recording, with a lower CHADS2 score and more prior failed ablation (74% vs 63%) and had fewer males (74% vs 87%)	1. Not blinded to treatment assignment; 2. Not blinded outcome assessment				
Pokushalov (2013)[26,]	3. Allocation concealment unclear: "coded envelope system"; "although not statistically significant, the CA group enrolled more patients with persistent AF" (44% vs 37%)	1. Not blinded to treatment assignment; 2. Not blinded outcome assessment	1. Not registered until study completion			
Adiyaman (2018)[27,]	3. Allocation concealment unclear; not described	1. Not blinded to treatment assignment; 2. Not blinded outcome assessment				

AF: atrial fibrillation; CA: catheter ablation; RCT: randomized controlled trial.
The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.
[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other

Nonrandomized Comparative Studies

Several small, single-center observational studies have compared maze and related minimally invasive surgical ablation procedures as a stand-alone treatment for AF to matched comparison groups of patients who received CA (Tables 7 and 8).[29,30,31,32,] Studies varied in the prognostic variables used to match the patient groups, the type of surgical ablation used, the proportion of patients with

prior failed CA (0% to 100%), and follow-up duration (range 1.5 years to 5.5 years). All studies consistently found higher success rates with surgical ablation.

Table 7. Summary of Characteristics of Comparative Observational Studies with Matched Comparison Groups

Study	Study Type	Country	Dates	Participants	Surgical Ablation Type	Catheter Ablation	Follow-Up	Matching variables
Mahapatra (2011)[30,]	Case series with matched control groups	US	2007-2009	Persistent or LSP AF who have failed ≥ 1 prior CA	Combined epicardial-surgical and endocardial-catheter, N=15	Repeat CA, N=30	20.7 m	LA size by echo, AF duration, AF type, use of post-ablation AAD, lack of prior cardiac surgery, and left ventricular ejection fraction
Stulak (2011)[31,]	Case series with matched control groups	US	1993-2007	Lone AF, 10% with prior CA	Isolated biatrial cut-and-sew Cox-Maze III procedure, N=97	CA, N=194	5.6 y for SA; 3.1 y for CA	Median age, age range, male, intermittent AF
Wang (2011)[32,]	Case series with matched control groups	China	2006-2009	Long-standing persistent AF (i.e., continuous AF for ≥ 1 year), resistant to either electrical or pharmacological cardioversion; no previous CA	Video-assisted minimally invasive ablation, N=83	CA, N=83	2.2 y	AF duration, left atrial dimension, and sex

AAD: anti-arrhythmic drug; AF: atrial fibrillation; CA: catheter ablation; LA: left atrial; LSP: long-standing persistent; SA: surgical ablation; US: United States.

Table 8. Summary of Results of Comparative Observational Studies with Matched Comparison Groups

Study	Free of atrial arrhythmia and off of AAD	Freedom from recurrence	Need for repeat ablation	Death	Overall Complications
Mahapatra (2011)[30,]	45	45	45	45	45
SA+CA	86.7% (13/15)	93.3% (14/15)	0	0	0
Repeat CA	53.3% (16/30)	56.7% (17/30)	10% (3/30)	0	3.33% (1/30)
Measure of association	p=.04	p=.01	p=.15	NR	NR
Stulak (2011)[31,]	N=265	N=265	N=265	N=265	N=265
SA	82%	NR	6.5% (6/93)	0	NR
CA	56%	NR	24% (41/172)	0	NR
Measure of association	p<.001		NR		NR
Wang (2011)[32,]	166	166	166	166	
SA	61.4%	NR	6.0% (5/83)	1.2% (1/83)	NR
CA	44.6%	NR	27.7% (23/83)	2.4% (2/83)	NR
Measure of association	p=.043	HR, 0.555 (95% CI, 0.354 to 0.872)	NR	NR	NR

AAD: anti-arrhythmic drug; CA: catheter ablation; CI: confidence interval; HR: hazard ratio; NR: not reported; SA: surgical ablation.

Other observational studies have reported outcomes for stand-alone AF treatment. Kwon et al (2021) reported a case series of 353 patients with paroxysmal or persistent AF who underwent RFA (n=125), cryoablation (n=97), or totally thoracoscopic surgical ablation (n=131).[29,] Unlike the studies described in Tables 7 and 8, this study did not include matched controls. Patients who underwent thoracoscopic ablation were more likely to have a history of stroke or TIA (p<.001), persistent (as opposed to paroxysmal) AF (p<.001), and enlarged left atrium (p<.001) based on diameter and volume when compared with the CA groups. At 12-month follow-up, similar proportions of patients were free from AF in the RFA (84%), cryoablation (74%), and thoracoscopic ablation groups (85%; p=.07). After controlling for demographic and clinical characteristics, RFA (HR, 1.33; 95% CI, 0.72 to 2.30) and cryoablation (HR, 1.77; 95% CI, 1.03 to 3.06) were associated with an increased risk of AF recurrence relative to thoracoscopic ablation, though the difference was not statistically significant for RFA. Procedural complications occurred in 2% to 4% of patients across treatment groups with no difference among treatments (p=.74).

In a retrospective cohort study, Lawrance et al (2014) compared patients who underwent a Cox maze IV procedure either by right mini-thoracotomy (n=104) or sternotomy (n=252) at a single-center from 2002 to 2014.[33,] Freedom from atrial tachyarrhythmias off antiarrhythmic drugs did not differ significantly between groups. The overall complication rate was lower in the mini-thoracotomy group (6%) than in the sternotomy group (13%; p=.044).

