Medical Coverage Policy

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Transcatheter Closure of Cardiovascular Defects

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Related Coverage Resources

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Overview

This coverage policy addresses the transcatheter approach for closure of secundum atrial septal defect (ASD), patent ductus arteriosus (PDA), fenestration following a Fontan procedure, muscular or perimenbranous ventricular septal defect (VSD), known patent foramen ovale, ostium primum or sinus venosus atrial septal defect, and perventricular (transmyocardial) closure of VSDs using cardiac occlusion devices in neonates, infants, children, and adults.

Coverage Policy

Transcatheter closure with a U.S. Food and Drug Administration (FDA)-approved device used according to FDA labeling is considered medically necessary for ANY of the following conditions:

- secundum atrial septal defect (ASD)
- patent ductus arteriosus (PDA)
- fenestration following a Fontan procedure
- muscular or perimembranous ventricular septal defect (VSD) when ALL of the following criteria are met:
  - The VSD is of significant size to warrant closure.
  - The individual is considered to be at high risk for standard transatrial or transarterial surgical closure.
  - The individual is ≥5.2kg
- closure of a known patent foramen ovale (PFO) when BOTH of the following criteria are met:
  - History of ischemic stroke presumed to be secondary to a paradoxical embolism following a negative workup for other causes of ischemic stroke.
  - Age 18 to 60 years

Transcatheter closure of a cardiovascular defect for any other indication (e.g., migraine, decompression illness prevention) is considered not medically necessary.

Transcatheter closure of ostium primum or sinus venosus atrial septal defects (ASDs) is considered not medically necessary.

Perventricular (transmyocardial) closure of ventricular septal defects (VSDs) is considered experimental, investigational, or unproven.

Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation, and neighborhoods; racism, discrimination and violence; education, job opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

Congenital heart defects are the most common types of birth defects and affect nearly 40,000 (1%) of births per year in the United States. They can be considered mild (e.g., small hole in the heart) or severe (e.g., missing or poorly formed cardiac anatomy). Examples of congenital heart defects include: atrial septal defect, Ebstein anomaly, single ventricle, ventricular septal defect. Depending on the severity of the defect, there may be no signs or symptoms at all. More severe defects may result in, for example, cyanosis, tachypnea, fatigue, or death. Some defects can be diagnosed during pregnancy with a fetal echocardiogram, however, some are not diagnosed until later in life. Treatment varies and is dependent on the severity of the defect (CDC, 2024).

Kaltman et al. (2020) found in a cross-sectional, population-based sample of birth and infant death data files from the National Center for Health Statistics at the Centers for Disease Control and Prevention that disparities exist in congenital heart disease infant mortality rates based upon the maternal proximity to a top 50 specialized pediatric cardiac center (PCC) (i.e., as reported by the U.S. News & World Report in 2017). The infant mortality rate for infants whose mothers lived proximal to a PCC (0.28/1000 live births) was significantly lower than the infant mortality rate for infants whose mothers did not live proximal to a PCC (0.37/1000 live births) ($p<0.0001$). The infant mortality rate was 28% greater for infants whose mothers did not live proximal to a top 50 PCC compared to those infants whose mothers did. These findings suggest that geographic proximity to a specialized pediatric cardiac center contributes to the overall risk for infant mortality in those with congenital heart disease.

General Background

Atrial Septal Defect (ASD)
ASDs represent a communication between the left and right atria and account for 7–10% of all congenital heart defects. ASDs may be located at different sites in the septum and range in size from small to large. The three major types of ASD (ostium secundum, ostium primum and sinus venosus) are named for their position in the atrial septum. Ostium secundum ASDs constitute 75–80% of all atrial septal defects and are located in the central portion of the septum (i.e., fossa ovalis). Ostium primum ASDs account for 15% of all ASDs and are located in the lower portion of the septum just above the atrioventricular valves. Sinus venosus or venous ASDs, which constitute 10% of all ASDs, occur at the junction of the superior vena cava and the right atrium. Moderate or large ASDs may be associated with significant left-to-right shunting, increase in pulmonary blood flow, and right ventricular volume overload. Risk factors associated with increased mortality from untreated ASD include the development of pulmonary vascular obstructive disease (i.e., pulmonary arteries thicken from prolonged left-to-right shunting), right atrial or ventricular enlargement, tricuspid regurgitation, pulmonary hypertension, cardiac rhythm disturbances, and stroke. Transcatheter closure using implantable occlusive devices has evolved as an alternative to open surgical intervention in selected patients with secundum septal defects and has been shown to be safe and effective. Transcatheter closure is not an option for ostium primum and sinus venosus ASDs. These defects are located at the very lower and upper edges of the atrial septum, respectively, and are often associated with other valve abnormalities.

Although the indications for the procedure are the same as for surgical closure, the selection criteria are stricter in terms of defect size and surrounding rim tissue. Depending on the device,

transcatheter closure can be performed only for patients with a secundum ASD with a stretched diameter of less than 41 mm and with adequate rims to enable secure device deployment. This technique is generally precluded in patients with anomalous pulmonary venous connection or with proximity of the defect to the AV valves, coronary sinus or systemic venous drainage. Major complications occur in less than 1% of patients, and clinical closure is achieved in more than 80% of patients. Device closure of an ASD improves functional status in symptomatic patients and exercise capacity in asymptomatic and symptomatic patients. Based on intermediate follow-up data, ASD device closure is safe and effective, with better preservation of right ventricular function and lower complication rates than with surgery (Webb, et al., 2019; 2015a).

U.S. Food and Drug Administration (FDA): The Amplatzer® Septal Occluder (Abbott, Abbott Park, IL) received FDA approval through the PMA process on December 5, 2001 (P000039), for the occlusion of atrial septal defects in secundum position and for patients who have undergone a fenestrated Fontan procedure and require closure of the fenestration. According to the FDA approval order, the Amplatzer system is indicated for patients who have echocardiographic evidence of ostium secundum atrial septal defect and clinical evidence of right ventricular volume overload (i.e., 1.5:1 degree of left-to-right shunt or right ventricle enlargement) (FDA, 2024).

The GORE HELEX™ Septal Occluder (W.L. Gore & Associates, Flagstaff, AZ) received FDA approval through the PMA process (P050006) on August 11, 2006, for percutaneous transcatheter closure of ostium secundum atrial septal defects. Per the manufacturer website, the GORE HELEX product was discontinued and replaced by the GORE CARDIOFORM Septal Occluder (W.L. Gore & Associates, Flagstaff, AZ). This device received FDA approval through the PMA process (P050006 Supplement S044) on April 30, 2015. The GORE CARDIOFORM Septal Occluder is indicated for the percutaneous, transcatheter closure of ostium secundum atrial septal defects (FDA, 2024).

Literature Review : Transcatheter closure of secundum ASDs has been evaluated in case series reports and cohort reviews (Baroutidou, et al., 2023; Ghaderian, et al., 2021; Alnasser, et al., 2018; de Hemptinne, et al., 2017; Turner, et al., 2017; Smith, et al., 2014; Fischer, et al., 2003; Chessa, et al., 2002; Du, et al., 2002; Berger, et al., 1999). The consensus in these studies was that transcatheter closure is safe and effective in the majority of cases. Complications and complete closure rates were comparable to those seen with surgical closure and transcatheter closure offered the advantages of less morbidity and shorter hospitalizations.

