NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of endovascular insertion of an intrasaccular wire-mesh blood-flow disruption device for intracranial aneurysms

An intracranial aneurysm is a bulge in a blood vessel in the brain, caused by a weakness in the blood vessel wall. In this procedure, a wire-mesh device is inserted through a thin tube (catheter) into the brain via a large blood vessel (endovascular) in the groin. It is guided into the aneurysm (intrasaccular) and left there to act as a plug (a blood clot forms in the device). The aim is to block the flow of blood into the aneurysm to reduce the chance of it rupturing or to stop further bleeding from an aneurysm that has already ruptured.

Contents

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in January and updated in June 2019.

Procedure name

- Endovascular insertion of an intrasaccular wire-mesh blood-flow disruption device for intracranial aneurysms

Specialist societies

- UK Neurointerventional Group
- Society of British Neurological Surgeons
- The British Society of Neuroradiologists
- Royal College of Radiologists.

Description of the procedure

Indications and current treatment

An intracranial aneurysm is a bulge in a blood vessel in the brain caused by a weakness in the blood vessel wall, usually where it branches. Most brain aneurysms only cause noticeable symptoms if they rupture. However, large aneurysms may cause local compression symptoms before they rupture, such as headache. Rupture of intracranial aneurysms causes subarachnoid haemorrhage and is associated with a very poor prognosis. About 10% of people die before reaching hospital and a further 50% die within 4 weeks. About 50% of people who survive a subarachnoid haemorrhage have a persistent neurological deficit.

If an intracranial aneurysm is detected before it ruptures, treatment may be recommended to prevent it rupturing in the future. This is typically only done if the risk of a rupture is particularly high.

Current options for managing intracranial aneurysms include coiling, often with stent placement (stent-assisted coiling), neurosurgical clipping through a craniotomy (with or without bypass procedures), parent vessel occlusion (by open neurosurgery or by endovascular means) and conservative management. Flow diverter embolisation devices, which are placed in the parent blood vessel to divert blood flow away from the aneurysm itself, may be an option for some people with intracranial aneurysms.

What the procedure involves

Endovascular insertion of an intrasaccular wire-mesh blood-flow disruption device for intracranial aneurysms is used for the embolisation of ruptured and unruptured intracranial aneurysms. It may be particularly suitable for people with wide-necked aneurysms. The procedure is usually done under general anaesthesia. A catheter is inserted into the femoral artery and advanced into the cerebral circulation under X-ray guidance. A second, smaller catheter is put inside the first and is inserted into the aneurysm. A basket-like device made of fine wire mesh is then pushed through the second catheter and placed into the aneurysm sac. The mesh device covers the aneurysm neck and obstructs blood flow into the aneurysm sac, creating blood stasis and promoting endothelial growth across the neck of the aneurysm. The appropriate device size is selected according to the aneurysm width and height.

The aim is to prevent the aneurysm from rupturing or to stop further bleeding from an aneurysm that has already ruptured.

Outcome measures

Modified Rankin Scale (mRS)

This is a functional assessment scale that measures the degree of disability or dependence of people who have suffered a stroke.

The scale runs from perfect health without symptoms to death:

- 0: no symptoms
- 1: no significant disability; able to carry out all usual activities, despite some symptoms

- 2: slight disability; able to look after own affairs without assistance, but unable to carry out all previous activities
- 3: moderate disability; needs some help, but able to walk unassisted
- 4: moderately severe disability; unable to attend to own bodily needs without assistance, and unable to walk unassisted
- 5: severe disability; needs constant nursing care and attention, bedridden, incontinent
- 6: dead.

Efficacy summary

Technical success

In a systematic review of 940 patients, successful placement of an intrasaccular blood-flow disruption device was achieved in 97% of procedures (95% confidence interval [CI] 95% to 99%).[1]

In a case series of 48 patients, successful device placement was achieved in 96% (50/52) of procedures.[4]

In a case series of 39 patients, the technical success rate was 100% (39/39).[6]

In a case series of 120 patients, the technical success rate was 93% (112/120).[11]

Need for additional devices

In the systematic review of 940 patients, 10% of patients needed additional devices, such as coils or stents, to complete the procedure (95% CI 5% to 15%, I^2=76%).[1]

In the case series of 48 patients, additional devices were needed in 22% (11/52) of procedures (10 stent insertions and 1 coiling).[4]

In the case series of 39 patients, adjunctive stent placement was needed in 5% (2/39) of procedures.[6]

In the case series of 120 patients, the procedure was used with other endovascular techniques in 23% (26/112) of patients.[11]

Aneurysm occlusion

In the systematic review of 940 patients, adequate occlusion (defined as either complete occlusion or neck remnant) was reported in 81% (95% CI 73% to 88%) of patients.[1]