De Maat et al (2013) published results of a retrospective observational study of minimally invasive surgical treatment for AF in 86 patients with symptomatic, drug-refractory paroxysmal or permanent AF.[34,] Patients were treated at 3 centers, via bilateral video-assisted mini-thoracotomy, from 2005 to 2007 (n=13 patients) and subsequently via a totally thoracoscopic approach from 2007 to 2011 (n=73 patients). Fifteen (17%) patients had had transcatheter ablation performed. The percentages of patients free from atrial arrhythmias without the use of antiarrhythmic drugs were 71% at 12 months, 72% at 24 months, and 69% at 36 months. Half of the 24 treatment failures underwent an additional transcatheter ablation. Major periprocedural adverse events occurred in 8%, which included 3 sternotomy or mini-thoracotomy procedures due to complications, 2 cases of late pericardial tamponade, 1 case of pericardial effusion requiring video-assisted thoracoscopic surgery, and 1 stroke.

Massimiano et al (2013) reported on outcomes for 292 consecutive patients from a single institution who underwent minimally invasive mitral valve surgery (n=177), surgical ablation for AF (n=81), or both (n=34).[35,]Among the 115 patients who underwent AF ablation, the percentages of patients in sinus rhythm at 6, 12, and 24 months were 93%, 93%, and 88%, respectively; the percentage of patients in sinus rhythm and not taking class I and III antiarrhythmic medications at 6, 12, and 24 months were 85%, 85%, and 77%, respectively.

Single-Arm Studies

Numerous single-arm case series have reported high success rates following a minimally invasive surgical procedure.[36,37,38,39,40,41,42,43,44,45,46,] Most series lacked a control group, generally only reported short-term outcomes, and did not consistently report adverse events. Vos et al (2020) reported on outcomes for 82 consecutive patients that underwent totally thoracoscopic ablation including left appendage closure.[46,]After a mean follow-up of 4.0 years, 60% of patients were free from atrial arrhythmia; long-term complications were not studied. Harlaar et al (2022) reported long-term outcomes for a consecutive series of 77 individuals with symptomatic long-standing persistent AF.[47,] At 5 years, freedom from AF was 50% in those who had a single thoracoscopic procedure and 68% in those who had a thoracoscopic procedure and also had an endocardial touch-up procedure. Only short-term, procedure-related complications were described.

Several single-arm case series of minimally invasive epicardial ablation have been reported in patients who had failed CA. Ad et al (2011) reported on 40 patients who had failed CA, with a mean of 2.3 prior ablations per patient.[48,] The percentages of patients maintaining sinus rhythm at 6, 12, and

24 months were 76% (29/38), 89% (23/26), and 93% (13/14), respectively. Castella et al (2010) enrolled 34 patients who had failed a mean of 2 prior CAs; 17 with paroxysmal AF, 12 with persistent AF, and 5 with long-standing persistent AF.[49,] At 1-year follow-up, sinus rhythm was maintained in 82% of patients with paroxysmal AF, 60% with persistent AF, and 20% with long-standing persistent AF. MacGregor et al (2022) reported long-term outcomes of 236 individuals who underwent a stand-alone Cox-Maze IV procedure (via sternotomy or a minimally invasive approach) for refractory AF.[50,] Median follow-up was approximately 5 years and maximum follow-up was 10 years; 59% of participants had failed a previous CA. Freedom from AF was 94% (187/199), 89% (81/91), and 77% (24/31) at 1, 5, and 10 years, respectively.

Section Summary: Maze and Related Procedures as a Stand-Alone Treatment for Atrial Fibrillation

The evidence on the role of maze and related procedures as stand-alone options consists of 4 RCTs (samples sizes ranging from 52 to 126), 3 observational studies (samples sizes ranging from 45 to 291), and many case series, some with matched control groups. The RCTs have had mixed results. Two RCTs reported significantly higher rates of freedom from AF at 1-year with surgical ablation but also reported significantly higher rates of serious adverse events. The remaining 2 RCTs found no significant differences between treatment groups in rates of freedom from AF and either did not assess or did not find significant differences in serious adverse events. The comparative observational studies consistently found significantly higher rates of freedom from atrial arrhythmias but lacked assessment of serious adverse events. This evidence does not support the superiority of 1 technique over the other but suggests that other factors (e.g., type of AF, prior treatments, inability to take anticoagulation, patient preference) may influence the decision for the type of procedure. Additionally, the studies do not permit conclusions about harm due to heterogeneous measurement across studies, with mixed results. Case series with matched control groups have reported higher success rates in maintaining sinus rhythm compared with CA. The single-arm case series have corroborated the high success rates following surgical treatment but does not provide sufficient evidence to form conclusions on the comparative efficacy of surgical treatment versus other treatments.

Some case series and a RCT have included only patients who have failed previous CA. These studies have also reported high success rates following thoracoscopic ablation, suggesting that patients who fail CA may still benefit from thoracoscopic ablation. However, the RCT reported higher adverse event rates than CA, and the risk-benefit ratio is not well-defined.

Additional multicenter RCTs are needed that compare stand-alone minimally invasive, off-pump thoracoscopic maze procedures to catheter ablation that use established techniques to control for bias, adhere to recommended reporting of harms, and clearly define the population for whom the technology is intended.

Hybrid Thoracoscopic and Endocardial Ablation Procedures

Clinical Context and Therapy Purpose

The purpose of hybrid thoracoscopic and endocardial ablation procedures in individuals who have AF is to provide a treatment option that is an alternative to or an improvement on existing therapies. "Hybrid" ablation refers to the use of both thoracoscopic and percutaneous approaches in the same patient. Ablation is performed on the outer surface of the heart (epicardial) via the thoracoscopic approach, and on the inner surface of the heart (endocardial) via the percutaneous approach. The rationale for a hybrid procedure is that a combination of both techniques may result in a complete ablation. Thoracoscopic epicardial ablation is limited by the inability to perform all possible ablation lines because the posterior portions of the heart are not accessible via thoracoscopy. Percutaneous, endoscopic ablation is limited by incomplete ablation lines that often require repeat procedures. By combining both procedures, a full set of ablation lines can be performed, and incomplete ablation lines can be minimized.