Professional Societies/Organizations: The 2018 American College of Cardiology (ACC)/American Heart Association (AHA) Guidelines for the Management of Adults with Congenital Heart Disease (Stout, et al., 2019) include the following evidence-based therapeutic recommendations for closure of atrial septal defects:

Guideline Class of Recommendation (COR) and Level of Evidence (LOE) are described as follows:

Class (Strength) of Recommendation:

- Class I (Strong) Benefit >>>Risk
- Class IIa (Moderate) Benefit>>Risk
- Class IIb (Weak) Benefit ≥ Risk
- Class III No Benefit (Moderate) Benefit=Risk
- Class III Harm (Strong) Risk>Benefit

Level (Quality) of Evidence:

- Level A if the data were derived from high-quality evidence from more than one randomized clinical trial(RCT), meta-analyses of high-quality RCTs, or one or more RCTs corroborated by high-quality registry.

Level B-R when data were derived from moderate quality evidence from one or more RCTs, or meta-analyses of moderate-quality RCTs.
Level B-NR was used to denote moderate-quality evidence from one or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies. This designation was also used to denote moderate-quality evidence from meta-analyses of such studies.
Level C-LD when the primary source of the recommendation was randomized or nonrandomized observational or registry studies with limitations of design or execution, meta-analyses of such studies, or physiological or mechanistic studies of human subjects.
Level C-EO was defined as expert opinion based on the clinical experience of the writing group.

COR I

- "In adults with isolated secundum ASD causing impaired functional capacity, right atrial and/or RV enlargement, and net left-to-right shunt sufficiently large to cause physiological sequelae (e.g., pulmonary–systemic blood flow ratio [Qp:Qs] ≥1.5:1) without cyanosis at rest or during exercise, transcatheter or surgical closure to reduce RV volume and improve exercise tolerance is recommended, provided that systolic PA pressure is less than 50% of systolic systemic pressure and pulmonary vascular resistance is less than one third of the systemic vascular resistance (LOE: B-NR^{SR}).
- Adults with primum ASD, sinus venosus defect or coronary sinus defect causing impaired functional capacity, right atrial and/or RV enlargement and net left-to-right shunt sufficiently large to cause physiological sequelae (e.g., Qp:Qs ≥1.5:1) without cyanosis at rest or during exercise, should be surgically repaired unless precluded by comorbidities, provided that systolic PA pressure is less than 50% of systemic pressure and pulmonary vascular resistance is less than one third of the systemic vascular resistance" (LOE: B-NR)."

COR IIa

- "In asymptomatic adults with isolated secundum ASD, right atrial and RV enlargement, and net left-to-right shunt sufficiently large to cause physiological sequelae (e.g., Qp:Qs 1.5:1 or greater), without cyanosis at rest or during exercise, transcatheter or surgical closure is reasonable to reduce RV volume and/or improve functional capacity, provided that systolic PA pressure is less than 50% of systemic pressure and pulmonary vascular resistance is less than one third systemic resistance (LOE: C-LD^{SR}).
- Surgical closure of a secundum ASD in adults is reasonable when a concomitant surgical procedure is being performed and there is a net left-to-right shunt sufficiently large to cause physiological sequelae (e.g., Qp:Qs 1.5:1 or greater) and right atrial and RV enlargement without cyanosis at rest or during exercise (LOE: C-LD).
- Percutaneous or surgical closure may be considered for adults with ASD when net left-to-right shunt (Qp:Qs) is 1.5:1 or greater, PA systolic pressure is 50% or more of systemic arterial systolic pressure, and/or pulmonary vascular resistance is greater than one third of the systemic resistance (LOE: B-NR)."

COR III: Harm

- "ASD closure should not be performed in adults with PA systolic pressure greater than two thirds systemic, pulmonary vascular resistance greater than two thirds systemic, and/or a net right-to-left shunt (LOE: C-D)."

The recommendations developed by the writing committee on the basis of the systematic review are marked with "SR".

Patent Foramen Ovale (PFO)

The foramen ovale, a remnant of the fetal circulation, is a tunnel-like space between the overlying septum secundum and septum primum. In fetal life, this interatrial communication directs blood flow from the umbilical vein to the left atrium. After birth, the left atrial pressure increases and the valve to the fossa ovalis closes. In approximately 25% of people, however, this fusion is not complete. This persistent communication is a variant of atrial septal defect (ASD), but differs from ASD in morphology and associated signs and symptoms. The flap-like opening seen with PFO however, is usually not clinically significant in healthy adults, and is generally not treated unless conditions such as pulmonary hypertension, chronic obstructive pulmonary disease or pulmonary embolism are present. These conditions may cause the right atrial pressure to be elevated, causing an increased potential for right-to-left shunting through the PFO. PFOs have been scrutinized for their implication in the mechanism of cryptogenic stroke (i.e. stroke with no other known cause of cerebral ischemia). Although basic principles linking PFO and stroke are plausible, this link has not been demonstrated. It has been proposed that PFOs may serve as a conduit for paradoxical embolization from the venous side to the systemic circulation, or as a point of origin for thrombus formation because of their tunnel-like structure and tendency for stagnant flow. A coordinated series of events is necessary for a paradoxical embolism through a PFO to occur, however. Therefore, even in patients with a history of cryptogenic stroke, the risk of recurrence may not be high (Webb, et al., 2019, 2015a; Almekhlafi et al., 2009).

Antiplatelet therapy may be indicated for patients with PFO who have had a cryptogenic stroke or transient ischemic attack (TIA). Warfarin may be recommended for patients with other indications for oral anticoagulation, including patients with an underlying hypercoagulation state, or those with evidence of venous thrombosis. There is no clear evidence to demonstrate whether warfarin or aspirin is superior in preventing recurrent stroke or death. It is also unclear whether patients treated medically following a cryptogenic stroke are at increased risk for a subsequent stroke or death because of the presence of PFO. Transcatheter closure has been proposed as an alternative to medical therapy in patients with PFO associated with cryptogenic stroke and has been shown to be safe and effective (Sacco, et al., 2006).

Several other clinical conditions have been attributed to the presence of a PFO. It has been proposed that PFO may be implicated in the pathophysiologic mechanism of migraine headaches, decompression sickness in deep sea divers (arterial gas embolism from the venous side), and platypnoea-orthodeoxia syndrome (dyspnea and arterial desaturation in the upright position, which improves on lying down). There is insufficient evidence to determine whether the presence of a PFO is involved in the pathophysiologic mechanisms of these conditions or to determine the safety and efficacy of transcatheter PFO closure for these indications. (Webb, et al., 2019, 2015a; Mattle, at al., 2010).

Numerous trials addressing transcatheter closure of PFO are listed in the ClinicalTrials.gov database.