In a case series of 113 patients, adequate occlusion was reported in 84% (82/98) of patients at 6-month follow up. In those patients who only had an intrasaccular wire-mesh blood-flow disruption device, the rate of adequate occlusion was 90% (64/71).[3]

In the case series of 48 patients, adequate occlusion was reported in 96% of aneurysms at short-term follow up (mean 5 months, n=45) and 100% at long-term follow up (mean 39 months, n=25).[4]

In the case series of 39 patients, adequate occlusion was reported in 87% of patients at short-term follow up (3 to 6 months, n=38) and 88% of patients at long-term follow up (18 months or longer, n=24).[6]

In a case series of 16 patients, total occlusion immediately after device insertion was 75% (12/16) and 19% (3/16) of patients had neck remnants. At long-term follow up (median 36 months), 4 of the 8 patients who did not have retreatment had total occlusion and 3 patients had neck remnants.[7]

In a case series of 150 patients, complete occlusion was reported in 54% (77/143) and adequate occlusion was reported in 85% (121/143) of patients.[10]

In a non-randomised comparative study of 132 patients, immediate complete aneurysm occlusion was reported in 59% (39/66) of patients who had an intrasaccular wire-mesh blood-flow disruption device and 92% (61/66) of patients who had stent-assisted coiling. After 6 months, complete occlusion was reported in 83% (55/66) and 85% (56/66) of patients respectively (p=1.0).[12]

In a non-randomised comparative study of 123 patients, complete aneurysm occlusion was reported in 88% (28/32) of patients who had an intrasaccular wire-mesh blood-flow disruption device and 69% (20/29) of propensity score-matched patients who had stent-assisted coiling after mean follow ups of 11 and 18 months respectively (p=0.08).[13]

Retreatment

In a case series of 168 patients, retreatment was needed in 7% (11/160) of patients (4 stent and coils, 4 flow diverters, 1 stent, 1 intrasaccular blood-flow disruption device and stent, and 1 intrasaccular blood-flow disruption device).[2]

In the case series of 113 patients, retreatment was reported in 15% (15/98) of patients (4 coiling, 7 stent-assisted coiling, 3 flow diversion, 1 additional intrasaccular blood-flow disruption device).[3]

In the case series of 48 patients, retreatment was needed after 16% (8/49) of procedures (11 retreatments: 5 stent-assisted coiling, 3 intrasaccular blood-flow disruption device insertion, 2 coiling and 1 flow diverter stent placement).[4]

In the case series of 39 patients, retreatment was needed after 5% (2/39) of procedures.[6]

In the case series of 16 patients, retreatment was needed in 47% (7/15) of patients by the end of follow up (median 36 months).[7]

In the case series of 150 patients, the overall retreatment rate was 10% (14/143) after 12 months of follow up.[10]

In the non-randomised comparative study of 132 patients, retreatment was reported in 11% (7/66) of patients who had an intrasaccular wire-mesh blood-flow disruption device and 12% (8/66) of patients who had stent-assisted coiling at 6-month follow up (p=1.0).[12]

In the non-randomised comparative study of 123 patients, retreatment was reported in 3% (1/32) of patients who had an intrasaccular wire-mesh blood-flow disruption device and 14% (4/29) of propensity score-matched patients who had stent-assisted coiling after mean follow ups of 11 and 18 months respectively (p=0.13).[13]

Clinical outcome

In the case series of 113 patients, a favourable clinical outcome (mRS score 2 or less) was reported in 81% (92/113) of patients at 6-month follow up. The rate was higher for patients with unruptured aneurysms compared with those with ruptured aneurysms (96% and 49% respectively).[3]

In the case series of 48 patients, 92% (44/48) of patients had a good clinical outcome (mRS score 2 or less) at last clinical follow up (mean 25 months).[4]

In the case series of 120 patients, 80% (96/120) of all patients had a favourable outcome at discharge and 83% (100/120) had a favourable outcome at 6-month follow up. For patients with subarachnoid haemorrhage, 42% (16/38) and 53% (20/38) had favourable outcomes at discharge and 6-month follow up respectively.[11]

In the non-randomised comparative study of 132 patients, a favourable outcome was reported in 86% (57/66) of patients who had an intrasaccular wire-mesh

blood-flow disruption device and 86% (57/66) of patients who had stent-assisted coiling at 6-month follow up (p=1.0).[12]

In the non-randomised comparative study of 123 patients, there was no statistically significant difference in the proportion of patients with an mRS score of 2 or less at 6-month follow up (100% [38/38] of patients who had an intrasaccular wire-mesh blood-flow disruption device compared with 97% [37/38] of patients who had coiling in the propensity score-matched analysis, p=1.0).[13]