The following PICO was used to select literature to inform this review:

Populations
The relevant population of interest is individuals with symptomatic drug-resistant AF or flutter not undergoing cardiac surgery with bypass. Hybrid techniques are of particular interest in individuals with persistent and long-standing persistent AF.

Interventions
The therapies being considered are hybrid thoracoscopic and endocardial ablation procedures. The hybrid approach first involves epicardial ablation. The epicardial portion of the hybrid approach can be performed thoracoscopically or endoscopically through a subxiphoid incision. The procedure is called 'hybrid convergent' when utilizing endoscopic subxyphoid access.

Following the epicardial procedure, an electrophysiologic study is performed percutaneously followed by endocardial ablation as directed by the results of electrophysiology. Most commonly, the electrophysiology study and endocardial ablation are done immediately after the thoracoscopy as part of a single procedure. However, some hybrid approaches perform the electrophysiology study and endocardial ablation on separate days, as directed by the electrophysiology study.

Comparators
The following practice is currently being used to treat individuals with symptomatic drug-resistant AF or flutter not undergoing cardiac surgery with bypass: medical management or CA. The success rate of CA remains low for long-standing persistent AF.

Outcomes
Relevant outcomes of interest are overall survival, medication use, and treatment-related morbidity. The 2017 joint expert consensus statement (including Heart Rhythm Society) on catheter and surgical ablation of AF affirmed that freedom from any atrial arrhythmia, defined as AF, atrial flutter, or atrial tachycardia, lasting for more than 30 seconds off antiarrhythmic drug therapy, is the gold standard for reporting the efficacy of ablation in AF trials. The statement also suggests that there should be a minimum of 12 months follow-up.[7,]

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence
Systematic Reviews
Mhanna et al (2021) conducted a systematic review and meta-analysis of 8 controlled studies (including the DeLurgio 2020 RCT and the Kress 2016 and Maclean 2020 nonrandomized studies, discussed below) of 797 patients with AF undergoing hybrid epicardial/endocardial (convergent) ablation (n=366) or standard endocardial ablation (n=431) (Table 9).[51,] Across the studies, the mean age of study participants was 61 years, 77% were male, 93% had persistent AF, and 18% had undergone a previous ablation. The included studies were all assessed as having low to moderate risk of bias. Based on pooled analyses, hybrid ablation was associated with greater freedom from atrial arrhythmia, but also an increased risk of adverse events that included bleeding, pericardial effusion, and cardiac tamponade (Table 10). The study authors noted that across studies 5 deaths were

reported among hybrid ablation patients while no endocardial ablation patients died, but no risk estimate was reported.

Eranki et al (2022) conducted a systematic review and meta-analysis of 4 RCTs and propensity score-matched studies (N=422) of hybrid convergent ablation.[52,] All of the included studies are described in more detail in the following sections. Hybrid convergent participants had significantly higher rates of freedom from AF than endocardial ablation participants (OR=2.8; 95% CI, 1.8 to 4.2; p<.01). Major post-operative complications were also significantly higher in hybrid convergent participants (OR=5.1; 95% CI; 1.7 to 15.5; p<.01). One death was reported in the hybrid convergent participants; no deaths were reported in the in the endocardial ablation participants.

Table 9. SR & M-A Characteristics

Study	Dates	Studies	Participants	N (Range)	Design	Duration
Mhanna et al (2021)[51,]	2011-2020	8	Patients with AF undergoing hybrid convergent ablation or standard endocardial ablation	797 (45-222)	RCTs or controlled observational studies	16 to 30 months
Eranki et al (2022)[52,]	Through 2022	4	Patients with AF undergoing hybrid convergent ablation or standard endocardial ablation	422 (50-153)	RCTs or propensity score-matched studies	NR

AF: atrial fibrillation; MA: meta-analysis; NR: not reported; RCT: randomized controlled trial; SR: systematic review;

Table 10. SR & M-A Results

Study	Freedom from Atrial Arrhythmia	Periprocedural Adverse Events[a]	Length of Hospital Stay
Mhanna et al (2021[51,]			
Total N	N=789 (8 studies)	N=797 (8 studies)	N=355 (3 studies)
Pooled effect (95% CI)	RR 1.48; 95% CI 1.13 to 1.94	RR, 3.64 (95% CI, 2.06 to 6.43)	MD, 3.91 (95% CI, 1.68 to 6.14)
I^2	77%	0%	99%
Eranki et al (2022)[52,]			NR
Total N	N=418 (4 studies)	N=417 (4 studies)	
Pooled effect (95% CI)	OR 2.78; 95% CI 1.82 to 4.24	OR 5.14; 95% CI 1.70 to 15.54	
I^2	0%	0%	

CI: confidence interval; MD: mean difference; NR: not reported; OR: odds ratio; RR: risk ratio.
[a] The most common periprocedural adverse events were bleeding, pericardial effusion, and cardiac tamponade

Randomized Controlled Trials

DeLurgio et al (2020) evaluated the efficacy and safety of a minimally invasive epicardial/endocardial ablation approach with pericardial access achieved via a transdiaphragmatic or subxiphoid incision (hybrid convergent) as compared to CA in 153 patients with persistent and long-standing persistent AF in the Convergence of Epicardial and Endocardial Ablation for the Treatment of Symptomatic Persistent AF (CONVERGE; NCT01984346) trial.[53,] Patients were randomly assigned to hybrid convergent (n=102) or CA (n=51) at 27 sites in the United States and United Kingdom. The primary effectiveness endpoint was freedom from AF/atrial flutter/atrial tachycardia absent of class I/II antiarrhythmic drugs through the 12 months post-procedure. Secondary efficacy endpoints included AF burden reduction (defined as the proportion of patients achieving at least 90% reduction in AF burden at 12 months when compared with baseline) and AF freedom at 12 months. The primary safety endpoint was the incidence of major adverse events which included cardiac tamponade; severe pulmonary vein stenosis; excessive bleeding; MI, stroke, transient ischemic attack, atrioesophageal fistula, phrenic nerve injury, and death. No deaths, cardiac perforations, or atrioesophageal fistulas occurred in the trial. The safety rate was primarily driven by inflammatory pericardial effusions observed between 1 and 3 weeks postprocedure in the hybrid convergent arm; best practices for management of this adverse event such as adequate drain management, anti-inflammatory prophylaxis, and improved patient monitoring should be implemented. Race/ethnicity of participants was not reported in the primary publication but was

reported in the registration on ClinicalTrials.gov. Tables 11 and 12 present a summary of the key characteristics and main results of the CONVERGE trial. Study relevance, design, and conduct limitations are presented in Tables 13 and 14.

