

07.01.32 Percutaneous Intracranial Angioplasty and Stenting

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Related Policies:

- None

Summary

Description

Intracranial arterial disease includes thromboembolic events, vascular stenoses, and aneurysms. Endovascular techniques have been investigated for the treatment of intracranial arterial disease. Endovascular therapy is used as an alternative or adjunct to intravenous tissue plasminogen activator and supportive care for acute stenosis and as an adjunct to risk-factor modification for chronic stenosis. For cerebral aneurysms, stent-assisted coiling and the use of flow-diverting stents have been evaluated as an alternative to endovascular coiling in individuals whose anatomy is not amenable to simple coiling.

Summary of Evidence

For individuals who have intracranial aneurysm(s) who received endovascular coiling with intracranial stent placement or intracranial placement of a flow-diverting stent, the evidence includes randomized controlled trials (RCTs), several nonrandomized comparative studies, and multiple single-arm studies. Relevant outcomes are overall survival, morbid events, functional outcomes, and treatment-related mortality and morbidity. The available nonrandomized comparative studies have reported occlusion rates for stent-assisted coiling that are similar to or higher than coiling alone and recurrence rates that may be lower than those for coiling alone. For stent-assisted coiling with self-expanding stents, some evidence has also shown that adverse event rates are relatively high, and a nonrandomized comparative trial has reported that mortality is higher with stent-assisted coiling than with coiling alone. For placement of flow-diverting stents, a pragmatic RCT and registry study have compared flow diversion with standard management (observation, coil embolization, or parent vessel occlusion) in patients for whom flow diversion was considered a promising treatment. The pragmatic study was stopped early after crossing a predefined safety boundary when 16% of patients treated with flow diversion were dead or dependent at 3 months or later. Flow diversion was also not as effective as the investigators had hypothesized. A systematic review comparing the flow-diverting stents with endovascular coiling for intracranial aneurysms has demonstrated higher rates of aneurysm obliteration in those treated with the Pipeline endovascular device than those treated with coiling, with similar rates of good clinical outcomes. The evidence does not provide high certainty whether stent-assisted coiling or placement of a flow-diverting stent improves outcomes for patients with intracranial aneurysms because the risk-benefit ratio cannot be adequately defined. One randomized study demonstrated adequate aneurysm occlusion with the Surpass flow diverter device. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome. However, it is recognized that individuals who are candidates for endovascular therapy for aneurysms frequently have aneurysms in locations not amenable to surgical therapy, making comparisons with surgical therapy unlikely. Given the relative rarity of intracranial aneurysms, there may be legitimate barriers to clinical trials. Even though there is a paucity of data in the peer-reviewed scientific evidence based on clinical input and relevant professional society guidelines in which endovascular therapy for aneurysms is supported in select individual's, it will be considered medically necessary when the criteria below are met, see [Policy](#).

For individuals who have symptomatic intracranial arterial stenosis due to atherosclerosis who receive intracranial percutaneous transluminal angioplasty with or without stenting, the evidence includes systematic reviews and 3 major RCTs. Relevant outcomes are overall survival, symptoms, morbid events, functional outcomes, and treatment-related mortality and morbidity. All available RCTs have demonstrated no significant benefit with endovascular therapy. In particular, the Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial was stopped early due to harms, because the rate of stroke or death at 30 days posttreatment was higher in the endovascular arm, which received percutaneous angioplasty with stenting. Follow-up of SAMMPRIS subjects has demonstrated no long-term benefit from endovascular therapy. Although some nonrandomized studies have suggested a benefit from endovascular therapy, the available evidence from 3 RCTs does not suggest that intracranial percutaneous transluminal angioplasty with or without stenting improves outcomes for individuals with symptomatic intracranial stenosis. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Additional Information

Not applicable.

OBJECTIVE

The objective of this evidence review is to determine whether endovascular therapies improve the net health outcome in individuals with intracranial arterial stenosis, or intracranial aneurysm.

PRIOR APPROVAL

Not applicable.

POLICY

Intracranial Stent Placement

Intracranial stent placement may be considered **medically necessary** as part of the endovascular treatment of an intracranial aneurysm for individuals when **ALL** the following criteria are met:

- When surgical treatment is not appropriate; **and**
- Standard endovascular techniques do not allow for complete isolation of the aneurysm due to its anatomy, e.g., wide-neck aneurysm (≥ 4 mm) or sack-to-neck ratio less than 2:1.

Intracranial Flow-Diverting Stents

Intracranial flow-diverting stents with U.S. Food and Drug Administration (FDA) approval (*see Regulatory Status information below*) for the treatment of intracranial aneurysms may be considered **medically necessary** as part of the endovascular treatment of intracranial aneurysms for individuals meeting **ALL** the following criteria:

- Not amendable to surgical treatment or standard endovascular therapy; **and**
- The treatment is for large or giant wide-necked aneurysm with a size of ≥ 10 mm and has a neck diameter ≥ 4 mm in the internal carotid artery from the petrous to the superior hypophyseal segments.

Intracranial stent placement and intracranial flow-diverting stents is considered **investigational** in the treatment of intracranial aneurysms except as indicated above because the evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Percutaneous Intracranial Transluminal Angioplasty

Percutaneous intracranial transluminal angioplasty with or without stenting is considered **investigational** for the treatment of atherosclerotic cerebrovascular disease because the evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

POLICY GUIDELINES

Flow-diverting stents are indicated for the treatment of large or giant wide-necked intracranial aneurysms, with a size of 10 mm or more and a neck diameter of 4 mm or more, in the internal carotid artery from the petrous to the superior hypophyseal segments.

This policy only addresses endovascular therapies used on intracranial vessels.

Coding

See the [Codes](#) table for details.

BACKGROUND

Cerebrovascular Diseases

Cerebrovascular diseases include a range of processes affecting the cerebral vascular system, including arterial thromboembolism, arterial stenosis, and arterial aneurysms, all of which can restrict cerebral blood flow due to ischemia or hemorrhage. Endovascular techniques, including endovascular mechanical embolectomy with various types of devices (i.e., stents), and angioplasty with or without stenting have been investigated for the treatment of cerebrovascular diseases.

Intracranial Arterial Stenosis

It is estimated that intracranial atherosclerosis causes about 8% of all ischemic strokes. Intracranial stenosis may contribute to stroke in 2 ways: either due to embolism or low-flow ischemia in the absence of collateral circulation. Recurrent annual stroke rates are estimated at 4% to 12% per year with atherosclerosis of the intracranial anterior circulation and 2.5% to 15% per year with lesions of the posterior (vertebrobasilar) circulation.

Intracranial Aneurysms

Compared with acute ischemic stroke, cerebral aneurysms have a much lower incidence in the United States, with prevalence between 0.5% and 6% of the population. However, they are associated with significant morbidity and mortality due to subarachnoid hemorrhage resulting from aneurysm rupture.

Regulatory Status

Table 1. Summarizes Devices with FDA Clearance

Device	Description
Enterprise™ Vascular Reconstruction Device and Delivery	In 2007, based on a series of approximately 30 patients with 6-month follow-up, the Enterprise™ Vascular Reconstruction Device and Delivery (Cordis Neurovascular) was approved by the FDA through the humanitarian device exemption process (H060001) for use with embolic coils for