U.S. Food and Drug Administration (FDA): The CardioSEAL® Septal Occlusion System (Nitinol Medical Technologies, Inc., Boston, MA) and the Amplatzer® PFO Occluder (Abbott, Abbott Park, IL) received FDA HDE approval on February 1, 2000 and April 5, 2002 respectively. However, the manufacturers of both devices voluntarily withdrew their HDEs, effective October 31, 2006 following receipt of a notification from the FDA of their intent to withdraw HDE approval because they no longer met HDE criteria. The FDA found that the patient population described by the approved indication significantly exceeded the 4,000 people or less criteria required for HDE approval. Because of the larger number of patients eligible for these devices, the FDA concluded that a demonstration of reasonable assurance of both safety and effectiveness is required, as is the case with all class III (highest risk) devices not eligible for HDE status (FDA Information Sheet, Center for Devices and Radiological Health, Aug. 16, 2006). Subsequently, both devices were only available in the United States through an FDA approved Investigational Device

Exemption which would allow the devices to be used when part of a clinical study in order to collect safety and effectiveness data required to support a premarket approval (PMA). However, the manufacturer of the CardioSEAL device ceased operations in 2011 (FDA, 2024b, FDA, 2024c).

The manufacturer of the Amplatzer PFO Occluder received FDA approval through the PMA process on October 28, 2016 (P120021) (FDA, 2024). The device is indicated for percutaneous transcatheter closure of a patent foramen ovale (PFO) to reduce the risk of recurrent ischemic stroke in patients, predominantly between the ages of 18-60 years, who have had a cryptogenic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude known causes of ischemic stroke.

The Amplatzer PFO Occluder is contraindicated for use in:

- Patients with intra-cardiac mass, vegetation, tumor or thrombus at the intended site of implant, or documented evidence of venous thrombus in the vessels through which access to the PFO is gained;
- Patients whose vasculature, through which access to the PFO is gained, is inadequate to accommodate the appropriate sheath size;
- Patients with anatomy in which the Amplatzer PFO device size required would interfere with other intracardiac or intravascular structures, such as valves or pulmonary veins;
- Patients with other source of right-to-left shunts, including an atrial septal defect and/or a fenestrated atrial septum; and/or
- Patients with active endocarditis or other untreated infections.

In 2007, the FDA convened a meeting of the Circulatory System Devices Panel (CSDP) to address several issues regarding PFO closure devices, and issued the following recommendations (Slottow et al., 2007):

- Randomized controlled trials of PFO closure to prevent recurrent stroke are required.
- A "proof of principle" trial with pooled data demonstrating that PFO closure does prevent recurrent stroke could allow this question to be answered in a timely fashion, if sponsors are amenable to cooperating and sharing data. "Proof of device" trials demonstrating that an individual device effectively closes a PFO could be done separately.
- "Off-label" closure should be discouraged. Enrollment in ongoing trials should be encouraged.
- Patients and physicians should be educated about the lack of evidence of benefit of closure and the need for completion of trials.

In March 2018 (P050006/S060) the FDA expanded the PMA indication for the GORE® CARDIOFORM Septal Occluder (W.L. Gore & Associates, Inc., Flagstaff, AZ) to include closure of a patent foramen ovale (PFO). The Summary of Safety and Effectiveness Data states the device is a permanently implanted device indicated in PFO to reduce the risk of recurrent ischemic stroke in individuals (predominantly between 18-60 years of age) who have had a cryptogenic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude known causes of ischemic stroke. The device is contraindicated in individuals who are unable to take antiplatelet or anticoagulation therapy. The FDA approval is based on data reported by Søndergaard et al. (2017) from the REDUCE (NCT00738894) study (FDA, 2024).

Literature Review: Transcatheter closure for a known patent foramen ovale (PFO) is an established treatment option for individuals who have a history of ischemic stroke presumed to be secondary to a paradoxical embolism. Case series and retrospective reviews reporting up to 5.9 years of data demonstrated outcomes comparable to medical therapy following transcatheter

closure. Some outcomes suggested closure is associated with a lower risk of stroke recurrence or other cerebrovascular events. Complication rates are similar between closure and medical therapy with the exception of atrial fibrillation; which may occur more frequently in patients treated with PFO closure. Studies are limited by the heterogeneity of the types of devices used and the treatment parameters. (Kavinsky, et al., 2022; Vaduganathan, et al., 2018; Hayes, 2017, updated 2019; Kheiri, et al., 2019; Nasir, et al., 2019; Hayes, 2018, updated 2019; Lee, et al., 2018; Riaz, et al., 2018; Sa, et al., 2018; Mas., et al., 2017; Saver, et al., 2017; Søndergaard, et al., 2017; FDA, 2016; Chen, et al., 2014; Carroll, et al., 2013; Meier, et al., 2013; Furlan, et al., 2012; Almedhlafi, et al., 2009; Harms, et al., 2007; Demkow, et al., 2004).

Other Indications

Migraine: Transcatheter closure of a known patent foramen ovale has also been proposed for the treatment of migraine. Migraine with aura has been associated with PFO and with other causes of right-to-left shunts. The evidence in the published peer-reviewed literature does not support the effectiveness of PFO closure for this indication. Available studies are limited by small patient populations, short-term follow-ups, incomplete data reporting and conflicting results (Wang, et al., 2022; Zhang, et al., 2022; Mojadidi, et al., 2021; Zhang, et al., 2021; Dowson, et al., 2008).

Mojadidi et al. (2021) conducted a pooled analysis of two randomized controlled trials (RCT) (i.e., Tobis, et al., 2017, Mattle, et al., 2016) to evaluate the safety and efficacy of percutaneous PFO closure in individuals with migraine compared with medical therapy alone. Participants in the Mattle, et al. (2016) study (n=107) were not blinded to treatment allocation. Participants in the Tobis, et al. (2017) study (n=230) were blinded initially, but were then un-blinded after one year. In both studies, participants were treated with 1–3 months of clopidogrel and six months of aspirin. Participant ages ranged from 18–65 years. The intervention consisted of percutaneous PFO closure using the Amplatzer PFO Occluder device combined with medical management. The comparator in Mattle, et al. (2016) was medical treatment alone and the comparator in Tobis, et al. (2017) was sham PFO closure (e.g., right heart catheterization) with medical treatment. The pooled analysis included the following primary endpoints: mean reduction in monthly migraine days, mean reduction in monthly migraine attacks, responder rate (i.e., ≥ 50% reduction in migraine attacks), and complete migraine cessation. Subgroup analysis took place for those participants who experienced migraine with aura or frequent aura. Secondary outcomes included adverse events, vascular procedural complications, atrial fibrillation, or major bleeding episode. Significant improvement in monthly migraine days, migraine attacks, and complete migraine cessation at 12 months post-intervention was observed in the PFO closure group compared to the control group (p=0.02, p=0.01, p=<0.001, respectively). Improvement in responder rate did not achieve statistical significance between the PFO closure group and control group (p=.13). Compared with the control group, subgroup analysis for those participants with aura or frequent aura demonstrated a significant reduction in migraine days (p=0.03) and complete headache cessation (p=0.002). However, statistical significance was not achieved for those without aura compared with the control for migraine days (p=0.53) or complete headache cessation (p=0.16). The responder rate was significantly greater in participants with frequent aura compared with control (p=0.005) but not in participants with infrequent aura (p=0.69). Adverse events included: access-site bleeding, hematoma, hypotension, tachycardia, vasovagal episode, fatigue, non-sustained atrial fibrillation, and syncope. Author noted limitations included: heterogeneity of treatment parameters and patient characteristics (e.g., history of head trauma, mood disorders, palpitations, steroid use) and the short-term follow-up. Additional limitations included participant attrition and the small patient population.