Lee et al (2022) reported results of the Epicardial Approach in Recurred Atrial Fibrillation (EPIREAF; NCT02979847) RCT comparing a combined epicardial and endocardial ablation approach (n=50) with a conventional endocardial ablation approach (n=50).[54,] In the combined approach, subxiphoid epicardial access was obtained under fluoroscopic guidance (hybrid convergent). Participants had symptomatic, persistent AF refractory or intolerant to antiarrhythmic drugs and prior endocardial ablation. EPIREAF was a single-center, open-label, unblinded trial enrolling participants from June 2016 to November 2019. Rhythm monitoring occurred via 12-lead ECG and 24 hour Holter monitoring at 1, 3, 6, 9, and 12 months after the procedure and then every 6 months thereafter. The primary efficacy outcome was time to recurrence of sustained (>30 seconds) AF or atrial tachycardia following the 90-day blanking period within 12 months of the procedure. The reported safety outcome was occurrence of procedure-related complications within 24 hours after the procedure. Complications included death, any event requiring emergent surgery, severe bradycardia requiring cardiac pacing, pericardial effusion with tamponade or requiring transfusion, ischemic stroke, and procedure-related hematoma or vessel injury. The median age of participants was 59 years and 16% were women. Race/ethnicity of participants was not reported. The median CHA2DS2-VASc score was 1 and the median number of prior ablations was 1. The median procedure time was 232.5 minutes in the hybrid convergent group and 226 minutes in the CA group. Tables 11 and 12 present a summary of the key characteristics and main results of the EPIREAF trial. Study relevance, design, and conduct limitations are presented in Tables 13 and 14.

van der Heijden et al (2023) reported results of the Hybrid Versus Catheter Ablation in Persistent AF (HARTCAP-AF; NCT02441738) RCT.[55,] HARTCAP-AF was a single-center, open-label, unblinded trial randomizing 41 ablation-naive adults with symptomatic, long-standing persistent AF to either hybrid ablation (n=19) or CA (n=22) between October 2016 and December 2018. All randomized participants received their allocated treatment. The hybrid ablation was performed by an experienced surgeon and electrophysiologist in a single-stage procedure. Rhythm observation was performed with a 12-lead ECG and 24-hour-Holter monitor at 3 and 6 months or following report of symptoms. A 7-day-Holter was collected at 12 months. The primary efficacy outcome was freedom from any atrial tachyarrhythmia (lasting >5 minutes) off antiarrhythmic drugs after the 3-month blanking period until 12 months. The primary safety outcome was a composite of major adverse events and complications occurring within 12 months of follow-up. Major adverse event included death, stroke, bleeding requiring transfusion and/or reoperation, cardiac tamponade or pericardial effusion requiring intervention, empyema, myocardial infarction, pericarditis requiring pericardiocentesis or (prolongation of) (re)hospitalization, pneumothorax requiring intervention (after removal of chest tubes), gastroparesis, symptomatic pulmonary vein stenosis >70%, or (persistent) diaphragmatic paresis. The median age of participants was approximately 65 years; approximately 90% of participants had persistent but not long-standing AF and approximately 10% had persistent, long-standing AF. Several baseline characteristics were not balanced between the 2 treatment groups: women (5% in hybrid vs 18% in CA); median AF duration (22 months in hybrid vs 33 months in CA); CHA2DS2-VASc score >3 (53% in hybrid vs 27% in CA); and congestive heart failure (5% in hybrid vs 27% in CA). Race/ethnicity of participants was not reported. Median procedure time (4 hours 16 minutes vs 2 hours 53 minutes; p<.001) and length of hospital stay (4 days vs 2 days; p<.001) were significantly longer in the hybrid group. Radiation dose (31 cGycm^2 vs 67 cGycm^2; p=.004) and radiation exposure time (23 minutes vs 1 hour 54 minutes; p<.001) were significantly higher in the CA group. Tables 11 and 12 present a summary of the key characteristics and main results of the HARTCAP-AF trial. Study relevance, design, and conduct limitations are presented in Tables 13 and 14.

Table 11. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator

Study	Countries	Sites	Dates	Participants	Interventions	
Jan (2018)[56,]	Slovenia	1	2018	Adults with paroxysmal AF Mean age, 59 years; 26% women	Hybrid Convergent; n=24	CA; n=26
DeLurgio (2020); CONVERGE[53,]	US; UK	27	Dec 2013-Aug 2018	Adults with symptomatic persistent AF refractory or intolerant to at least 1 class I/II antiarrhythmic drug and a left atrium size of ≤6 cm and no prior CA Mean age, 64 years; Mean years since diagnosis of AF, 4.4; 70% men; Hispanic or Latino, 2%; 4% Black; 95% White	Hybrid Convergent, n=102	CA, n=51
Lee (2022); EPIREAF[54,]	Korea	1	Jun 2016-Nov2019	Adults with symptomatic, persistent AF refractory or intolerant to antiarrhythmic drugs after prior endocardial ablation Median age, 59 years; 16% women	Hybrid Convergent, n=50	CA; n=50
van der Heijden (2023); HARTCAP-AF[55,]	Netherlands	1	Oct 2016-Dec 2018	Adults with symptomatic, persistent AF refractory to 1 or more class I or III antiarrhythmic drugs and no prior CA Median age, 64 years	Hybrid; n=19	CA; n=22

AF: atrial fibrillation; CA: catheter ablation; RCT: randomized controlled trial; UK: United Kingdom; US: United States.