	the treatment of wide-neck, intracranial, saccular, or fusiform aneurysms.
Low-Profile Visualized Intraluminal Support Device	In 2014, the Low-Profile Visualized Intraluminal Support Device (LVIS™ and LVIS™ Jr.; MicroVention) was approved by the FDA through the humanitarian device exemption process (H130005) for use with embolic coils for the treatment of unruptured, wide-neck (neck, ≥ 4 mm or dome-to-neck ratio, < 2), intracranial, saccular aneurysms arising from a parent vessel with a diameter of 2.5 mm or greater and 4.5 mm or smaller. In 2018, the LVIS™ and LVIS™ Jr. were approved through the PMA process (P170013).
Neuroform™ Atlas Stent System	In 2019, the Neuroform™ Atlas Stent System (Stryker) was approved by the FDA through the PMA process (P190031) based on the pivotal ATLAS study including 201 patients with up to 12 months of follow-up. The approved indication is "for use with neurovascular embolization coils in the anterior circulation of the neurovasculature for the endovascular treatment of patients greater than or equal to 18 years of age with saccular wide-necked (neck width greater or equal to 4 mm or a dome-to-neck ratio of < 2) intracranial aneurysms arising from a parent vessel with a diameter of greater than or equal to 2.0 mm and less than or equal to 4.5 mm."
Neuroform™ Microdelivery Stent System	In 2002, the Neuroform™ Microdelivery Stent System (Stryker) received HDE approval (H020002) from the FDA for use with embolic coils for treatment of wide-neck intracranial aneurysms that cannot be treated by surgical clipping.
Neurolink® System	The Neurolink® system, marketed by the Guidant Corporation, received HDE approval from the FDA and is indicated for the treatment of patients with recurrent intracranial stroke attributable to atherosclerotic disease refractory to medical therapy in intracranial vessels ranging from 2.5 to 4.5 mm in diameter with a stenosis greater than or equal to 50% and that are accessible to the stent system.
Pipeline® Embolization Device	In 2011, the Pipeline® Embolization Device (Covidien/eV3 Neurovascular), an intracranial aneurysm flow-diverter, was approved by the FDA through the premarket approval process (P100018) for the endovascular treatment of adults (≥ 22 years) with large or giant wide-necked intracranial aneurysms in the internal carotid artery from the petrous to the superior hypophyseal segments. Approval was based on the Pipeline for Uncoilable for Failed Aneurysms Study, a single-arm, open-label feasibility study, reported by Becske et al (2013) that included 108 patients, aged 30 to 75

	years, with unruptured large and giant wide-necked aneurysms.
PulseRider® Aneurysm Neck Reconstruction Device	In 2017, the PulseRider® Aneurysm Neck Reconstruction Device (Pulsar Vascular, Inc.) was approved by the FDA through the humanitarian device exemption process (H160002) for use with neurovascular embolic coils for treatment of unruptured wide-necked intracranial aneurysms with neck width at least 4 mm or dome to neck ratio greater than 2.
Surpass Streamline Flow Diverter	In 2018, Surpass Streamline Flow Diverter (Stryker Neurovascular) was approved by the FDA through the premarket approval process (P170024) for use in the endovascular treatment of patients (18 years of age and older) with unruptured large or giant saccular wide-neck (neck width ≥ 4 mm or dome-to-neck ratio < 2) or fusiform intracranial aneurysms in the internal carotid artery from the petrous segment to the terminus arising from a parent vessel with a diameter ≥ 2.5 mm and ≤ 5.3 mm. The approval was based on 1- year results of the Surpass Intracranial Aneurysm Embolization System Pivotal Trial to Treat Large or Giant Wide Neck Aneurysms (SCENT) study. The SCENT study is continuing follow-up to 5 years post-procedure as a post-approval study.
Wingspan Stent System with Gateway™ PTA Balloon Catheter	The Wingspan™ Stent System with Gateway™ PTA Balloon Catheter, marketed by Boston Scientific, received HDE approval (H050001) from the FDA in 2005 to treat refractory intracranial atherosclerotic disease resulting in 50 percent or greater narrowing in the intracranial arteries. Following analysis of data from the SAMMPRIS study, the original HDE clinical study and other clinical studies performed after the stent's HDE approval, the FDA revised the use and labeling for the Wingspan™ stent in August 2012. The new labeling approves the use of Wingspan™ stent for a very select group of patients who are between 22 and 80 years of age and meet all the following criteria: • Have had two or more strokes despite aggressive medical management. • Their most recent stroke occurred more than seven days prior to Wingspan™ placement and • Have 70-99% stenosis due to atherosclerosis of the intracranial artery related to the recurrent strokes; and • Have made good recovery from previous stroke with a modified Rankin score of 3 or less prior to Wingspan™ treatment. The Wingspan™ Stent System should not be used for the treatment of TIAs or treatment of stroke with

	onset of symptoms within seven days or less of treatment.
Woven Endobridge (WEB®)	In 2018, the Woven Endobridge (WEB®) Aneurysm Embolization System (Sequent Medical™ Inc. [MicroVention, Inc.] Aliso Viejo, CA) received FDA premarket approval (P170032) for use at the middle cerebral artery (MCA) bifurcation, internal carotid artery (ICA) terminus, anterior communicating artery (AComm) complex, or basilar artery apex for the endovascular treatment of adults with saccular, wide neck, bifurcating intracranial aneurysms with dome diameter from 3 mm to 10 mm and either neck size of 4 mm or greater or a dome-to-neck ratio greater than 1 and less than 2.

RATIONALE

This evidence review was created in July 2006 and has been updated regularly with searches of the PubMed database. The most recent literature update with performed through June 2026.

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, including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to 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 one 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.

Endovascular Interventions for Symptomatic Intracranial Atherosclerotic Disease

Clinical Context and Therapy Purpose

The purpose of endovascular interventions in individuals with intracranial atherosclerotic disease is to prevent stroke or recurrent stroke.

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

Populations

The relevant population of interest is individuals with severe stenosis (70% to 99% of the diameter of a major intracranial artery).

Interventions

Devices for treatment of intracranial stenosis have received the FDA approval through the humanitarian device exemption process. The Neurolink System was approved based on the Stenting of Symptomatic Atherosclerosis Lesions in the Vertebral or Intracranial Arteries (SSYL VIA) trial, a prospective, nonrandomized, multicenter, international study of 61 individuals. The Wingspan Stent System was evaluated in a prospective study of 45 individuals enrolled at 12 international centers. The SSYL VIA study reported an all-stroke rate of 13.1% over a mean follow-up of 216 days; the Wingspan study reported an all-stroke rate of 9.5% over a mean follow-up of 174 days.

The FDA summary of safety and effectiveness for the Wingspan device offered the following conclusions and the FDA appears to have based its approval of Wingspan in part on the favorable comparison with the Neurolink device:

“...the probable benefit to health from using the Wingspan Stent System with Gateway PTA [percutaneous transluminal angioplasty] Balloon Catheter for treating transcranial stenosis outweighs the risk of illness or injury when used in accordance with the Instructions for Use and when taking into account the probable risks and benefits of currently available alternative forms of treatment.”

Comparators

Medical treatment typically includes either anticoagulant therapy (i.e., warfarin) or antiplatelet therapy (e.g., aspirin). The Warfarin-Aspirin Symptomatic Intracranial Disease trial assessed the incidence of stroke brain hemorrhage or death among individuals randomized to aspirin or warfarin. The trial found that over a mean 1.8 years of follow-up, warfarin provided no benefit over aspirin and was associated with a significantly higher rate of complications. Also, if symptoms could be attributed to low-flow ischemia, agents to increase mean arterial blood pressure and avoid orthostatic hypotension may be recommended. However, medical therapy has been considered less than optimal. For example, in individuals with persistent symptoms despite antithrombotic therapy, the subsequent rate of stroke or death has been extremely high, estimated in 1 study at 45%, with recurrent events within 1 month of the initial event. Surgical approaches have been met with limited success. The widely cited extracranial-intracranial bypass study randomized 1377 individuals with symptomatic atherosclerosis of the internal carotid or middle cerebral arteries to medical care or extracranial-intracranial bypass. Outcomes in both groups were similar, suggesting that the extracranial-intracranial bypass is ineffective in preventing cerebral ischemia. Due to inaccessibility, surgical options for the posterior circulation are even more limited.

Percutaneous transluminal angioplasty has been approached cautiously for use in intracranial circulation, due to technical difficulties in the catheter and stent design and the risk of embolism, which may result in devastating complications if occurring in the posterior fossa or brain stem. However, improvement in the ability to track catheterization, allowing catheterization of tortuous vessels, and the increased use of stents have created ongoing interest in percutaneous transluminal angioplasty as a minimally invasive treatment of this difficult-to-treat population. Most published studies of intracranial percutaneous transluminal angioplasty have focused on vertebrobasilar circulation.

Outcomes

The outcomes of interest are stroke, death, function, and quality of life. Treatment-related adverse effects, including vessel perforation, hemorrhage, or thrombus formation in a new site, are important safety outcomes. Evidence for both short-term (30 day) and long-term (out to 2 years) outcomes are needed.