Dowson et al. (2008) conducted a prospective, double-blind, randomized controlled trial to evaluate the effectiveness of PFO closure in patients with migraine with aura who experienced frequent migraine attacks, had failed ≥ two classes of prophylactic treatments, and had moderate to large right-to-left shunts consistent with the presence of PFO. Patients were randomized to

transcatheter closure with the STARFlex implant (NMT Medical, Inc., Boston MA) (n=74) or to a sham procedure (n=73). The primary efficacy endpoint was migraine headache cessation 91–180 days after the procedure. There was no significant difference in the primary outcome between the two groups; in the treatment group, 3 of 74 patients experienced headache cessation, compared to 3 of 73 patients in the sham group.

Schwedt et al. (2008) conducted a systematic review to evaluate the association of PFO and migraine and to assess the effect of PFO closure on migraine. Six retrospective studies met the inclusion criteria for the effect of PFO closure on migraine. The authors stated that the low-to-moderate grade of evidence from observational studies supports an apparent association between PFO and migraine, and that although PFO closure seemed to have a favorable effect on migraine patterns, the very low grade of available evidence to support this association precludes definitive conclusions.

Professional Societies/Organizations: In a 2022 guideline on the management of PFO, the Society for Cardiovascular Angiography and Interventions gave a conditional recommendation with a moderate certainty of evidence against PFO closure in persons experiencing migraines without a prior PFO-associated stroke. The recommendation is based on three randomized controlled trials (n=83–230) that failed to achieve their primary efficacy endpoints of eliminating or reducing migraine attacks per month (Kavinsky, et al., 2022; Tobis, et al., 2017; Mattle, et al., 2016; Dowson, et al., 2008).

Secondary Prevention of Recurrent Paradoxical Embolism in Deep Sea Divers: Patent foramen ovale (PFO) closure has been proposed as a means of secondary prevention of recurrent paradoxical embolism in deep sea divers. Inert gas accumulates within blood and tissues during a dive. Assuming appropriate decompression schedules are followed, on ascent that gas is excreted by the lungs. During a deep or long dive, venous gas emboli can form and in the presence of a PFO, these emboli can become arterialized resulting in symptoms of a stroke. This is referred to as neurological decompression illness (NICE, 2010). According to Anderson, et al. (2019), the risk of neurological decompression sickness in divers with a PFO is approximately 4-6 out of 10,000 dives or, in other words, 4-6 times that of a diver without a PFO. Conservative risk mitigation strategies include diving cessation and diving more conservatively to prevent the presence of post-dive venous gas bubbles.

Anderson et al. (2019) conducted a prospective, observational study of divers (n=65) to compare the effectiveness of patent foramen ovale (PFO) closure (n=42) and conservative diving (n=23) in decompression sickness (DCS) risk mitigation. The mean age of patients in the conservative group was 52 years and in the closure group was 45.5 years old. Adult participants were included in the study if they: were certified divers, had a diagnosis of PFO regardless of the DCS history, and planned to continue diving. After diagnosis with a PFO, divers who decided to continue diving without undergoing PFO closure were classified as "conservative". Those who decided to undergo PFO closure were classified as "closure". The primary outcome followed was "confirmed DCS" defined as cases diagnosed by a medical professional and requiring treatment in a recompression chamber. Secondary outcomes followed were cases of "possible DCS" which was defined as subjective reports of: vertigo, joint pain, skin itching and rash, post-dive skin mottling, breast swelling, muscular weakness, or use of in-water recompression or surface oxygen to alleviate symptoms. Additional secondary outcomes were: return to diving, frequency and intensity of diving after the intervention, and possible adverse events related to the closure. The median follow-up period was five years for the conservative group and six years for the closure group. The number of confirmed DCS cases in the conservative group decreased non-significantly from 12.8 to 6.2 while confirmed cases in the closure group decreased significantly from 13.1 to 2.7 ($p=<0.05$). The number of possible DCS cases in the conservative group increased significantly from 31.3 to 131.2 ($p=<0.0001$). The number of possible DCS cases in the closure group

decreased significantly from 144.5 to 42.1 (p=<0.0001). The authors postulated that the increase in possible DCS in the conservative group may have been attributed to the fact that the divers may have become more vigilant of DCS symptoms after PFO diagnosis. On average, fewer dives were reported in both groups per year after intervention. Stratification by PFO size suggested that divers with large PFOs who underwent closure would reduce incidences of possible DCS while those with small PFOs would not. Of those who underwent closure, adverse events occurred in 19% of divers and included: post-surgical bleeding, transient atrial fibrillation, migraine with aura, dysrhythmia, heart palpitations, premature atrial and ventricular contractions, supraventricular tachycardia, and allergic reaction to a muscle relaxant used during surgery. Author reported limitations of the study included: small sample size, bias due to self-enrollment, subjective reports of DCS, heterogeneity of clinical practices, and a lack of available medical documentation. The authors concluded that PFO closure could benefit healthy deep sea divers with a significant DCS burden and large PFO who wish to pursue advanced diving. Additional high quality studies are needed to fully assess the value of PFO closure as a risk mitigation strategy for deep sea divers.

Pearman et al. (2015) conducted a retrospective review of one cardiologist's practice to assess the safety and efficacy of PFO closure for the prevention of decompression illness in divers (n=106). Patients ranged in age from 16–63 years. Patients were implanted with either the Amplatzer (n=89), Gore Septal Occluder (n=7), Premere (n=6), Helex (n=3), or Starflex (n=1). Data from the RESPECT study, which evaluated PFO closure for the indication of cryptogenic stroke, served as the benchmark for evaluation. Outcomes measured included: the efficacy of PFO closure, complications related to the procedure, and the likelihood of being able to return to diving. Eighty percent of patients were considered fit for unrestricted diving after closure as evidenced by the lack of a shunt or the presence of a mild shunt on bubble contrast echocardiography. At the time of writing the review, 81/98 divers were followed up on and cleared to resume unrestricted diving, three patients had residual shunts, and 14 were given restrictions on their diving depths. Complications were found to be similar to those observed in the RESPECT trial and included: atrial fibrillation, atrial flutter, stroke, transient inferior ST segment elevation, retroperitoneal hematoma, vagal symptoms, palpitations, chest pain, nausea, and dizziness. Limitations of the review include the retrospective design, small patient population, and use of a benchmark study that did not evaluate PFO closure for the prevention of decompression illness in divers. Additional, high quality studies are needed to assess the safety and efficacy of PFO closure for the prevention of decompression illness in deep sea divers.

Professional Societies/Organizations: In a 2022 guideline on the management of PFO, the Society for Cardiovascular Angiography and Interventions gave a conditional recommendation with a very low certainty of evidence against PFO closure to prevent decompression illness (DCI) in SCUBA divers with prior DCI and without a prior PFO-associated stroke. The recommendation is based on three observational studies (n=35–153) that showed PFO closure may reduce the incidence of recurrent DCI. However, the literature is limited by observational and non-randomized trials that are inconclusive and fail to define optimal risk stratification for management (Kavinsky, et al., 2022; Honěk, et al., 2020; Anderson, et al., 2019; Koopsen, et al., 2018).