Aneurysm recurrence

In the case series of 113 patients, aneurysm recurrence was reported in 15% (15/98) of patients at 6-month follow up; 7 were minor and 8 were major recurrences.[3]

Safety summary

Thromboembolic complications

Thromboembolic complications were reported in 10% (91/940) of patients in the systematic review of 940 patients.[1]

Thromboembolic complications were reported after 6% (3/52) of procedures in the case series of 48 patients. Two patients had intravenous abciximab and stent placement with no further consequences. In the third patient with a ruptured aneurysm, abciximab was not given to avoid haemorrhagic complications. There was a subsequent occlusion of a temporal M2 branch, resulting in temporo-parietal ischaemia with right hemiparesis and dysphasia (mRS score 4). The patient gradually recovered with slight hemiparesis at follow up (mRS score 2).[4]

Thromboembolic events were reported in 8% (3/39) of patients in the case series of 39 patients: 2 patients had no clinical deficit and 1 patient had a permanent deficit related to stent placement.[6]

A major stroke was reported in 1 patient in a case series of 150 patients; a delayed ipsilateral parenchymal haemorrhage, unrelated to the treated aneurysm, happened on day 22 after the procedure. Minor ischaemic stroke and transient ischaemic attack were reported in 5% (7/150) and 3% (5/150) of patients respectively. Arterial thrombosis in parent or branch vessels near the device was reported in 2% (3/150) of patients.[8]

Thromboembolic events were reported in 9% (11/120) of patients in the case series of 120 patients. Symptomatic infarction was reported in 3% (3/120) of patients, 1 of these patients was moderately disabled at discharge.[11]

Thromboembolic complications were reported in 12% (8/66) of patients who had an intrasaccular wire-mesh blood-flow disruption device and 18% (12/66) of patients who had stent-assisted coiling in the non-randomised comparative study of 132 patients (p=0.3). Neurological complications were reported in 2% (1/66) and 8% (5/66) of patients respectively (p=0.2) and ischaemic stroke was reported in 2% (1/66) and 6% (4/66) of patients respectively (p=0.4).[12]

Haemorrhage

Procedure-related haemorrhage was reported in 2% (14/940) of patients in the systematic review of 940 patients.[1]

Intraprocedural subarachnoid haemorrhage was reported in 1% (2/150) of patients in the case series of 150 patients (both patients were discharged without neurological symptoms).[8]

Haemorrhagic complications were reported in none of the patients who had an intrasaccular wire-mesh blood-flow disruption device and 3% (2/66) of patients who had stent-assisted coiling in the non-randomised comparative study of 132 patients (p=0.5).[12]

Aneurysm rupture during procedure

Intraprocedural rupture was reported in 1% (2/167) of patients in the case series of 168 patients.[2]

Aneurysm rupture during device placement was reported in 1 patient in the case series of 48 patients. This was treated by coils and glue; subsequent symptomatic vasospasm resulted in a hemiplegia that remained stable at follow up, with an mRS score of 3.[4]

Aneurysm rupture was reported in 2% (2/120) of patients in the case series of 120 patients. One intraoperative aneurysm rupture happened because of misplacement of the device and resulted in subarachnoid haemorrhage; the patient died from brain oedema. In the second patient, a peri-interventional aneurysmal rupture resulted in intraventricular haemorrhage; the patient developed a hemiparesis and was discharged with a modified Rankin Scale score of 5.[11]

Other vascular damage

Cervical artery dissection was reported in 4% (2/48) of patients in the case series of 48 patients: 1 case was identified during the procedure and treated by stenting with no clinical consequences. The other was diagnosed 24 hours after the procedure because the patient showed mild left hemiparesis, and was then

treated by stenting. The patient had left upper limb paresis at follow up (mRS score 2). Femoral artery dissection was reported in 1 patient in the same study; this was treated by surgical bypass with no further clinical consequences.[4]

Inflammatory response

Inflammatory response around the blood-flow disruption device was reported in 1 patient in the case series of 16 patients. This was seen on MRI as perianeurysmal oedema from 10 months after the procedure, and constantly increased thereafter. The patient also had an increasing neck remnant, which needed clipping.[7]

Mortality

Mortality was 5% (95% CI 1% to 10%) at last clinical follow up in the systematic review of 940 patients.[1]

Mortality was 3% (3/113) at 6-month follow up in a case series of 113 patients; 1 death was procedure related.[3]

One patient died from aneurysm rupture 3 years and 10 months after the original blood-flow disruption device insertion, in the case series of 16 patients. There was progressive aneurysm growth with increasingly slow circulation between the Woven EndoBridge (WEB) device and the aneurysm wall. This patient had the largest aneurysm of the series, originating from the basilar tip.[7]