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 long-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

Luo et al (2023) completed a Cochrane review that evaluated endovascular therapy plus conventional medical treatment versus medical treatment alone for symptomatic intracranial artery stenosis. The review included 4 RCTs (N=989) and identified 2 ongoing RCTs. All trials had a high risk of performance bias, and the certainty of included evidence ranged from low to moderate. Characteristics and moderate certainty results of the review are found in Tables 2 and 3. The review also included various subgroup analyses. Overall, endovascular therapy plus conventional medical treatment was found to increase the risk of the primary outcome (short-term stroke and death [i.e., within 3 months of randomization]) in patients with recent symptomatic intracranial artery stenosis. It was also found to increase the risk of short-term ipsilateral stroke (RR, 3.26; 95% CI, 1.94 to 5.48; moderate certainty), short-term ischemic stroke (RR, 2.24; 95% CI, 1.30 to 3.87; moderate certainty), and long-term death or stroke (RR, 1.49; 95% CI, 1.12 to 1.99; moderate certainty). Long-term results that were reported appeared to be due to the early risks of endovascular therapy.

Table 2. Systematic Review and Meta-Analysis Characteristics

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Luo et al (2023)	NR - 2022	4	Adults with symptomatic intracranial artery stenosis related to atherosclerotic factors	989 (NR)	RCT	Short-term follow-up: mean 30 days Long-term follow-up: mean 12 months

NR: not reported; RCT: randomized controlled trial.

Table 3. Systematic Review and Meta-Analysis Results

Study	Short-term death or stroke	Short-term ipsilateral stroke	Short-term ischemic stroke	Long-term death or stroke
Luo et al (2023)				
Total N	989	989	989	970
Risk ratio (95% CI)	2.93 (1.81 to 4.75)	3.26 (1.94 to 5.48)	2.24 (1.30 to 3.87)	1.49 (1.12 to 1.99)
I^2	0%	0%	0%	45%
Test for overall effect: Z (p)	4.36 (p<.0001)	4.47 (p<.00001)	2.89 (p=.004)	2.71 (p=.007)

CI: confidence interval.

Other meta-analyses support the Luo et al (2023) Cochrane review. Yeo et al (2024) conducted a patient-level meta-analysis of RCTs that compared stenting and best medical therapy for intracranial arterial stenosis. Among the 7 included RCTs (N=1425), the risk of stroke or death within the first 30 days was higher with stenting than with best medical therapy (RR, 2.22; interquartile range, 1.28 to 3.86; $I^2=0\%$). Intracranial hemorrhage and death were significantly higher among patients who received a stent. Similarly, an analysis of 11 studies (N=1915) by Shi et al (2023) did not identify a benefit of endovascular therapy combined with medical therapy over medical therapy alone among patients with symptomatic intracranial artery stenosis, but there was a suggestion of harm due to increased incidence of death or stroke, cerebral hemorrhage, and disabling stroke or death.

Randomized Controlled Trials

Gao et al (2022) published the results of the CASSISS trial, which randomized 380 patients with stroke or transient ischemic attack due to severe intracranial stenosis (70% to 99%) to either stenting plus medical therapy or medical therapy alone. The trial was conducted to determine whether more selective patient inclusion criteria or more experience among surgeons might overcome the lack of benefit or harm identified in prior RCTs. The study was conducted at 8 centers in China and patients were followed for 3 years. The primary outcome (a composite of stroke within 30 days, death within 30 days, or stroke in the qualifying artery territory between 30 days and 1 year) was similar in both groups (hazard ratio, 1.10; 95% CI, 0.52 to 2.35; p=.82). Mortality at 3 years was similar between groups (p=.08).

Zaidat et al (2015) published the results of the Vitesse Intracranial Stent Study for Ischemic Stroke Therapy (VISSIT) trial, a RCT comparing a balloon-expandable stent plus medical management with medical management alone among patients who had symptomatic intracranial stenosis of 70% or greater. Eligible patients had stenosis of 70% to 99% of the internal carotid, middle cerebral, intracranial vertebral, or basilar arteries with a transient ischemic attack (TIA) or stroke attributable to the territory of the target lesion within the prior 30 days. Enrollment was planned for up to 250 participants. However, an early unplanned analysis was conducted by the trial sponsor after the results of the Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial were published. A total of 112 patients were enrolled from 2009 to 2012 and randomized to the balloon-expandable stent (Vitesse stent) plus medical management (stent group; n=59) or medical management alone (medical group; n=53). Medical management included clopidogrel (75 mg daily) for the first 3 months post-enrollment and aspirin (81 to 325 mg/d) for the duration of the study, along with management of hypercholesterolemia and/or hypertension, if necessary. The trial used a primary composite endpoint that included any stroke in the same territory as the presenting event within 1 year of randomization and “hard TIA” in the same territory as the presenting event from 2 days to 1 year after

randomization. Among 29 patients who met 1 of the primary endpoints within 1 year of randomization, 8 (15.1%) patients were in the medical group, and 21 (36.2%) were in the stent group (risk difference, 21.1%; 95% CI, 5.4 to 36.8; $p=.02$). The rates of stroke within 30 days of randomization or TIA were 9.4% in the medical group and 24.1% in the stent group (risk difference, 14.7%; 95% CI, 1.2 to 28.2; $p=.05$). The 30-day all-cause mortality rate was 5.2% and 0% in the stent and the medical groups, respectively (risk difference, 5.2%; 95% CI, -0.5 to 10.9; $p=.25$). The authors concluded that results did not support the use of a balloon-expandable stent for patients with symptomatic intracranial stenosis.

The SAMMPRIS trial was a RCT comparing aggressive medical management alone with aggressive medical management plus stenting in patients who had symptomatic cerebrovascular disease and intracranial stenosis between 70% and 99%. This trial used the Wingspan stent system implanted by experienced neurointerventionalists credentialed to participate in the trial. The authors planned to enroll 750 patients based on power calculations. However, the trial was stopped early for futility after 451 patients had been randomized, due to an excess of the primary outcome (stroke or death) at 30 days in the stenting group. In the stenting group, the rate of stroke or death at 30 days was 14.7% (95% CI, 10.7 to 20.1) compared with 5.8% (95% CI, 3.4 to 9.7; $p=.002$) in the medical management group. At the time of trial termination, mean follow-up was 11.9 months. Kaplan-Meier estimates of the primary outcome (stroke or death at 1 year) was 20.5% (95% CI, 15.2 to 26.0) in the stenting group and 12.2% (95% CI, 8.4 to 17.6; $p=.009$) in the medical management group. These results represented an excess rate of early adverse events with stenting over what was expected together with a decreased rate of stroke and death in the medical management group compared with expected values.

The SAMMPRIS investigators, as reported by Derdeyn et al (2014), also published results from long-term subject follow-up. Primary endpoints (in addition to stroke or death within 30 days of enrollment) included ischemic stroke in the qualifying artery beyond 30 days after enrollment or stroke or death within 30 days after a revascularization procedure of the qualifying lesion. During a median follow-up of 32.4 months, 34 (15%) of 227 patients in the best medical management group and 52 (23%) of 224 patients in the stenting group had a primary endpoint event, with a significantly higher cumulative probability of a primary endpoint in the stenting group than in the best medical management group ($p=.025$). Compared with the best medical management group, subjects in the stenting group had higher rates of any stroke (59/224 [26%] vs. 42/227 [19%], $p=.047$) and major hemorrhage (29/224 [13%] vs. 10/227 [4%], $p<.001$). The authors concluded the benefits of aggressive medical management over percutaneous angioplasty and stenting among patients with intracranial stenosis persist over long-term follow-up.

Lutsep et al (2015) published a subgroup analysis of the SAMMPRIS trial results to evaluate whether outcomes differed for patients whose qualifying events occurred on or off antithrombotic therapy. Similar to the overall trial results, outcomes were worse in the stent group than in the best medical management group. Of the 284 patients on antithrombotic therapy at the time of the qualifying event, 140 patients were randomized to medical management and 144 to stenting. In Kaplan-Meier analysis, 2-year rates of the primary endpoint were 15.6% in the medical management group and 21.6% in the stent group ($p=.043$). In other subgroup analyses of the SAMMPRIS trial results, 2-year event rates were higher in the stent group for most variables evaluated. The interaction between treatment and the subgroup variables was not significant for any variable.

The Carotid And Vertebral Artery Transluminal Angioplasty Study randomized 16 patients with symptomatic vertebral artery stenosis to endovascular therapy (balloon angioplasty or stenting) or best medical treatment alone. Endovascular intervention was technically successful in all 8 patients, but 2 patients experienced transient ischemic attacks. During a mean follow-up of 4.7 years, no patient in either treatment group experienced a vertebrobasilar territory stroke, but 3 patients in each arm died of myocardial infarction or carotid territory stroke, and 1 patient in the endovascular arm had a nonfatal

carotid territory stroke. The investigators concluded that patients with vertebral artery stenosis were more likely to have carotid territory stroke and myocardial infarction during follow-up than recurrent vertebrobasilar stroke. While they noted the trial failed to show a benefit of endovascular treatment of vertebral artery stenosis, the small number of patients enrolled severely limits conclusions.