After a review of the literature, the American Academy of Neurology (AAN) (Messe, et al., 2020) issued a practice advisory regarding patent foramen ovale (PFO) closure in individuals with cryptogenic stroke. They found that percutaneous PFO closure "probably reduces the risk of stroke recurrence", has a periprocedural complication rate of 3.9%, and "probably is associated with the development of serious nonperiprocedural atrial fibrillation". The AAN included the following recommendations in their advisory:

- "In patients being considered for PFO closure, clinicians should ensure that an appropriately thorough evaluation has been performed to rule out alternative mechanisms of stroke, as was performed in all positive PFO closure trials.

- In patients being considered for PFO closure, clinicians should obtain brain imaging to confirm stroke size and distribution, assessing for an embolic pattern or a lacunar infarct (typically involving a single deep perforator, <1.5 cm in diameter).
- In patients being considered for PFO closure, clinicians should obtain complete vascular imaging (MRA or CTA) of the cervical and intracranial vessels to look for dissection, vasculopathy, and atherosclerosis.
- In patients being considered for PFO closure, clinicians must perform a baseline ECG to look for atrial fibrillation.
- Select patients being considered for PFO closure thought to be at risk of atrial fibrillation should receive prolonged cardiac monitoring for at least 28 days.
- In patients being considered for PFO closure, clinicians should assess for cardioembolic sources using TTE followed by TEE assessment if the first study does not identify a high-risk stroke mechanism. Studies should use bubble contrast, with and without Valsalva maneuver, to assess for right-to-left shunt and determine degree of shunting.
- In patients being considered for PFO closure, clinicians should perform hypercoagulable studies that would be considered a plausible high-risk stroke mechanism that would lead to a change in management such as requiring lifelong anticoagulation (e.g., persistent moderate- or high-titer antiphospholipid antibodies in a younger patient with cryptogenic stroke).
- Before undergoing PFO closure, patients should be assessed by a clinician with expertise in stroke to ensure that the PFO is the most plausible mechanism of stroke.
- If a higher risk alternative mechanism of stroke is identified, clinicians should not routinely recommend PFO closure.
- In patients younger than 60 years with a PFO and an embolic appearing infarct and no other mechanism of stroke identified, clinicians may recommend closure following a discussion of potential benefits (reduction of stroke recurrence) and risks (procedural complication and atrial fibrillation)."

The American Heart Association (AHA)/American Stroke Association (ASA) Guidelines for the Prevention of Stroke in Patients with Stroke and Transient Ischemic Attack (Kleindorfer, et al., 2021) include the following recommendations for patent foramen ovale (PFO):

Classification (strength) of Recommendations:
- Class 1: Strong; Benefit >>>Risk
- Class 2a: Moderate; Benefit>>Risk
- Class 2b: Weak; Benefit ≥ Risk
- Class 3: No Benefit (Moderate); Benefit = Risk
- Class 3: Harm (Strong); Risk > Benefit

Levels of Evidence:
- Level A
  - High-quality evidence from more than 1 RCT
  - Meta-analysis of high-quality RCTs
  - One or more RCTs corroborated by high-quality registry studies
- Level B-R
  - Moderate-quality evidence from 1 or more RCTs
  - Meta-analyses of moderate-quality RCTs
- Level B-NR
  - Moderate-quality evidence from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
  - Meta-analysis of such studies
- Level C-LD

    - Randomized or nonrandomized observational or registry studies with limitations of design or execution
    - Meta-analysis of such studies
    - Physiological or mechanistic studies in human subjects
- Level C-EO
    - Consensus of expert opinion based on clinical experience

Class 1

- "In patients with a nonlacunar ischemic stroke of undetermined cause and a PFO, recommendations for PFO closure versus medical management should be made jointly by the patient, a cardiologist, and a neurologist, taking into account the probability of a causal role for the PFO (Level C-EO).

Class 2a

- In patients 18 to 60 years of age with a nonlacunar ischemic stroke of undetermined cause despite a thorough evaluation and a PFO with high-risk anatomic features, it is reasonable to choose closure with a transcatheter device and long-term antiplatelet therapy over antiplatelet therapy alone for preventing recurrent stroke (Level B-R).

Class 2b

- In patients with ischemic stroke or TIA in whom patent foramen ovale (PFO) closure would be contemplated, TCD (transcranial Doppler) with embolus detection might be reasonable to screen for right-to-left shunt (Level C-LD).
- In patients 18 to 60 years of age with a nonlacunar ischemic stroke of undetermined cause despite a thorough evaluation and a PFO without high-risk anatomic features, the benefit of closure with a transcatheter device and long-term antiplatelet therapy over antiplatelet therapy alone for preventing recurrent stroke is not well established (Level C-LD).
- In patients 18 to 60 years of age with a nonlacunar ischemic stroke of undetermined cause despite a thorough evaluation and a PFO, the comparative benefit of closure with a transcatheter device versus warfarin is unknown (Level C-LD)."

The American College of Chest Physicians Evidence-Based Clinical Practice Guideline, Antithrombotic Therapy and Prevention of Thrombosis (Guyatt, et al., 2012) includes the following recommendations for patients with PFO and atrial septal aneurysms:

- In patients with cryptogenic stroke and PFO or atrial septal aneurysm, we recommend aspirin (50-100 mg) over no aspirin (Grade 1A, strong recommendation, high quality evidence)
- In patients with cryptogenic stroke and PFO or atrial septal aneurysm, who experience recurrent events despite aspirin therapy, we suggest treatment with vitamin K antagonist (VKA therapy), and consideration of device therapy over aspirin therapy (Grade 2C, weak recommendation, low or very low quality evidence)
- In patients with cryptogenic stroke and PFO, with evidence of deep vein thrombosis, we recommend VKA therapy for three months and consideration of device therapy over no VKA therapy or aspirin therapy (Grade 2C, weak recommendation, low-or very low quality evidence)

A science advisory on percutaneous device closure of patent foramen ovale for secondary stroke prevention was issued by the American Heart Association/American Stroke Association and the American College of Cardiology, and was affirmed by the American Academy of Neurology (O'Gara et al., 2009). According to the advisory, the optimal therapy for prevention of recurrent stroke or transient ischemic attack in patients with cryptogenic stroke and patent foramen ovale has not been defined. Although a strong association between patent foramen ovale and cryptogenic stroke has been suggested by numerous observational studies, a causal relationship has not been convincingly established for the majority of affected patients. The advisory further states:

"The choice between medical therapy and percutaneous device closure has been the subject of intense debate over the past several years, albeit one that has not been adequately informed by randomized, prospective clinical trial data to permit an objective comparison of the relative safety and efficacy of these respective approaches. Enrollment in clinical trials has lagged considerably despite frequent calls for participation from the US Food and Drug Administration and major professional societies. Completion and peer review of ongoing trials are critical steps to establish an evidence base from which clinicians can make informed decisions regarding the best therapy for individual patients. The present advisory strongly encourages all clinicians involved in the care of appropriate patients with cryptogenic stroke and patent foramen ovale—cardiologists, neurologists, internists, radiologists, and surgeons—to consider referral for enrollment in these landmark trials to expedite their completion and help resolve the uncertainty regarding optimal care for this condition."