Other safety issues

Hydrophilic polymer embolism after intrasaccular blood-flow disruption device insertion was described in a case report. The patient developed status epilepticus and pneumonia and died 24 days after admission. The cause of death was certified as 'intracerebral and subarachnoidal haemorrhage from ruptured aneurysm of the left anterior cerebral artery'. The authors noted that the precise role of hydrophilic polymer embolism in the sequence of events leading to death remain a matter for speculation.[9]

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, specialist advisers listed the following anecdotal adverse events: displacement of a deployed device from

the aneurysm sac into the lumen of the parent artery, the need for an additional intravascular device such as a stent, groin haematoma, clot formation and aneurysm rupture. They considered that the following were theoretical adverse events: delay in time to treatment if treatment is for a ruptured aneurysm, and risks from the use of antiplatelet therapy.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to endovascular insertion of an intrasaccular wire-mesh blood-flow disruption device for intracranial aneurysms. The following databases were searched, covering the period from their start to 30 April 2019: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	People with an intracranial aneurysm.
Intervention/test	Endovascular insertion of an intrasaccular blood-flow disruption device.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on about 1,500 patients from 1 systematic review, 2 non-randomised comparative studies, 9 case series and 1 case report (there is some patient overlap between the studies).[1–13]

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) are listed in the appendix.

Table 2 Summary of key efficacy and safety findings on endovascular insertion of an intrasaccular wire-mesh blood-flow disruption device for intracranial aneurysms

Study 1 Tau N (2018)

Details

Study type	**Systematic review**
Country	Europe and US
Recruitment period	Search date: December 2017
Study population and number	**n=940 (12 studies)** Patients with bifurcation intracranial aneurysms, either ruptured or unruptured
Age and sex	Mean 57 years; 69% female
Patient selection criteria	Studies of any design were included, without language restriction, except for commentaries, letters, technical notes, case reports and case series with fewer than 10 patients. The population of interest was patients with bifurcation aneurysms, either ruptured or unruptured, with any aneurysm anatomic characteristics. The intervention was endovascular treatment with any of the WEB devices.
Technique	Endovascular treatment with any WEB device (Sequent Medical, US).
Follow up	**Clinical follow up: median 7 months (range 1 to 13.8)**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Losses to follow up were not discussed in the review.

Study design issues: The review was reported according to the 'Preferred Reporting Items for Systematic Reviews and Meta-analyses' (PRISMA) guidelines. When an overlapping cohort was identified, only the most comprehensive and latest report was included in the final analysis. If the reviewers were unable to verify the uniqueness of participating patients, the paper was excluded from final analysis. Study quality was assessed using the 'Quality Assessment Tool for Case Series Studies' published by the National Institutes of Health. All studies were uncontrolled case series. There were 7 prospective, 4 retrospective and 1 combined retrospective and prospective. Three studies were single centre and 9 were multicentre. Five studies were rated as 'good', 1 was 'poor' and 6 were 'adequate'. The authors noted large heterogeneity between studies.

Study population issues: The most common aneurysm location was the middle cerebral artery bifurcation (37%), followed by anterior communicating artery (25%), basilar artery (22%), and internal carotid artery (8%). The aneurysmal neck was more than 4 mm in 75% to 100% of patients. Two studies exclusively included patients with ruptured aneurysms, while in other studies the proportion of patients with ruptured aneurysms was less than 50%.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **940** **Successful placement of device=97% (95% CI 95% to 99%)** Proportion of patients needing additional devices (such as coils or stents)=10% (95% CI 5% to 15%; I^2=76.4%) **Adequate occlusion (defined as either complete occlusion or neck remnant)=81% (95% CI 73% to 88%)** There were no significant differences according to the duration of follow up. Angiographic evaluation was done at a median of 7 months (range 3 to 28).	**Periprocedural complications=14% (130/940)** **(95% CI 9% to 19%, I^2=76.9%)** • Thromboembolic complications, n=91 • Procedure-related haemorrhage, n=14 • Other complications included intracranial aneurysm rupture and brain oedema. **Mortality** At last clinical follow up, mortality was 5% (95% CI 1% to 10%) and was increased in studies with higher proportions of patients with ruptured intracranial aneurysms.
Abbreviations used: CI, confidence interval; WEB, Woven EndoBridge	

Study 2 Pierot L (2018)