Qureshi et al (2013) published results from another small RCT comparing angioplasty alone with angioplasty plus a balloon-expanding stent for 18 subjects who had moderate intracranial stenosis ($\geq 50\%$) with documented failure of medical treatment or severe stenosis ($\geq 70\%$) with or without failure of medical treatment. Technical success ($< 30\%$ residual stenosis on immediate post-procedure angiography) occurred in 5 of 10 patients treated with angiography (9 randomized to angiography, 1 crossover from the group randomized to stent placement) and 5 of 8 patients treated with stent placement. Rates of stroke or death were low in both groups (1 of 10 in the angiography group vs. none in the stent placement group). This trial suggests that angioplasty with stenting is feasible in patients with severe intracranial stenosis, but the small sample size and lack of statistical comparisons limit conclusions that can be drawn.

Post market Surveillance

Alexander et al (2019) reported results from Wingspan Stent System Post Market Surveillance (WEAVE) post marketing surveillance study. WEAVE was an FDA-mandated, prospective, single-arm study evaluating the rate of stroke and death within 72 hours post-stenting in patients who met FDA on-label usage criteria. One hundred fifty-two consecutive patients were enrolled at 24 hospitals. The study was designed to enroll 389 patients but was stopped early when the second, predetermined interim data analysis indicated that the safety benchmarks were met. The primary outcome included 2 nonfatal strokes and 2 deaths from strokes for a total of 4 patients (2.6%) with an event of stroke, bleed or death.

Section Summary: Endovascular Interventions for Symptomatic Intracranial Atherosclerotic Disease

The strongest evidence on the efficacy of endovascular treatment for symptomatic intracranial stenosis is from the SAMMPRIS, VISSIT, and CASISS RCTs. The SAMMPRIS trial was stopped early due to harms because the rate of stroke or death at 30 days following treatment was higher in the endovascular arm, which received percutaneous angioplasty with stenting. Follow-up of the SAMMPRIS subjects has demonstrated no long-term benefit from endovascular therapy. The VISSIT and CASISS RCTs similarly found no benefit with endovascular treatment. These studies support the conclusion that outcomes of endovascular treatment are worse than medical therapy in patients with symptomatic intracranial stenosis.

Stent-Assisted Endovascular Treatment of Intracranial Aneurysms

Clinical Context and Therapy Purpose

The purpose of endovascular interventions in individuals with intracranial aneurysm is to remove the aneurysm from the circulation and prevent possible rupture (or if the aneurysm had already ruptured, to stop bleeding and prevent re-rupture) or to divert blood flow away from an aneurysm.

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

Populations

The population of interest is individuals with intracranial aneurysms. Treatment decisions depend on patient and aneurysm characteristics. Small (<7 mm) asymptomatic aneurysms can generally be observed. Larger and asymptomatic aneurysms may be considered for treatment according to anatomical location and morphological characteristics of the aneurysm and relative risks for specific treatments. The FDA-approved endovascular treatments have specific specifications regarding aneurysm characteristics (see Regulatory section) although they have been used off-label for challenging lesions in other locations.

Interventions

Self-expanding stents have FDA approval through the humanitarian device exemption program for the endovascular treatment of intracranial aneurysms.

Intracranial stents are being used to treat cerebral aneurysms. Stent-assisted coiling began as an approach to treat fusiform or wide-neck aneurysms in which other surgical or endovascular treatment strategies may not be feasible. As experience has grown, stenting has also been used in smaller berry aneurysms as an approach to decrease the rate of retreatment needed in individuals who receive coiling.

In 2011, the Pipeline Embolization Device, which falls into a new device category called “intracranial aneurysm flow diverters,” or flow-diverting stents, received FDA premarket approval for the endovascular treatment of large or giant wide-necked intracranial aneurysms in the internal carotid artery. The Pipeline device is a braided, wire mesh device that is placed within the parent artery of an aneurysm to redirect blood flow away from the aneurysm, with the goal of preventing aneurysm rupture and possibly decreasing aneurysm size. According to FDA documentation, the Surpass Streamline Flow Diverter has the same mechanism of action as the approved Pipeline Embolization Device.

Comparators

Small asymptomatic aneurysms can generally be observed without surgery. Surgical clipping of intracranial aneurysms has been used since the 1960s, but the feasibility of clipping for aneurysms depends on the aneurysm location.

Outcomes

The Executive Summary of an FDA meeting of the Neurological Devices Advisory Panel in 2018 states the primary safety outcomes for regulatory review have traditionally been focused on neurological deaths and major ipsilateral strokes (defined as an increase of ≥ 4 points in the National Institutes of Health Stroke Scale score during the stroke event) and the percentage of individuals who had a disabling stroke (defined as a modified Rankin Scale score ≥ 3 assessed at a minimum of 90 days post-stroke event) within 6 months to 1 year of treatment. The FDA is considering an additional outcome to assess functional independence defined as the change in the modified Rankin Scale score at 1-year post-treatment compared to pre procedure. The FDA has traditionally used a composite efficacy outcome defined as the percentage of individuals demonstrating a Raymond I classification for complete occlusion (i.e., 100% aneurysmal occlusion) without retreatment of the target aneurysm or significant parent artery stenosis ($\geq 50\%$) evaluated within 1-year post procedure.

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 long-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

Randomized Controlled Trial

Darsaut et al (2023) conducted a pragmatic, unblinded RCT of surgical clipping compared to endovascular treatment in 291 patients with unruptured intracranial aneurysms. Adults with modified Rankin Scale score <3 with at least 10 years of life expectancy were included. Patients with multiple aneurysms were evaluated based on one aneurysm. The composite primary outcome was failure of aneurysm occlusion, intracranial hemorrhage during follow-up, or residual aneurysms at 1 year. The primary outcome occurred in 9% of patients who received surgical clipping and 19% of patients who received endovascular therapy (relative risk, 2.07; 95% CI, 1.12 to 3.83; $p=.021$). However, surgery was associated with a higher rate of complications including neurologic deficits ($p=.04$) and hospitalization beyond 5 days ($p<.001$).

Self-Expanding Stent-Assisted Coiling for Intracranial Aneurysms

A literature search did not identify any randomized trials of self-expanding stent-assisted treatment of intracranial aneurysms compared with standard neurosurgical treatment (i.e., surgical clipping or endovascular coils). The available evidence includes single-arm case series, registry studies, nonrandomized comparative studies, and a systematic review of nonrandomized comparative studies.

Systematic Reviews

Hong et al (2014) reported on the results of a systematic review and meta-analysis of studies that compared stent-assisted coiling with coiling alone for the treatment of intracranial aneurysms. Reviewers included 10 retrospective cohort studies, ranging in size from 9 to 1109 patients. In pooled analysis, compared with coiling alone, stent-assisted coiling was associated with higher rates of progressive thrombosis (37.5% vs. 19.4%; OR, 2.75; 95% CI, 1.95 to 3.86; $p<.000$) and lower rates of recurrence (16.2% vs. 34.4%; OR, 0.35; 95% CI, 0.25 to 0.49; $p<.000$). The mortality rate was 9.1% for stent-assisted coiling compared with 2.6% for coiling alone, although the difference was not statistically significant (OR, 2.31; 95% CI, 0.68 to 7.82; $p=.18$). Similarly, permanent complication rates and thromboembolic complication rates did not differ significantly between the 2 groups.

Ryu et al (2015) conducted a systematic review of studies reporting complications after stent-assisted coiling of ruptured intracranial aneurysms, with a focus on complications related to antiplatelet therapy. They included 33 studies, 3 of which were prospective and the other 30 were retrospective (N=1090 patients). In a pooled analysis, thromboembolic complications occurred in 108 patients (event rate, 11.2%; 95% CI, 9.2 to 13.6). Intraprocedural hemorrhage occurred in 46 patients (event rate, 5.4%; 95% CI, 4.1 to 7.1).