Patent Ductus Arteriosus (PDA)
The ductus arteriosus is the vessel leading from the bifurcation of the pulmonary artery to the aorta, just distal to the left subclavian artery. Under normal circumstances, this channel is open in the fetus and closes spontaneously during the first few days of life. PDA results from the failure of this duct to close following birth. It is a common finding in premature infants and progressively decreases in frequency with increasing gestational age. In premature infants with compromised respiratory status, closure may be attempted using fluid restriction, diuresis, maintenance of good oxygenation, and medications such as indomethacin or by surgical ligation. Treatment of PDA in a preterm infant varies and depends on the degree of shunting and the severity of hyaline membrane disease. There is general agreement that closure of a hemodynamically significant PDA is indicated in children and adults. The safety and efficacy of transcatheter closure of PDA is established, with achievement of complete ductal closure in more than 85% of patients by one year, with a mortality rate of less than 1%. Surgical closure is generally reserved for patients in whom the defect is too large for device closure, or in centers without access to device closure. Surgical closure has a marginally greater closure rate than device closure, but is associated with slightly higher morbidity and mortality (Webb, et al., 2019; 2015a).

U.S. Food and Drug Administration (FDA): On May 14, 2003, the Amplatzer Duct Occluder and 180° Delivery System (Abbott, Abbott Park, IL) received FDA approval through the PMA process (P020024) for the indication of nonsurgical closure of patent ductus arteriosus (PDA).

The Amplatzer Duct Occluder and 180° Delivery System is contraindicated for use in:

- "Patients weighing less than 6 kgs.
- Patients less than 6 months of age.
- Presence of thrombus at the intended site of implant, or documented evidence of venous thrombus in the vessels through which access to the defect is gained.
- Active endocarditis or other infections producing bacteremia.
- Patients whose vasculature, through which access to the defect is gained, is inadequate to accommodate the appropriate sheath size.
- Patients with pulmonary hypertension with pulmonary vascular resistance of >8 Woods units or Rp/Rs of >0.4 (FDA, 2024)."

On July 9, 2020, the Amplatzer Piccolo™ Occluder was added to the Abbott Amplatzer Family of Duct Occluders and is designed to occlude small ducts including those of neonates and infants. The occluder is contraindicated for use in:

- "Weight <700 grams at time of the procedure

- Age <3 days at time of procedure
- Coarctation of the aorta
- Left pulmonary artery stenosis
- Cardiac output that is dependent on right to left shunt through the PDA due to pulmonary hypertension
- Intracardiac thrombus that may interfere with the implant procedure
- Active infection requiring treatment at the time of implant
- Patients with a PDA length smaller than 3 mm
- Patients with a PDA diameter that is greater than 4 mm at the narrowest portion (FDA, 2024; Abbott, 2024)."

Literature Review: The safety and efficacy of transcatheter device closure for patent ductus arteriosus smaller than 8 mm has been established over the past 20 years, with complete ductal closure achieved in more than 85% of patients by one year with a mortality rate of less than 1%. Transcatheter closure has become the method of choice in centers with appropriate resources and experience. Although surgical closure has a marginally greater closure rate than device closure, the surgical mortality in adults is 1–3.5%, due to the presence of pulmonary arterial hypertension and difficult ductal morphology (e.g., calcified or aneurismal) frequently seen in adults. Surgical closure is therefore generally reserved for patients in whom the PDA is too large for device closure or centers without access to device closure (Bischoff, et al., 2021; Sathanandam, et al., 2020; Webb, et al., 2019; 2015a; Gruenstein, et al., 2017; Butera, et al., 2004; Pass, et al., 2004).

Bischoff, et al. (2021) conducted a systematic review and meta-analysis of observational case series to assess the safety and efficacy of percutaneous patent ductus arteriosus (PDA) closure with either a coil or device in infants ≤ 1.5 kg with subgroup analysis of infants ≤ 6.0 kg. There were 28 studies comprising 373 infants in the ≤ 1.5 kg group and 69 studies comprising 1,794 infants in the ≤ 6 kg subgroup. Studies evaluating infants weighing ≤ 6 kg at the time of PDA closure and studies including a comparator were included. Case reports or case series with < 3 participants, studies without data on the patient's weight or adverse events, and studies with mixed populations were excluded. The comparators included no treatment, medical therapy, and surgical closure. The primary outcome measured was technical success while adverse events served as the secondary outcome measured. Technical success was defined as successful placement of the device or coil in the PDA at the time the patient left the procedure room or cases of device or coil embolization that were retrieved and replaced with a different size device or coil during the same procedure. In the ≤ 1.5 kg group, technical success was achieved in 96% of percutaneous procedures, adverse events occurred in 27% of cases, and age at the time of the procedure was identified as a significant predictor for technical success (p=0.004). The incidence of major adverse events was 8% (p=0.63) and minor adverse events was 18% (p=<0.001). Ten cases (2.7%) were considered technical failures including: cardiac perforation or hemopericardium resulting in death (n=3), conversion to surgical ligation (n=3), procedure abortion due to inferior vena cava dissection at the time of sheath advancement (n=1), cardiac tamponade converted to surgical ligation (n=1), iatrogenic aorta coarctation requiring surgical removal of the device and surgical ligation (n=1), and embolization to the left pulmonary artery that required surgical removal of the device and surgical ligation of the PDA (n=1). In a comparison between infants ≤ 1.5 kg and infants between 1.5-6.0 kg, the authors found that technical success and incidence of adverse events were higher in patients weighing 1.5-6.0 kg. Author noted limitations of the study included the absence of randomized controlled trials, heterogeneity of the indication for PDA closure, and heterogeneity of practice parameters. Additional limitations of the study include the small patient populations and short-term follow-up. The authors concluded that percutaneous PDA closure is successful and associated with a limited number of adverse events.

Professional Societies/Organizations: The 2018 ACC/AHA Guidelines for the Management of Adults with Congenital Heart Disease (Stout, et al., 2019) include the following evidence-based therapeutic recommendations for patent ductus arteriosus (PDA) closure:

Guideline Class of Recommendation (COR) and Level of Evidence (LOE) are described as follows:

Class (Strength) of Recommendation:
Class I (Strong) Benefit >>>Risk
Class IIa (Moderate) Benefit>>Risk
Class IIb (Weak) Benefit ≥ Risk
Class III No Benefit (Moderate) Benefit=Risk
Class III Harm (Strong) Risk>Benefit

Level (Quality) of Evidence:
Level A if the data were derived from high-quality evidence from more than one randomized clinical trial(RCT), meta-analyses of high-quality RCTs, or one or more RCTs corroborated by high-quality registry.
Level B-R when data were derived from moderate quality evidence from one or more RCTs, or meta-analyses of moderate-quality RCTs.
Level B-NR was used to denote moderate-quality evidence from one or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies. This designation was also used to denote moderate-quality evidence from meta-analyses of such studies.
Level C-LD when the primary source of the recommendation was randomized or nonrandomized observational or registry studies with limitations of design or execution, meta-analyses of such studies, or physiological or mechanistic studies of human subjects.
Level C-EO was defined as expert opinion based on the clinical experience of the writing group.

COR I
- PDA closure in adults if left atrial or left ventricular (LV) enlargement is present and attributable to PDA with net left-to-right shunt, PA systolic pressure less than 50% systemic and pulmonary vascular resistance less than one third systemic (LOE: C-LD).