Details

Study type	**Case series (3 single-arm prospective multicentre studies: WEBCAST, WEBCAST-2 and French Observatory)**
Country	Denmark, France, Germany, Hungary
Recruitment period	2010 onwards
Study population and number	**n=168 (169 aneurysms)** Patients with bifurcation intracranial aneurysms, ruptured or unruptured
Age and sex	Mean 56 years (range 27 to 77); 67% female
Patient selection criteria	Inclusion criteria: age 18 years or over, ruptured (Hunt and Hess grade I, II, or III) aneurysms or unruptured aneurysms in the basilar artery, middle cerebral artery, internal carotid artery terminus or anterior communicating artery complex, diameter suitable for WEB use, dome-to-neck ratio ≥1. The French Observatory study also specified recanalised aneurysms as an inclusion criterion and the WEBCAST studies also specified neck size ≥4 mm and no additional implant. Exclusion criteria: age over 75 years, more than 1 aneurysm to be treated within 30 days, microcatheter could not reach target aneurysm, tumour or arteriovenous malformation. The WEBCAST studies also specified subarachnoid haemorrhage or intracranial haemorrhage within 3 months of treatment as an exclusion criterion for unruptured aneurysms.
Technique	The WEB-DL (Sequent Medical, US) device was initially used. This was subsequently replaced by WEB-SL, which has a barrel shape, and WEB-SLS, which is spherical. The most recent evolution of the device (WEBEV) has enhanced visualisation, which incorporates composite wire strands made from nitinol and platinum. Different microcatheters were also used throughout the studies. Treatment with ancillary devices (balloon, coils and stents) could be done, if necessary, in the French Observatory. In the WEBCAST trials, the use of ancillary devices was authorised as a rescue treatment only.
Follow up	**1 year**
Conflict of interest/source of funding	All 3 studies were funded by Sequent. A number of authors are consultants for companies including Sequent, Balt, Microvention, Neuravi, Penumbra, Medtronic, Stryker, Codman, Covidien and Cerus Endovascular.

Analysis

Follow-up issues: 91% (153/168) of patients were clinically evaluated with a mRS scoring at the 12-month follow up. Of the remaining 15 patients, 2 withdrew consent, 6 patients did not have a WEB device implanted, 5 patients had retreatment, 1 patient was lost to follow up and 1 patient missed the follow up.

Study design issues: Cumulative population of 3 single-arm, prospective, consecutive, multicentre studies. Clinical data, including all adverse events, were independently monitored and analysed by the same medical monitor. Thromboembolic events were diagnosed intraoperatively by angiography. Postoperative thromboembolic events were diagnosed by MRI or digital subtraction angiography done in patients with sudden neurological compromise. An expert interventional neuroradiologist independently evaluated aneurysm location on the initial angiogram, and aneurysm occlusion at the last angiographic follow up, using a previously validated 3-grade scale: complete occlusion, neck remnant and aneurysm remnant.

Study population issues: At baseline, 8% (14/169) of aneurysms were ruptured, 89% (150/169) were unruptured and 3% (5/169) were recanalised (after coiling). Aneurysm locations were: middle cerebral artery (51%), anterior communicating artery (21%), basilar artery (18%), and internal carotid artery terminus (10%). Aneurysm size was 2.8 to 17.0 mm (mean 7.6±2.5 mm). Aneurysm neck size was 2.4 to 13.8 mm (mean 5.2±1.6 mm). The neck was wide (≥4 mm) in 85% (144/169) of aneurysms.

Other issues: Study is included in systematic review by Tau et al. (study 1)

Key efficacy and safety findings

Efficacy

Number of patients analysed: **168**

Successful device placement=96.4% (163/169) (causes of failure were protrusion and subsequent retrieval of the device in 2 aneurysms, lack of appropriate device sizing in 3 aneurysms, and inability to deploy device in 1 aneurysm)

Adjunctive devices were used in 7.4% (12/163) of aneurysms (coils alone in 7, stents of flow diverters in 5).

Aneurysm occlusion at 1 year follow up

	All (n=153)	WEB-DL (n=72)	WEB-SL/SLS (n=81)	p value
Complete occlusion	81 (52.9%)	38 (52.8%)	43 (53.1%)	1.00
Neck remnant	40 (26.1%)	19 (26.4%)	21 (25.9%)	
Aneurysm remnant	32 (20.9%)	15 (20.8%)	17 (21.0%)	

Evolution of aneurysm occlusion between postoperative DSA and 1-year follow up

	All (n=153)	WEB-DL (n=72)	WEB-SL/SLS (n=81)	p value
Improved	94 (61.8%)	46 (63.9%)	48 (60.0%)	0.911
Stable	53 (34.9%)	24 (33.3%)	29 (36.3%)	
Worsened	5 (3.3%)	2 (2.8%)	3 (3.8%)	

No neck or aneurysm remnant was associated with bleeding or rebleeding during the follow-up period.

Retreatment=6.9% (11/160) (4 stent and coils, 4 flow diverters, 1 stent, 1 WEB and stent, and 1 WEB).