Randomized Controlled Trial

Boisseau et al (2023) published results of the Stenting in the Treatment of Aneurysm Trial (STAT), which was a multicenter RCT that compared stent-assisted coiling of unruptured intracranial aneurysms compared to coiling alone. Study subjects (n=205) had a risk of aneurysm recurrence (e.g., large aneurysms ≥ 10 mm], post coiling recurrent aneurysm, or small aneurysms with a wide neck ≥ 4 mm]). The primary outcome was treatment failure, which was a composite of initial failure to treat the aneurysm, aneurysm rupture, need for retreatment, dependency, death, or residual aneurysm seen on angiography at 12 months). The primary outcome occurred in 30.1% of patients who underwent stent-assisted coiling versus 27.3% of patients who underwent coiling alone (relative risk, 1.10; 95% CI, 0.7 to 1.7; $p=.66$). These results may be limited by Type 2 error, since the difference between groups was smaller than expected possibly due to the study being underpowered.

Nonrandomized Comparative Studies

The largest comparative series describing the use of stents and coiling alone for treating intracranial aneurysms was described by Piotin et al (2010). They reported on a series of 1137 patients (1325 aneurysms) treated between 2002 and 2009. In this series, 1109 (83.5%) aneurysms were treated without stents (coiling), and 216 (16.5%) were treated with stents (15 balloon-expandable and 201 self-expandable stents). Permanent neurologic procedure-related complications occurred in 7.4% (16/216) of those with stents versus 3.8% (42/1109) of those without stents (logistic regression $p=.644$; OR, 1.289; 95% CI, 0.439 to 3.779). Procedure-induced mortality occurred in 4.6% (10/216) of the procedures with stents versus 1.2% (13/1109) in those without (logistic regression $p=.006$; OR, 0.116; 95% CI, 0.025 to 0.531). At the time of publication, the authors had followed 53% (114/216) of aneurysms treated with stents and 70% (774/1109) of aneurysms treated without, with angiographic recurrence in 14.9% (17/114) versus 33.5% (259/774), respectively ($p<.001$; OR, 0.349; 95% CI, 0.204 to 0.596).

Additional smaller nonrandomized comparative studies, both prospective and retrospective, have evaluated stent-assisted coiling, compared with coiling alone, balloon-assisted coiling, or surgical clipping.

Hetts et al (2014) compared outcomes for patients treated using stent-assisted coiling with those treated using coiling alone for patients who had unruptured intracranial aneurysms who were enrolled in the prospective, nonrandomized, multicenter Matrix and Platinum Science Trial. The trial compared bare-metal aneurysm coils with polymer-coated aneurysm coils. One hundred thirty-seven patients received a stent-assisted coil, and 224 patients received coiling alone. Patients treated with stent-assisted coiling more often had wide-neck aneurysms (62% vs. 33%; $p<.000$) and had aneurysms with a lower dome-to-neck ratio (1.3 vs. 1.8; $p<.000$). Periprocedural serious adverse events occurred in 6.6% of those treated with stent-assisted-coiling, compared with 4.5% of those treated with coiling alone ($p=.039$). At 1 year, ischemic strokes were more common in patients who received a stent-assisted coil than in patients who received a coil alone (8.8% vs. 2.2%; $p=.005$). However, in multivariable analysis, stent use did not independently predict ischemic stroke at 2 years (adjusted OR, 1.1; $p=.94$).

Consoli et al (2016) compared stent-assisted coiling with balloon-assisted coiling in patients who had unruptured wide-necked intracranial aneurysms treated at a single-center. The study included 268 patients (286 aneurysms), 117 (122 aneurysms) of whom were treated with stent-assisted coiling and 151 (164 aneurysms) of whom were treated with balloon-assisted coiling. At discharge, 97.9% and 97.3% of those in the balloon-assisted and stent-assisted groups, respectively, had modified Rankin Scale scores of 0 or 1 (statistical comparison not reported). After 6 months, 97.9% and 98% of those in the balloon-assisted and stent-assisted groups, respectively, had modified Rankin Scale scores of 0 or 1, while

mortality rates were 2.6% and 1.7% in the balloon-assisted and stent-assisted groups, respectively (statistical comparisons not reported). At 6 months, aneurysm recurrence rates were 11.1% and 5.8% in the balloon-assisted and stent-assisted groups, respectively. In multivariable analysis, the use of stent-assisted coiling was significantly associated with complete occlusion at the end of the procedure (regression coefficient not reported; $p=.024$) and complete occlusion after 6 months (regression coefficient not reported; $p=.05$).

Liu et al (2014) retrospectively compared outcomes for patients who had posterior communicating artery aneurysms treated using stent-assisted coiling with those treated using coiling alone. A total of 291 coiling procedures were performed, including 56 aneurysms treated with a self-expandable stent. Complete aneurysm occlusion on initial angiography occurred in 41.1% of stent-assisted coiling patients compared with 35.3% of nonstented patients (statistical comparison not reported). At last follow-up (mean, 14.3 months for stent-assisted coiling and 13.2 months for nonstent patients), the aneurysm recurrence rates were 10.6% in stent-assisted coiling patients and 28.1% of nonstent patients ($p=.014$). Procedural complications occurred in 10.7% of stent-assisted coiling patients compared with 11.5% of nonstent patients ($p=NS$).

Comparison Between Endovascular Devices for Intracranial Aneurysms

Systematic Reviews

Nonrandomized studies, summarized in a systematic review by King et al (2015), have compared devices used for stent-assisted coiling of intracranial aneurysms. Reviewers evaluated published studies reporting on stent-assisted coiling with the Neuroform and Enterprise systems to assess outcomes between the devices. The analysis included 47 studies with a total of 4039 patients (4238 aneurysms; 2111 treated with Neuroform and 2127 with Enterprise). Most (81%) studies were retrospective. Compared with those treated using the Enterprise system, patients treated using the Neuroform system were more likely to have deployment failure (2.3% vs. 0.2%; $p<.001$) and a higher mortality rate (2.8% vs. 1.8%; $p=.04$), less likely to have 100% aneurysm occlusion at last follow-up (61.1% vs. 74.7%; $p<.001$), and more likely to have recanalization (13.9% vs. 10.6%; $p=.02$). However, conclusions drawn from these findings are influenced by the potential for bias in the underlying studies and between-study heterogeneity.

Nonrandomized Comparative Studies

A large study, reported by Geyik et al (2013), included 468 patients with wide-necked cerebral aneurysms who underwent stent-assisted coiling with the Enterprise, Neuroform, Wingspan, or (self-expanding) Leo (Balt Extrusion) stents. The overall mortality rate was 1.9%; procedure-related complications occurred in 28 (6.9%) patients. Angiographic follow-up data, obtained from 6 months to 7 years post procedure (mean, 19.2 months), were available for 440 (94%) patients. For the total of 467 aneurysms with follow-up, complete occlusion occurred in 194 (41.6%) aneurysms, near-complete occlusion (>95% occlusion but minimal residual filling with coils at the neck) occurred in 242 (51.8%) aneurysms, and incomplete occlusion (<95%) occurred in 31 (6.6%) aneurysms. At 6-month follow-up, recanalization occurred in 38 aneurysms (8% of all aneurysms with follow-up available). The authors concluded that stents were associated with high rates of occlusion and low rates of recurrence over long-term follow-up.

In a larger study, Lee et al (2016) reported on 1038 patients treated with endovascular coiling, 296 of whom underwent stent-assisted coiling, with a focus on predictors of procedural rupture. Three cases of procedural rupture occurred among patients treated with stent-assisted coiling.

Other representative noncomparative studies in which at least some patients were treated with devices commercially available in the U.S. are summarized in Table 4. Interpretation of these studies is limited by potential selection bias and lack of comparison groups. In general, these series demonstrate high rates of technical success of stent deployment with high rates of aneurysm occlusion; however, variable complication rates, particularly related to thromboembolic events, were observed.