Table 12. Summary of Key RCT Results

Study	Freedom from AF	AF burden reduction	Cardioversions	Major adverse events
Jan (2018)[56,]	Recurrence of episode of AF/AFL/AT lasting 6 minutes or more Mean follow-up, 30.5 months			Periprocedural complication rates
Hybrid convergent	17% (4/24)	NR	4% (1/24)	12.5%
CA	38% (10/26)	NR	8% (2/26)	0%
Treatment effect	OR=3.78 (1.17 to 12.19); p=.05			
DeLurgio (2020); CONVERGE[53,]	Freedom from AF/atrial flutter/atrial tachycardia absent of class I/II antiarrhythmic	90% AF burden reduction 1-year	Freedom from cardioversions 1 year	Between 8- and 30-days postprocedure

Study	Freedom from AF	AF burden reduction	Cardioversions	Major adverse events
	drugs 1-year			
Hybrid Convergent	67.7% (67/99)	80% (60/75)	91%	7.8% (8/102)
CA	50% (25/50)	56.8% (25/44)	74%	0%
Treatment effect	RD=17.7% (RR, 1.35; p=.036)	RD=23.2% (RR, 1.41; p=.007)	p=.006	p=.0525
DeLurgio (2022); CONVERGE subanalysis[57,]	Long-standing persistent atrial fibrillation subgroup (n=65)			
Hybrid convergent	65.8% (25/38)	78.9% (30/38)		7.9% (3/38)
CA	37.0% (10/27)	46.2% (12/26)		0%
Treatment effect	RD=28.8% (95% CI, 5.1 to 52.4; p=.022)	RD=32.8% (95% CI, 9.7 to 55.9; p=.007)		
Lee (2022); EPIREAF[54,]	Recurrence of sustained (>30 seconds) AF or atrial tachycardia 1 year			Periprocedural complication rate 24 hours
Hybrid convergent	32% (16/50)	NR	NR	2%
CA	42% (21/50)	NR	NR	16%
Treatment effect	HR=0.72 (95% CI, 0.38 to 1.39); p=.33			OR=0.11 (0.00 to 0.87; p=.03
van der Heijden (2023); HARTCAP-AF[55,]	Freedom from any atrial tachyarrhythmia >5 minutes off antiarrhythmic drugs 1 year		Number of cardioversions 1 year	1 year
Hybrid	89% (17/19)	NR	5% (1/19)	1 (pericarditis)
CA	41% (9/22)	NR	23% (5/22)	1 (bleeding)
Treatment effect	p=.002		p=.19	p=1.000

AF: atrial fibrillation; AFL: atrial flutter;AT: atrial tachycardia; CA: catheter ablation; CI: confidence interval; HR: hazard ratio; RCT: randomized controlled trial; RD: risk difference;OR: odds ratio; RR: risk ratio.

Table 13. Study Relevance Limitations of Key RCTs

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Jan (2018)[56,]	5. Race/ethnicity not reported in publication; study conducted entirely in Slovenia	5. Procedures conducted at a single, highly specialized center			2. Safety only reported short term
DeLurgio (2020); CONVERGE[53,]	5. Study population is 95% White		2. Absence of empirical endocardial posterior wall ablation in the CA group	1. Major adverse events were only reported through 30 days and not through the 12-month follow-up	
Lee (2022); EPIREAF[54,]	5. Race/ethnicity not reported in publication;	5. Procedures conducted at a single, highly	4. 7/50 of the CA participants did not undergo the procedure	4. Intermittent rhythm monitoring	2. Safety only reported

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
	study conducted entirely in Korea	specialized center	(compared to 0/50 in the hybrid group)	post-procedure	at 24 hours
van der Heijden (2023); HARTCAP-AF[55],	5. Race/ethnicity not reported in publication; study conducted entirely in Netherlands	5. Procedures conducted at a single, highly specialized center		4. Intermittent rhythm monitoring post-procedure	

CA: catheter ablation; RCT: randomized controlled trial.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use; 5. Enrolled study populations do not reflect relevant diversity; 6. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest; 5. Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 14. Study Design and Conduct Limitations of Key RCTs

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Jan (2018)[56],		1. Subjects and clinicians not blinded to treatment assignment				5. High uncertainty about rates of adverse events due to very small number of events and sample size
DeLurgio (2020); CONVERGE[53],	3. Allocation concealment was not described in the publication or the protocol.	1. Subjects and clinicians not blinded to treatment assignment				
Lee (2022); EPIREAF[54],	3. Allocation concealment was not described	1. Subjects and clinicians not blinded to treatment assignment		1. 13/50 in the hybrid group and 9/50 in the CA group were lost to follow-up before the 1-year primary assessment		4. Data on subsequent procedures (e.g., cardioversion) not provided by treatment group
van der Heijden (2023);	3. Allocation concealment was not described	1. Subjects and clinicians not blinded to				5. High uncertainty about rates of adverse events

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
HARTCAP-AF[55,]		treatment assignment				due to very small number of events and sample size

RCT: randomized controlled trial.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

Nonrandomized Studies

La Meir et al (2012) reported on a comparative study that enrolled 35 patients who underwent a hybrid procedure and 28 patients who underwent a standard percutaneous procedure.[58,] Approximately two-thirds (42/63) of the patients had a previous percutaneous ablation procedure. At 1 year, there were more patients in the hybrid group who were free of AF, but this difference was not statistically significant (91.4% vs 82.1%, p=.07). On subgroup analysis, the success rate was higher for the hybrid group in patients with long-standing persistent AF (81.8% vs 44.4%; p=.001). Significantly more patients in the hybrid group were on warfarin at 1 year (29% vs 13.4%, p<.001). There was no difference between groups in the frequency of adverse events.