Safety

Adverse events, morbidity and mortality at 1 month

Event type	All (n=167)	WEB-DL (n=80)	WEB-SL/SLS (n=87)	p value
Thromboembolic events	24 (14.4%)	15 (18.8%)	9 (10.3%)	0.130
- *asymptomatic*	11 (6.6%)	9 (11.3%)	2 (2.3%)	0.027
- *symptomatic without sequelae*	8 (4.8%)	4 (5.0%)	4 (4.6%)	1.00
- *symptomatic with sequelae*	5 (3.0%)	2 (2.5%)	3 (3.4%)	1.00
Intraprocedural rupture	2 (1.2%)	1 (1.3%)	1 (1.1%)	1.00
Intracranial haemorrhage	1 (0.6%)	1 (1.3%)	0 (0%)	0.479
Morbidity*	5 (3.0%)	3 (3.8%)	2 (2.3%)	0.671
Mortality	0 (0%)	0 (0%)	0 (0%)	-

* defined as an mRS score >2 if baseline ≤2, mRS +1 or more if baseline >2, mRS >2 and ruptured at baseline.

The intraoperative ruptures and intracranial haemorrhage (related to antiplatelet treatment) were asymptomatic.

Morbidity was related to a thromboembolic event in 2 patients (mRS score 3) with device protrusion in 1 patient, to initial aneurysm rupture in 2 patients (mRS scores 3 and 4), and to worsening of pre-existing aneurysm mass effect in 1 patient (mRS score 3). Morbidity was related to the device in 1 patient, to the procedure in 1 patient and to the disease in 3 patients.

Mortality at 1 year

3.3% (5/153) of patients died between the 1-month and 1-year follow up: 3 were unrelated to aneurysm disease or treatment (2 cancer and 1 cirrhosis), 1 from worsening of pre-existing mass effect and 1 as a consequence and complication of a retroperitoneal haematoma during the index procedure.

All-cause mortality at 1 year=3.3% (5/153)

Neuro-related mortality at 1 year=0.7% (1/153)

Procedure-related mortality at 1 year=0.7% (1/153)

Morbidity at 1 year

All-cause morbidity at 1 year=1.3% (2/153)

Neuro-related morbidity at 1 year=0% (0/153)

Procedure-related morbidity at 1 year=1.3% (2/153)

Abbreviations used: DL, double layer; DSA, digital subtraction angiography; EV, enhanced visualisation; mRS, modified Rankin Scale; SL, single layer; SLS, single-layer sphere; WEB, Woven EndoBridge

Study 3 Kabbasch C (2018)

Details

Study type	**Case series**
Country	Germany (3 centres)
Recruitment period	2011 to 2018
Study population and number	**n=113** (114 aneurysms) Patients with intracranial aneurysms, ruptured or unruptured
Age and sex	Mean 59 years; 66% (75/113) female
Patient selection criteria	Not described
Technique	All procedures were done using a transfemoral approach with the patient under general anaesthesia. The single-layer, double-layer, and single-layer sphere WEB devices were used (Sequent Medical, US). The use of additional devices was left to the neurointerventionalist's discretion. 77% of aneurysms were treated by WEB only and 23% were treated in conjunction with coiling or additional devices (stents or flow diverters).
Follow up	**6 months**
Conflict of interest/source of funding	2 authors are consultants for Acandis GmbH (Germany) and 1 is a proctor for Microvention Inc./Sequent Medical (US).

Analysis

Follow-up issues: An additional 8 patients had treatment during the study period, but were excluded from the study cohort because the implantation procedure failed. 86% (98/114) of aneurysms were available for the 6-month angiographic follow up.

Study design issues: Retrospective, multicentre, observational study of consecutive patients. Functional outcome was evaluated by the mRS score at 6-month follow up. Unfavourable outcome was defined as mRS score >2. The study aim was to evaluate factors influencing aneurysm occlusion and aneurysm recurrence after WEB embolisation.

Study population issues: 32% (36/114) of aneurysms were ruptured and were treated within 24 hours after ictus. 9% (10/113) of patients had recurrent aneurysms that had been previously treated with other modalities. 7 aneurysms were partially thrombosed and 13 had a lobular shape. 34% of aneurysms were located at the basilar tip, 28% at the anterior communicating artery and 14% at the middle cerebral artery bifurcation. 80% (91/114) of aneurysms were located at a bifurcation and 20% (23/114) were sidewall aneurysms. The maximum aneurysm diameter ranged from 3 to 27.2 mm (mean diameter 8.6±4.6 mm). The mean dome width was 7.3±3.6 mm, the mean aneurysm height 7.9±4.4 mm, the mean neck width 4.6±1.8 mm and the mean dome-to-neck ratio 1.7±0.8. A total of 104 (91%) aneurysms were classified as wide necked.