Table 4. Noncomparative Studies of Stent-Assisted Endovascular Treatment of Aneurysms

Study	Study Type	Population	Intervention	Primary Outcome
ATLAS IDE study: Jankowitz et al (2019) (30 patients enrolled through September 2015) FDA SSED (201 patients enrolled through October 2016)	Prospective, multicenter (25 sites)	201 patients with wide-necked intracranial aneurysm (neck ≥ 4 mm or dome-to-neck ratio < 2), parent vessel diameter of 2.0 to 4.5 mm, the aneurysm is intracranial (encompassing the entire posterior circulation and aneurysms at or distal to the superior hypophyseal artery in the anterior circulation)	Neuroform Atlas stent and approved coils	100% occlusion, without retreatment or significant stenosis: 84.7% (95% CI, 78.6 to 90.9) - Any serious adverse event: 51 (28%) - Cerebrovascular event: 18 (11%) unruptured - Any major ipsilateral stroke or neurologic death: 4.4% (95% CI, 1.9 to 8.5)
US LVIS pivotal trial: Fiorella et al (2018) FDA SSED	Prospective, multicenter (21 sites)	153 patients with unruptured or ruptured (> 30 days since occurrence) wide-necked (neck ≥ 4 mm or dome to neck ratio < 2) intracranial, saccular aneurysms (≥ 4 mm and < 20 mm maximum diameter in any plane) from a parent vessel with a diameter ≥ 2.0	LVIS devices	100% occlusion, without retreatment or significant stenosis: 71% (95% CI, 63 to 77) - Disabling stroke with mRS score ≥ 3 or neurological death: 6% (95% CI, 3 to 11)

Study	Study Type	Population	Intervention	Primary Outcome
		mm and ≤ 4.5 mm which were amenable to endovascular coil embolization		
Feng et al (2016)	Retrospective case series	97 patients with intracranial saccular aneurysms (13 with rupture)	Endovascular treatment with LVIS	100% of patients had technically successful treatment· 98.9% met the primary end point of safety (absence of new transient or permanent neurologic deficit or death) - Over mean 7.8-mo FU, no patient had new neurologic deterioration or died - Among 76 patients with DSA at FU, 59.21% had complete occlusion
Aydin et al (2015)	Retrospective case series	80 patients with wide-necked intracranial aneurysm (3 institutions)	Endovascular treatment with stent placement (Leo Baby stent)	97.5% of patients had technically successful treatment 7.5% had periprocedural or delayed thromboembolic events; 3 (3.8%) had permanent neurologic deficits
Chalouhi et al (2013)	Retrospective case series	76 patients with PCA aneurysms (1 institution)	Of 71 successful interventions: endovascular coiling (n=60) with or without Neuroform stent assistance (n=4) or balloon assistance (n=4), or parent vessel trapping (n=11)	93.4% of patients had technically successful treatment; remaining patients required surgical clipping - Among 67 patients who had successful endovascular treatments and who did not die in the hospital, 85% favorable outcomes (mild, moderate, no disability)
Chen et al (2013)	Retrospective case series	10 patients with large and giant fusiform	Endovascular treatment with stent placement (Neuroform	9 patients had good outcomes; 1 patient

Study	Study Type	Population	Intervention	Primary Outcome
		aneurysms of the vertebrobasilar arteries (1 institution)	or Leo self-expanding, 5 patients), stent-assisted coiling (3 patients), or occlusion of proximal artery (2 patients)	- died after stenting procedure - Stent deployment was generally feasible in the vertebrobasilar system
Gentric et al (2013)	Prospective cohort; industry-sponsored	107 patients with unruptured cerebral aneurysms (1 of 10 European institutions)	Endovascular treatment with Neuroform stent-assisted coiling	94.4% of patients had technically successful treatment; 66.4% of patients had complete occlusion immediately postprocedure - At 12- to 18-mo FU, 5 (5%) had delayed complications, with 3% having thromboembolic events - Of 93 patients with anatomic evaluation available, aneurysms recurred in 9.7%
Johnson et al (2013)	Retrospective case series	91 patients with complex MCA aneurysms not amenable to coiling enrolled (1 institution)	Endovascular treatment with coiling with stent assistance using Neuroform (62 aneurysms), Enterprise (32 aneurysms), Wingspan (1 aneurysm), or a combination (5 aneurysms) or stenting alone (2 aneurysms)	100% of patients had technically successful treatment 9 patients had new neurologic symptoms after procedure, 1 with long-term disability. One procedure-related death. - Of 85 aneurysms with initial FU imaging available (usually at 6 mo post procedure), 77 (90.6%) were completely occluded and 4 (4.7%) required retreatment
Kulcsar et al (2013)	Retrospective case series	117 patients with wide-necked cerebral aneurysms	Endovascular treatment with Neuroform stent-assisted coiling	- Stents successfully deployed in 113 patients with 117 aneurysms. 99 patients had grade 1 or 2 occlusion (complete or aneurysm neck) on immediate post procedure imaging - Intraprocedural major thrombotic events occurred in 7 (5.9%)

Study	Study Type	Population	Intervention	Primary Outcome
				and major infarcts on post procedure imaging in 9 (7.7%) Of 92 aneurysms with FU imaging available, 71 (77%) had grade 1 or 2 occlusion

CI: confidence interval; DSA: digital subtraction angiography; FDA: Food and Drug Administration; FU: follow-up; IDE: Investigational Device Exemption; LVIS: low-profile visualized intraluminal support; MCA: middle cerebral artery; mRS modified Rankin Scale; PCA: posterior cerebellar artery; SSED: Summary of Safety and Effectiveness Data; US: United States.

Subsection Summary: Self-Expanding Stent-Assisted Coiling for Intracranial Aneurysms

There is a lack of RCT evidence on the efficacy of self-expanding stent-assisted coiling compared with coiling alone or surgical clipping for the treatment of intracranial aneurysms. Nonrandomized studies have reported higher complete occlusion rates with stenting and lower recurrence rates. However, some evidence has shown that adverse event rates are relatively high with stenting, and 1 nonrandomized comparative trial reported higher mortality with stent-assisted coiling than with coiling alone. This evidence is insufficient to determine whether stent-assisted coiling improves outcomes for patients with intracranial aneurysms because the risk-benefit ratio cannot be adequately defined. However, it is recognized that patients who are candidates for endovascular therapy for aneurysms frequently have aneurysms in locations not amenable to surgical therapy, making comparisons with surgical therapy unlikely. Given the relative rarity of intracranial aneurysms, there may be legitimate barriers to clinical trials.

Flow-Diverting Stents for Intracranial Aneurysms

Pivotal Studies for Food and Drug Administration Approval

In 2011, the Pipeline Embolization Device, which is categorized as a flow-diverting stent, received FDA premarket approval. The device's approval was based on the industry-sponsored Pipeline for Uncoilable or Failed Aneurysms study, a multicenter, prospective, single-arm trial (2013) of the device for treatment of internal carotid artery aneurysms that were uncoilable or had failed coiling. Investigators enrolled 108 patients at 10 centers with unruptured large- or giant-necked aneurysms measuring at least 10 mm in diameter, with aneurysm necks of at least 4 mm, who underwent placement of 1 or more Pipeline devices. One patient was excluded from evaluations of the device effectiveness and safety due to unsuccessful catheterization. Four patients were excluded from the evaluation of the device effectiveness. Two patients had 2 qualifying aneurysms treated, so the "effectiveness cohort" was 106 aneurysms in 104 patients. Seventy-eight (73.6%) of 106 aneurysms met the study's combined primary effectiveness end point of complete occlusion at day 180 without major stenosis or use of adjunctive coils. For 6 (5.6%) of the 107 patients who underwent any catheterization, a primary safety endpoint (occurrence of major ipsilateral stroke or neurologic death at 180 days) occurred.

The Surpass Streamline Flow Diverter received FDA premarket approval in 2018. According to FDA documentation, the Surpass diverter has the same mechanism of action as the Pipeline diverter. The device was approved based on the pivotal Surpass Intracranial Aneurysm Embolization System Pivotal Trial to Treat Large or Giant Wide Neck Aneurysms (SCENT) prospective, single-arm study. Patients were enrolled and treated between 2012 and 2015 at 25 sites in the U.S. and 1 site in the Netherlands.

Two-hundred and thirty-six patients were enrolled and 180 had 1-year data included in the FDA report. Eligible patients had a single targeted intracranial aneurysm located in the internal carotid artery distribution up to the terminus with a neck ≥ 4 mm or no discernible neck and an aneurysm size ≥ 10 mm (including saccular, fusiform, and dissecting configuration) and had a vessel diameter between 2.5 mm and 5.3 mm at both the proximal and distal segments. The incidence of major ipsilateral stroke, defined as an increase in the National Institutes of Health Stroke Scale score from baseline by ≥ 4 points, and neurological death was 10.6% (19/180) and 2.8% (5/180), respectively. Five of the patients experiencing major ipsilateral stroke also suffered neurological death. The percent of patients experiencing disabling stroke defined as a modified Rankin Scale of 3 or higher measured at least 90 days after stroke event was 6.1% (11/180; 95% CI, 3.1 to 10.7). Forty-one (22.8%) patients had improved modified Rankin Scale scores at 12-months compared to baseline. The percent of patients with 100% occlusion (Raymond-Roy Class I) without clinically significant stenosis (defined as $>50\%$ stenosis) of the parent artery was 62.8% (113/180).