COR IIb
- PDA closure in adults may be considered in the presence of a net left-to-right shunt if PA systolic pressure is 50% or greater systemic, and/or pulmonary vascular resistance is greater than one third systemic (LOE: B-NR).

COR III: Harm
- PDA closure should not be performed in adults with a net right-to-left shunt and PA systolic pressure greater than two thirds systemic or pulmonary vascular resistance greater than two thirds systemic (LOE: C-LD).

Fenestration Following Fontan Procedure
The Fontan procedure is a palliation procedure that involves separating the pulmonary and systemic blood flows in patients with single ventricular defects. The technique reduces the mixing of unoxygenated and oxygenated blood by directing blood flow from the right atrium to the pulmonary artery, excluding the ventricle from right-sided circulation. The procedure is intended to produce a normal workload on the ventricle. One component of this procedure involves leaving a hole or fenestration in the septum of the repaired section of the heart, allowing for some mixing of blood for patients who are unable to tolerate the change in venous pressure. The size of the fenestration varies, and smaller holes can close spontaneously. Some patients require the creation

of larger holes and, in many of these patients, the fenestration will remain patent. In patients with cyanosis in the setting of a fenestrated Fontan, surgical or preferably transcatheter closure of the fenestration can be attempted. Postoperative closure of Fontan fenestrations using a test occlusion and subsequent permanent closure with an intracardiac device evolved based on growing experience with transcatheter techniques to close various intracardiac defects. Early and late closure after test occlusion has been reported to reduce mortality and morbidity after the Fontan procedure, especially in high-risk patients.

U.S. Food and Drug Administration (FDA): As previously stated, the Amplatzer® Septal Occluder received FDA approval through the PMA process on December 5, 2001, for the occlusion of secundum atrial septal defects and also for patients who have undergone a fenestrated Fontan procedure and require closure of the fenestration. According to the FDA approval order, the Amplatzer system is indicated for patients who have echocardiographic evidence of ostium secundum atrial septal defect and clinical evidence of right ventricular volume overload (i.e., 1.5:1 degree of left-to-right shunt or right ventricle enlargement). The FDA PMA submission for the Amplatzer Septal Occluder included registry data that evaluated the safety and effectiveness in patients with fenestrated Fontan. According to the Summary of Safety and Effectiveness, the effectiveness of the device was demonstrated by results consistent with those obtained for treatment of ASD and by the primary efficacy at 12 months' follow-up. There was no need for additional surgical repair in the 32 patients. In addition, the adverse events rates at 12 months were within the protocol-defined acceptable limits (4.2%) and the mortality rate was zero (FDA, 2024).

Literature Review: Because of the relative rarity of this condition, published studies evaluating transcatheter closure of fenestrations following Fontan procedure are limited. There is sufficient evidence, however, to indicate that transcatheter septal occlusion is safe and effective for closure of a fenestration following a Fontan procedure in patients with single ventricle physiology.

Goff et al. (2000) published a multicenter registry study of patients who underwent catheter closure of a fenestrated Fontan with either the Clamshell (n=91) or CardioSEAL (n=63) device. All 63 patients who had their fenestrations treated with the CardioSEAL device achieved successful implantation. Late closure of the fenestration (at greater than six months after surgery) was followed by improved oxygenation, reduced need for anticongestive medication, and improved somatic growth at follow-up.

Ventricular Septal Defect (VSD)
Congenital VSD can occur in isolation and as one part of a combination of cardiac anomalies. The natural history of congenital VSD may include spontaneous closure, development of pulmonary vascular obstruction, right ventricle outflow tract obstruction, aortic regurgitation, infective endocarditis, cardiomegaly, congestive cardiac failure and death in infancy. Many infants experience growth failure. Management of VSD is largely dependent on the size and pathophysiology of the defect. Patients with large defects and pulmonary hypertension are those at greatest risk of developing pulmonary vascular obstruction as well as respiratory infections. Large defects require correction early in life when pulmonary vascular disease is still reversible. Medical treatment may include diuretics, digitalis, and treatment of respiratory infections, as well as increased caloric density of feedings. Acquired VSD can occur post-myocardial infarction (MI), as well as following multiple trauma. It has been estimated that there is an 80–90% mortality rate within the first two months of the occurrence of a post-MI VSD with medical treatment alone. Rupture of the intraventricular septum is an uncommon but often fatal complication of acute MI or traumatic injury. Surgical closure of congenital and acquired ventricular septal defects is a well-established procedure with low perioperative mortality, a high closure rate, and positive immediate and short-term outcomes in patients with suitable anatomy. Since long-term data are

not yet available, transcatheter VSD closure should be reserved for patients with VSD of significant size to warrant closure who are at high risk for standard surgical closure.

U.S. Food and Drug Administration (FDA): The CardioSEAL® Septal Occlusion System with QuikLoad™ (NMT, Inc., Boston, MA) received FDA approval through the PMA process (P000049) on December 5, 2001, for use in patients with complex VSDs of significant size to warrant closure and who are considered at high risk for standard transatrial or transarterial surgical closure based on anatomical conditions and/or overall medical condition. According to the FDA approval order, high-risk anatomical factors for transatrial or transarterial surgical closure include:

- patients requiring a left ventriculotomy or an extensive right ventriculotomy
- patients with a failed previous VSD closure
- patients with multiple apical and/or anterior muscular VSDs ("Swiss cheese septum")
- patients with posterior apical VSDs covered by trabeculae

The FDA summary of safety and efficacy document indicates that the approval study used included individuals from Children's Hospital in Boston, MA. Study participants ranged in age from 0.3 years to 70.1 years with a median age of 3.7 years. The contraindications states that the device is contraindicated in individuals whose vasculature through which access to the defect is to be gained and the defect itself, isn't of sufficient size to accommodate the delivery sheath.

A modified version of the CardioSEAL device, to be marketed under the trade name STARFlex® Septal Occlusion System, received FDA PMA approval (P000049/S016) on March 5, 2009. The device as modified is indicated for use in patients with a complex ventricular septal defect of a significant size to warrant closure but that, based on location, cannot be closed with standard transatrial or transarterial approaches (FDA, 2024).

The Amplatzer Muscular VSD Occluder (Abbott, Abbott Park, IL) received FDA approval through the PMA process (P040040) on September 7, 2007. The device is indicated for use in patients with a complex VSD of significant size to warrant closure (large volume, left to right shunt, pulmonary hypertension and/or clinical symptoms of congestive heart failure) who are considered to be at high risk for standard transatrial or transarterial surgical closure based on anatomical conditions and/or based on overall medical condition. The approval letter lists the same high-risk anatomical factors included in the approval letter for the CardioSEAL Septal Occlusion System with QuikLoad™, listed above. The FDA summary of safety and efficacy document states that the device is contraindicated in individuals <5.2kg. The mean age of the individuals studied was 3.2 years with a range of 0.1 years–49.0 years (FDA, 2024).