Kress et al (2017) evaluated clinical outcomes in 133 patients with persistent and long-standing AF who underwent conventional endocardial ablation (only RFA; n=69) or a hybrid approach of endocardial CA and epicardial ablation (n=64).[59,] Results revealed that the hybrid approach was associated with less recurrence (37% vs. 58%; p=.013) and repeat ablation (9% vs. 26%, p=.012) as well as an improvement in AF-free survival (72% vs. 51%; p=.01). Although the hybrid intervention was associated with a longer length of stay (p<.001), the occurrence of 30-day periprocedural complications was similar between the groups (p=.205). Complications were evaluated based on the Heart Rhythm/European Heart Rhythm Association/European Cardiac Arrhythmia Society/Sociedad Latinoamericana de Estimulación Cardíaca y Electrofisiología consensus guidelines and included pericardial infusion, groin complications, cerebrovascular accident, and death. There were a total of 7 complications overall (5.3%): 5 (7.8%) in the hybrid group and 2 (2.9%) in the endocardial group.

Maclean et al (2020) compared the efficacy and safety of a hybrid convergent procedure (surgical AF ablation combined with CA) in 43 patients with longstanding persistent AF with a matched group of 43 patients who underwent CA alone.[60,] At 1 year, patients who had undergone the hybrid convergent procedure had an increased AF-free survival on (60.5% vs. 25.6%; p=.002) and off (37.2% vs. 13.9%; p=.025) antiarrhythmic drugs as compared to the CA group. Additionally, after 30.5 ± 13.3 months of follow-up, increased arrhythmia-free survival was significantly improved in the convergent, as compared to the CA group, both on (58.1% vs. 30.2%; p=.016) and off (32.5% vs. 11.6%; p=.036) antiarrhythmics. Complications were reported more frequently in the convergent group (11.6% vs. 2.3%; p=.2). Serious adverse events related to the epicardial procedure included an inferior vena cava rupture requiring emergency sternotomy (n=1) and a pericardial hernia requiring surgical correction 6

months postoperatively (n=1). During CA, tamponade requiring emergency pericardiocentesis occurred in 2 patients in the hybrid convergent group versus 1 patient in the CA alone group. Phrenic nerve palsy was also reported in 1 patient in the convergent group following CA.

Other relevant single-arm case series have included populations ranging from 19 to 104 patients.[61,62,63,64,65,66,67,68,69,70,71,72,73,] These series have consistently reported high success rates in maintaining sinus rhythm at 1-year follow-up, ranging from 65% to 91%. Some series have reported individual adverse events, but did so variably not systematically, resulting in an inability to accurately estimate adverse event rates.

Section Summary: Hybrid Thoracoscopic and Endocardial Ablation Procedures

The evidence on hybrid ablation consists of 4 RCTs (sample sizes ranging from 41 to 153) and nonrandomized comparative studies that compare a hybrid procedure to a standard percutaneous procedure, a number of single-arm case series, and a systematic review of these studies. The RCTs varied with respect to the procedure used in the hybrid arm and the populations included (persistent versus paroxysmal AF). Only 1 RCT (CONVERGE) was conducted in the US and population demographics are not reflective of general US populations. Most trial participants have been male. All RCTs were conducted at highly specialized centers. Results of the RCTs and nonrandomized comparative studies have generally found an increased rate of AF-free survival with the use of a hybrid procedure as compared to CA in patients with persistent and long-standing AF. However, the risk of harm is not well characterized. Data regarding serious adverse events for at least 1 year following the procedure were not reported in the available RCTs. Pooled evidence from randomized and nonrandomized studies found an increased risk of periprocedural adverse events with the hybrid procedure relative to standard ablation.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2013 Input

In response to requests, input was received from 2 physician specialty societies and 6 academic medical centers (4 reviewers) while this policy was under review in 2013. There was consensus on the medically necessary statements. For subgroups of populations (e.g., those who have failed percutaneous catheter ablation), there was mixed support without consensus. There was also mixed support for the use of hybrid ablation.

2010 Input

In response to requests, input was received from 1 physician specialty society and 3 academic medical centers (4 reviewers) while this policy was under review in 2010. There was unanimous support for the policy statement regarding with cardiopulmonary bypass maze procedure. There was mixed support for the policy statement on off-bypass (off-pump) maze procedure; some providing input indicated off-pump procedures might be useful in select patients (e.g., those who cannot tolerate anticoagulation). Several providing input also commented on the limited long-term data for off-pump procedures.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US

representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

Society of Thoracic Surgeons

In 2017, the Society of Thoracic Surgeons published guidelines on the surgical treatment of atrial fibrillation (AF).[74,] Recommendations are provided in Table 15.

Table 15. Guidelines on Surgical Treatment of Atrial Fibrillation

Recommendation	COR	LOE
Surgical ablation for AF is recommended at the time of concomitant mitral operations to restore sinus rhythm.	I	A
Surgical ablation for AF is recommended at the time of concomitant isolated aortic valve replacement, isolated CABG surgery, and aortic valve replacement plus CABG operations to restore sinus rhythm.	I	B
Surgical ablation for symptomatic AF in the absence of structural heart disease that is refractory to class I/III antiarrhythmic drugs or catheter-based therapy of both is reasonable as a primary stand-alone procedure to restore sinus rhythm.	IIa	B

AF: atrial fibrillation; CABG: coronary artery bypass graft; COR: class of recommendation; LOE: level of evidence.