Systematic Reviews

Zhou et al (2015) reported the results of a systematic review of studies comparing flow-diverting devices with endovascular coiling for intracranial aneurysms, which included 9 retrospective comparative studies (N=863 subjects). Reviewers included studies of patients with ruptured or unruptured aneurysms. Across the 9 studies, 305 patients were treated with flow-diverting devices, 558 with coil embolization therapy, and 324 with stent-assisted coiling alone. In the pooled analysis, the use of flow-diverting devices was associated with a significantly higher complete occlusion rate than coil embolization therapy (OR, 3.13; 95% CI, 2.11 to 4.65; $I^2=18\%$) or stent-assisted coiling (OR, 2.08; 95% CI, 1.34 to 3.24; $I^2=0\%$). Rates of overall morbidity did not differ significantly between patients treated with flow-diverting devices and coil embolization therapy or between flow-diverting devices and stent-assisted coiling. Xin et al (2019) reported results of a similar systematic review of 11 observational studies, several of which overlapped with Zhou. Results with respect to occlusion rate compared to coil embolization and mortality were similar.

Randomized Controlled Trials

No randomized trials evaluating intracranial aneurysms were identified comparing flow-diverting stent treatment with standard neurosurgical treatment (i.e., surgical clipping or endovascular coils) from the time of FDA approval of the first flow-diverter until 2017.

Raymond et al (2017) reported on results of the Flow Diversion in the Treatment of Intracranial Aneurysm Trial (FIAT). FIAT was an investigator-initiated, pragmatic, multicenter RCT and registry study integrated into clinical practice at 3 Canadian hospitals enrolling 112 patients, between May 2011 and February 2015. Seventy-eight patients were randomized (39 in each group) to flow diversion or standard management (physician's choice of observation, coil embolization, parent vessel occlusion, or clip placement), and 34 additional patients received flow diversion within the registry. Inclusion criteria were pragmatic; patients with an aneurysm for which flow diversion was considered a promising treatment were eligible unless they had a contraindication. The trial was originally powered to include 200 patients in the pilot phase and 250 patients in the pivotal phase but was stopped early due to safety concerns. Patients mean age was about 58 years, mean aneurysm size was approximately 16 mm in the RCT arm and 19 mm in the registry arm, and mean aneurysm neck was 5 mm. Approximately two-thirds of the aneurysms were in the proximal carotid, 13% were in another anterior location, and 18% were in posterior circulation. The physician's choice in the standard care group (selected at the time of randomization) was coil embolization (with or without stent placement) in 25 (64%) patients, parent vessel occlusion in 10 (26%) patients, observation in 4 (10%) patients, and surgical clipping in no patients. Twelve (16%) of 75 patients (95% CI, 9% to 27%) who were allocated to or received flow diversion were dead (n=8) or dependent

(n=4) at 3 months or more, which crossed a predefined safety boundary. In the RCT portion of the study, morbidity or mortality occurred in 5 patients in the flow diversion group (13%; 95% CI, 5 to 29) and 5 patients in the standard treatment group (13%; 95% CI, 5 to 28). The primary efficacy outcome was a composite including complete or near-complete occlusion of the aneurysm between 3 and 12 months and an independent functional outcome (modified Rankin Scale score ≤ 2). Sixteen (42%) patients (95% CI, 27 to 59) in the flow diversion group failed to reach the primary outcome compared with 14 (36%) patients in the standard treatment group (95% CI, 22 to 53). Characteristics of the trial are shown in Table 5. Results shown in Table 6 include all patients and the subset of patients with proximal carotid aneurysms.

Kiselev et al (2018) reported the results of the Study of Complex intracranial Aneurysms Treatment (SCAT) trial of flow diversion versus parent vessel occlusion and bypass in patients with complex anterior circulation aneurysms conducted in 2 neurosurgical centers in Russia. One hundred and eleven patients were randomized: 55 into the flow diversion group and 56 into the parent vessel occlusion with bypass group. There was a baseline imbalance with respect to age and aneurysm neck size, so the authors included only 40 patients in each group, selected after propensity score matching. The mean age of subjects was 54 years old and approximately three-quarters of the patients were women. Patients were followed for 12 months. The aneurysms were in the following segments: A2 segment of anterior cerebral artery (n=1), anterior communicating artery (n=3), cavernous carotid artery (n=29), ophthalmic segment of internal carotid artery (n=9), communicating segment of internal carotid artery (n=11), M1 segment (n=20) and M2 segment of middle cerebral artery (n=7). The median aneurysm size by magnetic resonance imaging (MRI) was 12 mm (interquartile range, 9 to 16.75) in the bypass group and 15 mm (interquartile range, 9 to 20.5) in the flow diversion group. Study characteristics are shown in Table 5 and results are shown in Table 6. Outcome definitions were unclear. Of the 40 patients included in analysis, 97.5% in the flow diversion group and 80% in the bypass group had a 'good clinical outcome' (difference between groups, $p=.029$). The overall morbidity and mortality rates were 15% and 5%, respectively, but rates by group were not reported. The rate of complete occlusion at 12 months was 65% in the flow diversion group and 97.5% in the bypass group ($p=.001$).

Table 5. Summary of Randomized Controlled Trial Characteristics of Flow-Diverting Stents for Intracranial Aneurysms

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Raymond et al (2017) (FIAT)	Canada	3	2011 to 2015	Patients with an aneurysm for which flow diversion was considered a promising treatment (clinical judgment)	n =39 Arterial (not intraaneurysmal) flow-diverting device with or without coil embolization	n=39 Best standard treatment selected according to clinical judgment
Kiseleva et al (2018) (SCAT)	Russia	2	2015 to 2017	Patients with anterior circulation complex aneurysms with neck wider than 4 mm, where dome/neck ratio $\leq 2:1$; suitable for flow diversion and occlusion with bypass; not eligible for coiling or direct clipping	n=55 Flow diversion: multiple flow-diverting devices used	n=56 Parent vessel occlusion and bypass

Table 6. Summary of Randomized Controlled Trial Results of Flow-Diverting Stents for Intracranial Aneurysms

Study	Primary Efficacy Outcome	Death	Any Stroke	Complications	Residual Aneurysm or complete occlusion
Raymond et al (2017) (FIAT)				Any SAE or Complication	Residual aneurysm
All patients					
N	77	77	77	77	77
Flow diversion (95% CI), %	58 (41 to 73) ^a	5 (1 to 19)	13 (5 to 29)	29 (16 to 46)	18 (8 to 35)
Standard treatment (95% CI), %	64 (47 to 78) ^a	5 (1 to 19)	10 (3 to 25)	10 (3 to 25)	21 (10 to 37)
Treatment effect (95% CI)	NR	NR	NR	NR	NR
Patients with proximal carotid aneurysms					
N	54	54	54	54	54
Flow diversion (95% CI), %	42 (NR) ^a	4 (NR)	8 (NR)	39 (NR)	12 (NR)
Standard treatment (95% CI), %	36 (NR) ^a	4 (NR)	11 (NR)	14 (NR)	21 (NR)
Kiseleva et al (2018) (SCAT)				Total major complications	Complete occlusion at 12 mo
N	80			80	80
Flow diversion (95% CI), %	97.5 ^b	NR by group	NR by group	5	65
Bypass treatment (95% CI), %	80 ^b			22.5	97.5
Treatment effect (95% CI)	NR; p=.029			NR; p=.048	NR; p<.01

CI: confidence interval; NR: not reported; SAE: serious adverse event.

^a The primary efficacy outcome was a composite of complete or near-complete occlusion of the aneurysm between 3 and 12 months and an independent functional outcome (modified Rankin Scale score ≤2).

^b The primary outcome was 'good' or 'acceptable' clinical outcome. It was variably defined as neurological deterioration and neurological morbidity defined as modified Rankin Scale score increase by more than 1 or modified Rankin Scale ≥4.

Study limitations related to relevance and design and conduct of trials of flow-diverting stents are shown below in Tables 7 and 8 respectively. FIAT was a pragmatic trial and as such, the population included both

on- and off-label aneurysms and allowed multiple flow diverters and best standard therapy comparator as per clinical judgment.