Literature Review: Transcatheter closure is an established treatment option for complex ventricular septal defect (VSD) repair. Although there is a limited number of studies investigating transcatheter closure for VSD repair, case series (n=30–848), retrospective reviews (n=104), and systematic review and meta-analysis of prospective and retrospective (randomized and non randomized) trials (n=6–462) reporting up to 7.5 years of data reported favorable success rates and long-term results. There is variability as to the type of device used for the closure (Cen, et al., 2021; Weryński, et al., 2021; Yang, et al., 2021; Yang, et al., 2010; Butera, et al., 2007; Masura, et al., 2005; Tanopoulos and Riby, 2005; Arora, et al., 2004).

Professional Societies/Organizations:
American Heart Association (AHA)/American College of Cardiology (ACC): The 2018 ACC/AHA Guidelines for the Management of Adults with Congenital Heart Disease (Stout, et al., 2019) include the following evidence-based therapeutic recommendations for closure of a ventricular septal defect (VSD). The authors added that transcatheter occlusion of muscular and perimembranous VSD has demonstrated good safety and efficacy profile.

Guideline Class of Recommendation (COR) and Level of Evidence (LOE) are described as follows:

Class (Strength) of Recommendation:
Class I (Strong) Benefit >>>Risk
Class IIa (Moderate) Benefit>>Risk
Class IIb (Weak) Benefit ≥ Risk
Class III No Benefit (Moderate) Benefit=Risk
Class III Harm (Strong) Risk>Benefit

Level (Quality) of Evidence:
Level A if the data were derived from high-quality evidence from more than one randomized clinical trial(RCT), meta-analyses of high-quality RCTs, or one or more RCTs corroborated by high-quality registry.
Level B-R when data were derived from moderate quality evidence from one or more RCTs, or meta-analyses of moderate-quality RCTs.
Level B-NR was used to denote moderate-quality evidence from one or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies. This designation was also used to denote moderate-quality evidence from meta-analyses of such studies.
Level C-LD when the primary source of the recommendation was randomized or nonrandomized observational or registry studies with limitations of design or execution, meta-analyses of such studies, or physiological or mechanistic studies of human subjects.
Level C-EO was defined as expert opinion based on the clinical experience of the writing group.

COR I
- Adults with a VSD and evidence of left ventricular volume overload and hemodynamically significant shunts (Qp:Qs ≥1.5:1) should undergo VSD closure, if pulmonary artery (PA) systolic pressure is less than 50% systemic and pulmonary vascular resistance is less than one third systemic (LOE: B-NR).

COR IIa
- Surgical closure of perimembranous or supracristal VSD is reasonable in adults when there is worsening aortic regurgitation (AR) caused by VSD (LOE: C-LD).

COR IIb
- Surgical closure of a VSD may be reasonable in adults with a history of infective endocarditis (IE) caused by VSD if not otherwise contraindicated (Level of Evidence: C-LD).
- Closure of a VSD may be considered in the presence of a net left-to-right shunt (Qp:Qs ≥1.5:1) when PA systolic pressure is 50% or more than systemic and/or pulmonary vascular resistance is greater than one third systemic (LOE: C-LD).

COR III: Harm
- VSD closure should not be performed in adults with severe pulmonary arterial hypertension (PAH) with PA systolic pressure greater than two thirds systemic, pulmonary vascular resistance greater than two thirds systemic and/or a net right-to-left shunt (LOE: C-LD).

American College of Cardiology (ACC): In a 2022 review (Turner, et al., 2022), the American College of Cardiology stated that limitations for percutaneous VSD closure still exist despite considerable growth in understanding, techniques, and device selection and that surgical closure remains the preferred treatment strategy. However, they point to several defects that can be considered for transcatheter closure including defects that are, "anatomically favorable for device

implantation, with adequate space to avoid injury to surrounding structures such as the aortic and atrioventricular valves". The ACC stated that, "transcatheter device closure of MVSDs is reasonable in patients who weigh ≥5 kg with hemodynamically significant defects and suitable anatomy (Class IIa, LOE B).

Perventricular/Transmyocardial Closure of Ventricular Septal Defects: The use of a perventricular approach, also referred to as a transmyocardial approach, has been explored as an alternative to the transcatheter approach for ventricular septal defect (VSD) closure. This hybrid approach has been investigated in the treatment of patients for whom transcatheter closure is challenging, including small infants and patients with poor vascular access. A perventricular approach was reported in five of 55 patients included in the first report of the multicenter CardioSEAL VSD registry. The registry was created following FDA approval of the CardioSEAL VSD Occluder in order to track the device's safety in closing high-risk, complex, muscular VSD. The five patients who were treated with perventricular implantation all weighed ≤ 7 kg. Four of these procedures were reported to be successful by the implanting center. One perventricular implant failed because the right ventricular arms of the device protruded the right ventricular free wall (Lim, et al., 2007). There is insufficient evidence in the published medical literature to demonstrate the safety and efficacy of perventricular closure of VSD. In addition, no devices have received FDA approval for this application.

U.S. Food and Drug Administration (FDA): No devices have received FDA approval for perventricular/transmyocardial closure of ventricular septal defects.

Literature Review: There is insufficient evidence in published peer-reviewed scientific literature to support the safety and effectiveness of the perventricular/transmyocardial approach to VSD closure. The body of evidence is largely comprised of case series, observational studies, and cohort studies with a few small randomized controlled trials. The studies are limited by hetergenous study designs, small patient populations, publication bias, and variability in the type of VSDs treated. Well-designed, randomized controlled studies are needed to determine the clinical utility of the perventricular/transmyocardial approach to VSD closure (Huan, et al., 2020; Li, et al., 2020; Hong, et al., 2019)

Bacha at al. (2005) described a perventricular hybrid approach, combining surgical and interventional techniques, utilized in a series 12 patients with muscular VSD. Using a sternotomy or subxyphoid approach, the right ventricle free wall was punctured under transesophageal echocardiography guidance. A guide wire was introduced across the largest defect, and a short delivery sheath was positioned in the left ventricle cavity. An Amplatzer muscular VSD occluder was deployed across the VSD. Cardiopulmonary bypass was required only for repair of concomitant lesions. At a median follow-up of 12 months, all patients were asymptomatic, and two patients had mild residual ventricular level shunts.

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	No National Coverage Determination found	
LCD		No Local Coverage Determination found	

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Notes:

1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare and Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
93580†	Percutaneous transcatheter closure of congenital interatrial communication (i.e., Fontan fenestration, atrial septal defect) with implant
93581	Percutaneous transcatheter closure of a congenital ventricular septal defect with implant
93582	Percutaneous transcatheter closure of patent ductus arteriosus
93662	Intracardiac echocardiography during therapeutic/diagnostic intervention, including imaging supervision and interpretation (List separately in addition to code for primary procedure)

†Note: Considered Not Medically Necessary when used to report transcatheter closure of ostium primum or sinus venosus atrial septal defects

HCPCS Codes	Description
C1817	Septal defect implant system, intracardiac

Considered Experimental/Investigational/Unproven when used to report perventricular (transmyocardial) closure of ventricular septal defect:

CPT®* Codes	Description
33999	Unlisted procedure, cardiac surgery
93799	Unlisted cardiovascular service or procedure

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Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	• Revised policy statement for ventricular septal defects. • Revised policy statement for 'transcatheter closure of CVD for any other indication' and 'closure of ostium primum or sinus venosus ASDs'.	11/15/2024
Annual Review	• No policy statement changes.	11/15/2023