American Heart Association et al

In 2019, the American Heart Association, American College of Cardiologists, and Heart Rhythm Society issued joint guidelines in collaboration with the Society of Thoracic Surgeons on the management of patients with AF.[75,] Recommendations on the use of surgical ablation to maintain sinus rhythm are provided in Table 16.

Table 16. Guidelines on the Management of Atrial Fibrillation

Recommendation	COR	LOE
"AF catheter ablation may be reasonable in selected patients with symptomatic AF and HF with reduced left ventricular (LV) ejection fraction (HFrEF) to potentially lower mortality rate and reduce hospitalization for HF (S6.3.4-1, S6.3.4-2)."	IIb	B-R

AF: atrial fibrillation; COR: class of recommendation; HF: heart failure; LOE: level of evidence.

Heart Rhythm Society et al

A 2017 expert consensus statement on catheter and surgical ablation of atrial fibrillationwas developed by the Heart Rhythm Society, European Heart Rhythm Association, and European Cardiac Arrhythmia Society.[7,] The statement was endorsed by 4 other cardiology associations. Recommendations on concomitant surgical ablation in patients undergoing cardiac surgery for other purposes and who have symptomatic AF are provided in Table 17.

Table 17. Guidelines on Concomitant Surgical Ablation in Patients Undergoing Cardiac Surgery[a]

Recommendation	COR	LOE
Paroxysmal: Surgical ablation is recommended for patients undergoing surgery for other indications	II	B-NR
Persistent: Surgical ablation is recommended for patients undergoing surgery for other indications	II	B-NR
Longstanding Persistent: Surgical ablation is recommended for patients undergoing surgery for other indications	II	NR

COR: class of recommendation; LOE: level of evidence ; NR: nonrandomized.
a: For patients with symptomatic AF prior to initiation of antiarrhythmic therapy with Class I or III antiarrhythmic medication and an indication for concomitant closed surgical ablation for AF, surgical ablation is reasonable for paroxysmal, persistent, and long-standing persistent disease (Class: IIa; LOE: B-NR).

The following recommendations were made on stand-alone and hybrid surgical ablation in patients with symptomatic AF refractory or intolerant to at least 1 class 1 or 3 antiarrhythmic medication (Table 18).

Table 18. Guidelines on Stand-Alone and Hybrid Surgical Ablation for Symptomatic Atrial Fibrillation Refractory or Intolerant to Antiarrhythmics

Recommendation[a]	COR	LOE
Paroxysmal		
Stand alone surgical ablation can be considered for patients who have not failed catheter ablation but prefer a surgical approach	IIb	B-NR
Stand alone surgical ablation can be considered for patients who have failed 1 or more attempts at catheter ablation	IIb	B-NR
Persistent		
Stand alone surgical ablation is reasonable for patients who have not failed catheter ablation but prefer a surgical approach	IIa	B-NR
Stand alone surgical ablation is reasonable for patients who have failed 1 or more attempts at catheter ablation	IIa	B-NR
Longstanding persistent		
Stand alone surgical ablation is reasonable for patients who have not failed catheter ablation but prefer a surgical approach	IIb	B-NR
Stand alone surgical ablation is reasonable for patients who have failed 1 or more attempts at catheter ablation	IIb	B-NR

COR: class of recommendation; LOE: level of evidence ; NR: nonrandomized.
a: The recommendations noted that "it might be reasonable to apply the indication for stand-alone surgical ablation described above to patients being considered for hybrid surgical AF ablation."

American Association for Thoracic Surgery

In 2017, the American Association for Thoracic Surgery published guidelines on surgical ablation for AF.[76] Recommendations on concomitant surgical ablation in patients with AF are provided in Table 19.

Table 19. Guidelines on Concomitant Surgical Ablation in Patients with Atrial Fibrillation

Recommendation	COR	LOE
"Addition of a concomitant surgical ablation procedure for AF does not increase the incidence of perioperative morbidity."	IIa	A, B-R, B-NR[a]
"Addition of a concomitant surgical ablation procedure for AF does not change the incidence of perioperative stroke/TIA."	IIa	A
"Addition of a concomitant surgical ablation procedure for AF does not change the incidence of late stroke/TIA, but subgroup analysis of nonrandomized controlled trials found a significant reduction in late stroke/TIA incidence."	IIa	A, B-NR[b]
"A surgical procedure that includes concomitant surgical ablation for AF does improve HRQL."	IIa	B-R
"Addition of concomitant surgical ablation for AF does improve AF-related symptoms, and this improvement is greater than in patients without surgical ablation for AF."	IIa	C-LD
"Addition of concomitant surgical ablation for AF does improve 30-day operative mortality."	I	A
"Addition of a concomitant surgical ablation procedure for AF improves long term survival."	IIa	A, B-NR[c]

AF: atrial fibrillation; COR: class of recommendation; HRQL: health-related quality of life; LOE: level of evidence ; NR: nonrandomized; R: randomized; TIA: transient ischemic attack
a: "LOE A for deep sternal wound infection, pneumonia, reoperation for bleeding, and renal failure requiring dialysis; LOE B-R for intensive care unit length of stay and total hospital length of stay; and LOE B-NR for readmission less than 30 days and renal failure."
b: "LOE A for no change in incidence of late stroke/ TIA (up to 1 year of follow-up after surgery) and LOE B-NR for reduction in incidence of late stroke/TIA (>1 year of follow-up after surgery)."
c: "LOE A for no change in long-term survival (up to 1 year after surgery) and LOE B-NR for improvement in long-term survival (>1 year after surgery)."

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in Table 20.