Table 7. Study Relevance Limitations

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Follow-Up ^e
Raymond et al (2017) (FIAT)	1. Population included both on-label and off-label use and several anatomic locations	1. Multiple flow-diverters were allowed	1. Best standard therapy not clearly defined		2. Death and dependency reported at 3 months
Kiseleva et al (2018) (SCAT)		1. Multiple flow-diverters were allowed		1: Key morbidity and mortality outcomes not reported by group	

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 8. Study Design and Conduct Limitations

Study	Allocation ^a	Blinding ^b	Selective Reporting ^c	Data Completeness ^d	Power ^e	Statistical ^f
Raymond et al (2017) (FIAT)		1, 2 Patients, staff, outcome assessors not blinded				
Kiseleva et al (2018) (SCAT)	1: Only a subset of randomized patients included and matched using propensity scores	1,2,3: Blinding unclear	2: Outcome definitions unclear	1,2: Only a subset of randomized patients included in analysis		

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.

^b Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

^c Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

^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).

^e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

^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.

Nonrandomized Studies

Kan et al (2022) evaluated the treatment of large and giant posterior communicating artery aneurysms with the Surpass streamline flow diverter (SCENT trial). The Surpass flow diverter was implanted in 180

patients with uncoilable or treatment failure internal carotid artery aneurysms. The 3-year safety and effectiveness outcomes were published by Hanel et al (2022). The primary effectiveness outcome in the 3-year follow-up data was the proportion of patients who had complete aneurysm occlusion without clinically significant stent stenosis or retreatment. The primary safety outcome was defined as either neurological death or disabling stroke (defined as an increase in the National Institutes of Health Stroke Scale score ≥ 4). The primary effectiveness endpoint was met by 71.8% (79 out of 110) of patients; no patients in the 3-year follow-up cohort who achieved complete occlusion underwent retreatment. The primary safety composite outcome was reported in 12.2% (22 out of 180) of patients, and there were 4 cases of aneurysm rupture. The study characteristics are summarized in Table 9 and the results in Table 10.

Table 9. Summary of Nonrandomized Trial Study Characteristics

Study	Study Type	Country	Dates	Participants	Treatment 1	Treatment 2	Follow-Up
Hanel et al (2022) (SCENT)	Cohort	USA and various European sites	2012 to 2015	Patients with with large (10–24mm) or giant (≥ 25 mm) wide-neck (≥ 4 mm) unruptured or not acutely ruptured internal carotid artery aneurysms	Flow diversion utilizing the Surpass Streamline flow diverter	N/A	3 years

N/A: not applicable.

Table 10. Summary of Nonrandomized Trials Study Results

Study	Complete aneurysm occlusion without stenosis ^a or retreatment	Composite of: disabling stroke ^b or neurological death
Hanel et al (2022) (SCENT)		
Total N	110	180
% of patients who met the endpoint (95% CI)	71.8% (62.4% to 80.0%)	12.2% (7.8% to 17.9%)

CI: confidence interval.

^a Clinically significant in-stent stenosis defined as $>50\%$.

^b Disabling stroke defined as National Institutes of Health Stroke Scale score of ≥ 4 .

Subsection Summary: Flow-Diverting Stents for Intracranial Aneurysms

Two RCTs have evaluated flow-diverting stents. The FIAT pragmatic RCT and registry study compared flow diversion with standard management (observation, coil embolization, or parent vessel occlusion) in patients for whom flow diversion was considered a promising treatment. FIAT was stopped early due to safety concerns after 112 participants (78 in the randomized part of the study and 34 in the registry) were enrolled. Sixteen percent of patients who were randomized to flow diversion or received flow diversion at any time were dead or dependent at 3 months or later, which crossed a predefined safety boundary. The efficacy of flow diversion was also below expectations. While morbidity and mortality were lower for proximal carotid aneurysms than for posterior circulation aneurysms and results of flow diversion were more encouraging for aneurysms amenable to coil embolization, patients allocated to standard treatment appeared to do at least as well as those assigned to flow diversion.

SCAT compared flow diversion to parent vessel occlusion and bypass in patients with complex anterior circulation aneurysms. The publication included analysis of only 80 of the 111 randomized patients. Outcome definitions were unclear in the publication. Of the patients included in the analysis, 'good clinical outcome' was higher in the flow diversion group. Rates of overall morbidity and mortality were not reported by group. The rate of complete occlusion at 12 months was higher in the bypass group.

One systematic review, which compared the flow-diverting stents with endovascular coiling for intracranial aneurysms, demonstrated higher rates of aneurysm obliteration in those treated with the Pipeline endovascular device than in those treated with coiling, with similar rates of good clinical outcomes. Single-arm series have suggested there are high rates ($\geq 70\%$) of aneurysmal occlusion after flow-diverting stent placement. One randomized study demonstrated adequate aneurysm occlusion with the Surpass flow diverter device. As for self-expanding stents for aneurysms, patients who are candidates for endovascular therapy for aneurysms frequently have aneurysms in locations amenable to surgical therapy, making comparisons with surgical therapy unlikely.

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.

2014 Input

In response to requests, input was received from 4 physician specialty societies and 2 academic medical centers while this policy was under review in 2014. Input focused on the use of flow-diverting stents such as the Pipeline Embolization Device for the treatment of intracranial aneurysms. There was general support for the use of intracranial stent placement for intracranial aneurysms meeting the criteria outlined in the policy statements. There was also general support for the use of flow-diverting stents for the treatment of intracranial aneurysms and general support for the statement that flow-diverting stents are preferable to other stents for certain aneurysm characteristics.

2011 Input

In response to requests, input was received from 3 physician specialty societies and 3 academic medical centers while this policy was under review in 2011. For treatment of intracranial stenosis, most providing input would consider the use of this technology in selected patients who remained symptomatic from intracranial atherosclerotic disease, despite maximum medical therapy. There was unanimous support for the use of this technology in select patients with intracranial aneurysms, i.e., in those patients for whom surgical treatment is not possible and for whom endovascular treatment (coils) does not completely isolate the aneurysm.

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.

American Heart Association (AHA) and American Stroke Association (ASA)

In 2015, the American Heart Association (AHA) published joint guideline with American Stroke Association (ASA) on the management of patients with unruptured intracranial aneurysms. These guidelines included the following recommendations relevant to the use of endovascular therapies for aneurysms.

Table 11. Recommendations on Management of Unruptured Intracranial Aneurysms

Recommendation	COR	LOE
"...coil embolization may be superior to surgical clipping with respect to procedural morbidity and mortality, length of stay, and hospital costs, so it may be reasonable to choose endovascular therapy over surgical clipping in the treatment of select unruptured intracranial aneurysms, particularly in cases for which surgical morbidity is high, such as at the basilar apex and in the elderly"	IIb	B
"Endovascular treatment of unruptured intracranial aneurysms is recommended to be performed at high-volume centers."	I	B

COR: class of recommendation; LOE: level of recommendation.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review can be located at clinicaltrials.gov.

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CODES

To report provider services, use appropriate CPT codes, HCPCS codes, Revenue codes, and/or ICD diagnosis codes.

Codes	Number	Description
CPT		
	61630	Balloon angioplasty, intracranial (e.g., atherosclerotic stenosis), percutaneous
	61635	Transcatheter placement of intravascular stent(s), intracranial (e.g., atherosclerotic stenosis), including balloon angioplasty, if performed
	61640	Balloon dilatation of intracranial vasospasm, percutaneous; initial vessel
	61641	Balloon dilatation of intracranial vasospasm, percutaneous; each additional vessel in same vascular family
	61642	Balloon dilatation of intracranial vasospasm, percutaneous; each additional vessel in different vascular family
HCPCS		
	None	
Type of Service	Surgery	
Place of Service	Inpatient	

POLICY HISTORY

Date	Action	Action
June 2026	Annual Review	Policy Revised
June 2025	Annual Review	Policy Renewed
June 2024	Annual Review	Policy Renewed

Date	Action	Action
June 2023	Annual Review	Policy Revised
June 2022	Annual Review	Policy Revised
June 2021	Annual Review	Policy Revised
June 2020	Annual Review	Policy Revised
June 2019	Annual Review	Policy Revised
June 2018	Annual Review	Policy Renewed
June 2017	Annual Review	Policy Revised
June 2016	Annual Review	Policy Renewed
June 2015	Annual Review	Policy Renewed
July 2014	Annual Review	Policy Revised
September 2013	Annual Review	Policy Revised
October 2012	Annual Review	Policy Renewed
October 2011	Annual Review	Policy Renewed

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
PO Box 9232
Des Moines, IA 50306-9232

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