Other issues: There may be some patient overlap with Pierot L et al., 2018 (study 2)

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **113 (114 aneurysms)** **Immediate angiographic outcomes after device insertion** • Complete occlusion=57.0% (65/114) • Neck remnants=19.3% (22/114) • Aneurysm remnants=23.7% (27/114) **Angiographic outcome at 6-month follow up** • Complete occlusion=62.2% (61/98) • Neck remnants=21.4% (21/98) • Aneurysm remnants=16.3% (16/98) • Adequate occlusion=83.7% (82/98) In multivariate analysis, aneurysm size (OR 1.2, 95% CI 1.01 to 1.38, p=0.034) was an independent risk factor for aneurysm remnants. Among the procedure-related factors, recurrent aneurysms (OR 7.5, 95% CI 1.5 to 37.3, p=0.013) and treatment by WEB and coiling (OR 7.9, 95% CI 1.8 to 33.9, p=0.005) were independently associated with aneurysm remnants. **Angiographic outcome at 6-month follow up for aneurysms treated by WEB device only** • Complete occlusion=67.6% (48/71) • Neck remnants=22.5% (16/71) • Aneurysm remnants=9.9% (7/71) • Adequate occlusion=90.1% (64/71) Aneurysm remnants were more often seen in male patients (21.9%) than in female patients (0%, p=0.003) and the rate of adequate occlusion was higher in patients with immediate complete occlusion. These factors were not statistically significant in multivariate analysis. **Favourable clinical outcome at 6-month follow up (mRS≤2)** • Overall=81.4% (92/113) • Unruptured aneurysms=96.2% (75/78) • Ruptured aneurysms=48.6% (17/35) (1 unfavourable outcome was procedure related and the others were related to subarachnoid haemorrhage itself.) **Aneurysm recurrence at 6 months=15.3% (15/98)** (7 were minor and 8 were major recurrences) Recurrence was statistically significantly associated with partial intrasaccular thrombosis (p<0.001), increasing aneurysm size (p=0.005) and additional coiling (p=0.001). In multivariate analysis, aneurysm size (OR 1.2, 95% CI 1.02 to 1.41, p=0.032) and additional coiling (OR 7.8, 95% CI 1.9 to 31.7, p=0.004) remained as independent predictors of recurrence. **Aneurysm recurrence at 6 months for aneurysms treated by WEB device only=11.3%** (8/71) (6 minor and 2 major) Recurrent aneurysms had a larger height (p=0.008) and aspect ratio (p=0.012) than aneurysms without recurrence (factors were dependent in multivariate analysis). **Retreatment=15.3% (15/98)** (4 coiling, 7 stent-assisted coiling, 3 flow diversion, 1 additional WEB device). Retreatment was feasible in all patients.	**Mortality** At 6-month follow up, there were 3 deaths (2.7%), 1 of which was procedure related.
Abbreviations used: CI, confidence interval; mRS, modified Rankin Scale; OR, odds ratio; WEB, Woven EndoBridge	

Study 4 Mine B (2018)

Details

Study type	**Case series**
Country	Belgium (3 centres)
Recruitment period	2010 to 2015
Study population and number	**n=48 (49 aneurysms)** Patients with intracranial aneurysms
Age and sex	Mean 57 years (range 35 to 76); 73% (35/48) female
Patient selection criteria	Not reported. The indication and modality of treatment were based in multidisciplinary discussion for all patients.
Technique	All procedures were done under general anaesthesia and systemic heparinisation. Overall, 52 WEB devices (Sequent Medical, US) were implanted: 33 WEB-DL, 15 WEB-SL, 4 WEB-SLS An additional device was used in 22% (11/52) of procedures.
Follow up	**Mean 25 months (range 3 to 72)**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Imaging follow-up protocol consisted of digital subtraction angiography (DSA) at 3, 6 and 12 months. MR angiography (MRA) was done at 12-month follow up and then every 2 years for unruptured aneurysms and yearly for ruptured aneurysms. In 1 procedure, the device was retrieved because of a major protrusion in the parent artery and in another procedure the device could not be implanted because of an acute angle between the parent artery and the aneurysmal neck. These 2 aneurysms were excluded for anatomical evaluation. Anatomical results were available for 74.5% (35/47) of aneurysms at 12-month follow up and 53.2% (25/47) of aneurysms at long-term follow up (mean 39 months, range 24 to 72).

Study design issues: Retrospective analysis of prospectively maintained database from 3 centres. All patients who had a WEB device inserted for an intracranial aneurysm were identified from the database. Clinical outcome was assessed using the mRS. Aneurysm occlusion was evaluated on DSA using a 3-point scale: grade I, complete occlusion; grade II, almost complete occlusion – neck remnant; grade III, incomplete occlusion – aneurysm remnant. Aneurysm occlusion was evaluated by 2 senior neuroradiologists, reaching consensus.