Table 20. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04506814	Comparison of Repeat Endocardial PVI Vs Epicardial Posterior Wall Isolation and LAA Clip Plus PVI for Recurrent Atrial Fibrillation After Prior PVI	162	Dec 2025
NCT03546374	Irrigated Radio Frequency Ablation to Terminate Non-Paroxysmal Atrial Fibrillation (Terminate AF Study)	160	Aug 2024
NCT05723536	LAI-AF Trial: Hybrid Endo-epicardial Partial Left Atrial Isolation vs. Endocardial Ablation in Patients With Persistent Atrial Fibrillation (PLAI-AF)	80	Dec 2025
NCT03732794	AtriCure CryoICE Lesions for Persistent and Long-standing Persistent Atrial Fibrillation Treatment During Concomitant On-Pump Endo/Epicardial Cardiac Surgery	150	Dec 2026
NCT02393885	Pivotal Study Of A Dual Epicardial & Endocardial Procedure (DEEP) Approach for Treatment of Subjects With Persistent or Long Standing Persistent Atrial Fibrillation With Radiofrequency Ablation	220	Dec 2027
NCT04715425	Thoracoscopic Surgical Versus Catheter Ablation Approaches for Primary Treatment of Persistent Atrial Fibrillation	170	Sep 2028
Unpublished			
NCT02047279	Left Atrium Reduction Versus no Left Atrium Reduction for Patients With Enlarged Left Atria and Persistent or Long Standing Persistent Atrial Fibrillation Undergoing Mitral Valve Surgery	120	Sep 2017 (completed)
NCT02441738	Hybrid Thoracoscopic Surgical and Transvenous Catheter Ablation Versus Transvenous Catheter Ablation in Persistent and Longstanding Persistent Atrial Fibrillation	41	Dec 2018 (completed)
NCT03737929	Comparison of the Efficacy of Hybrid Ablative Therapy for Patients With Persistent Atrial Fibrillation Versus Conventional Catheter Ablation	228	Jan 2022 (unknown)
NCT04237389	Comparative Assessment of Catheter and Thoracoscopic Approaches in Patients With Persistent and Long-standing Persistent Atrial Fibrillation	60	Aug 2022 (unknown)

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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Documentation for Clinical Review

Please provide the following documentation:

- History and physical and/or consultation notes including:
- Procedures planned; including indication and type for other cardiac surgery to be done at the same time as maze or modified maze
- Previous treatment(s) and response to treatment(s) for atrial fibrillation or flutter
- Reason why a less invasive alternative is not being done
- EKG

Post Service (in addition to the above, please include the following):

- Cardiac operative report

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	33254	Operative tissue ablation and reconstruction of atria, limited (e.g., modified maze procedure)
	33255	Operative tissue ablation and reconstruction of atria, extensive (e.g., maze procedure); without cardiopulmonary bypass
	33256	Operative tissue ablation and reconstruction of atria, extensive (e.g., maze procedure); with cardiopulmonary bypass
	33257	Operative tissue ablation and reconstruction of atria, performed at the time of other cardiac procedure(s), limited (e.g., 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 (e.g., 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 (e.g., maze procedure), with

Type	Code	Description
		cardiopulmonary bypass (List separately in addition to code for primary procedure)
	33265	Endoscopy, surgical; operative tissue ablation and reconstruction of atria, limited (e.g., modified maze procedure), without cardiopulmonary bypass
	33266	Endoscopy, surgical; operative tissue ablation and reconstruction of atria, extensive (e.g., maze procedure), without cardiopulmonary bypass
HCPCS	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
12/07/2006	BCBSA Medical Policy adoption
07/02/2010	Policy Revision with position change
07/01/2011	Policy revision without position change
11/26/2014	Policy title change from Maze Procedure Policy revision without position change
08/01/2016	Policy Revision with position change Policy title change from Open and Thoracoscopic Approaches to Treat Atrial Fibrillation (Maze and Related Procedures)
08/01/2017	Policy revision without position change
07/01/2018	Policy revision without position change
07/01/2019	Policy revision without position change
07/01/2020	Annual review. No change to policy statement. Literature review updated.
07/01/2021	Annual review. Policy statement, guidelines and literature updated.
07/01/2022	Annual review. No change to policy statement. Literature review updated.
07/01/2023	Annual review. Policy statement and Literature review updated.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT	
BEFORE Red font: Verbiage removed	**AFTER** Blue font: Verbiage Changes/Additions
Open and Thoracoscopic Approaches to Treat Atrial Fibrillation and Atrial Flutter (Maze and Related Procedures) 7.01.14 **Policy Statement:** I. The maze or modified maze procedure, performed on a non-beating heart during cardiopulmonary bypass with concomitant cardiac surgery, may be considered **medically necessary** for the treatment of symptomatic atrial fibrillation or flutter. II. Stand-alone minimally invasive, off-pump maze procedures (i.e., modified maze procedures), including those done via mini-thoracotomy, are considered **investigational** for the treatment of atrial fibrillation or flutter. III. Hybrid ablation (defined as a combined percutaneous and thoracoscopic approach) is considered **investigationa**l for the treatment of atrial fibrillation or flutter. IV. The use of an open maze or modified maze procedure performed on a non-beating heart during cardiopulmonary bypass without concomitant cardiac surgery is considered not medically necessary for the treatment of atrial fibrillation or flutter.	**Open and Thoracoscopic Approaches to Treat Atrial Fibrillation and Atrial Flutter (Maze and Related Procedures) 7.01.14** **Policy Statement:** I. The maze or modified maze procedure, performed on a non-beating heart during cardiopulmonary bypass with concomitant cardiac surgery, may be considered **medically necessary** for the treatment of symptomatic atrial fibrillation or flutter. II. Stand-alone minimally invasive, off-pump maze procedures (i.e., modified maze procedures), including those done via mini-thoracotomy, are considered **investigational** for the treatment of atrial fibrillation or flutter. III. Hybrid ablation (defined as a combined percutaneous and thoracoscopic approach) is considered **investigationa**l for the treatment of atrial fibrillation or flutter. IV. The use of an open maze or modified maze procedure performed on a non-beating heart during cardiopulmonary bypass without concomitant cardiac surgery is considered investigational for the treatment of atrial fibrillation or flutter.