Study population issues: Mean aneurysm diameter was 8.6 mm (range 4 to 22) and mean neck diameter was 4.9 mm (range 2 to 10). There were 41 unruptured aneurysms, 3 recurrent aneurysms after treatment with coils, and 5 ruptured aneurysms. 59% (29/49) of aneurysms were located on the middle cerebral artery, 14% (7/49) on the basilar tip, 10% (5/49) on the anterior communicating artery, 4% (2/49) on the posteroinferior cerebellar artery and 2% (1/49) on the vertebral artery.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: 48 (49 aneurysms)

Successful device placement=96% (50/52) of procedures
Two devices were needed in 2 procedures. Two aneurysms needed more than 1 procedure: 1 needed a second WEB placement because of a significant remnant after the first procedure and the other needed 3 procedures because of persistent growth (in a previously ruptured and recanalised giant partially thrombosed anterior communicating artery aneurysm).

Additional devices=22.4% (11/52)
Of the 10 stent placements, 1 was planned before the procedure and 9 were decided during the procedure because of a WEB protrusion or clot formation. In 1 patient, additional coiling was done because of a significant aneurysm remnant after WEB placement.

Clinical outcome
At discharge, 83% (40/48) of patients had a normal (n=38, mRS=0) or unchanged neurological examination. 8.3% (4/48) of patients had neurological deterioration, 3 of whom showed a good clinical evolution at follow up (2 had an mRS score of 0 and 1 had mRS score of 1). One patient retained left paresis (mRS 3).

mRS score at last clinical follow up (mean 25 months)
• 0=79.2% (38/48)
• 1=6.2% (3/48)
• 2=6.2% (3/48)
• 3=4.2% (2/48)
• 6=4.2% (2/48)

Permanent neurological morbidity=6.2% (3/48)
Good clinical outcome (mRS≤2)=92% (44/48)

Retreatment=16.3% (8/49) (11 retreatments: 5 stent-assisted coiling, 3 WEB placement, 2 coiling, 1 flow diverter stent placement)

Anatomical outcomes – aneurysm occlusion grade (including retreatments)
<table>
<tr><th>Follow up</th><th>Grade I</th><th>Grade II</th><th>Grade III</th><th>Adequate occlusion (grade I and II)</th></tr>
<tr><td>Short term (mean 5 months), n=45</td><td>68.9%</td><td>26.7%</td><td>4.4%</td><td>95.6%</td></tr>
<tr><td>Mid-term (12 months), n=35</td><td>74.3%</td><td>20%</td><td>5.7%</td><td>94.3%</td></tr>
<tr><td>Long term (mean 39 months), n=25</td><td>72%</td><td>28%</td><td>0%</td><td>100%</td></tr>
</table>
Occlusion was stable between mid-term and long-term follow up in 82.6% (19/23) of aneurysms.

Overall occlusion at latest available follow up (mean 25 months, range 3 to 72)
• Grade I=72.3% (34/47)
• Grade II=27.7% (13/47)
</td><td>
Unexpected procedural events=14% (7/52) of procedures
• Thromboembolic complications=6% (3/52)
• Aneurysm rupture during device placement, n=1 (treated by coils and glue; subsequent symptomatic vasospasm resulted in a hemiplegia that remained stable at follow up with mRS score of 3)
• Cervical artery dissection, n=2 (1 was identified during the procedure and treated by stenting with no clinical consequences. The other was diagnosed 24 hours after the procedure because the patient showed mild left hemiparesis, and was then treated by stenting. The patient had left upper limb paresis at follow up, mRS score 2)
• Femoral artery dissection, n=1 (treated by surgical bypass with no further clinical consequences)

The 3 thromboembolic complications were clot formation at the neck: 2 were treated by intravenous abciximab and stent placement with no further consequences. In the third patient with a ruptured aneurysm, abciximab was not given to avoid haemorrhagic complications. There was a subsequent occlusion of a temporal M2 branch, resulting in temporo-parietal ischaemia with right hemiparesis and dysphasia (mRS score 4). The patient gradually recovered with slight hemiparesis at follow up (mRS score 2).

Mortality
2 patients died from unrelated causes during follow up.
</td></tr>
<tr><td colspan="2">Abbreviations used: DL, double layer; mRS, modified Rankin Scale; SL, single layer; SLS, single-layer sphere; WEB, Woven EndoBridge</td></tr>
</table>

Study 5 Lawson A (2018)

Details

Study type	**Case series**
Country	UK (14 centres)
Recruitment period	2012 to 2014
Study population and number	**n=109** (109 aneurysms, 112 procedures) Patients with intracranial aneurysms
Age and sex	Mean 56.5 years; 69% female
Patient selection criteria	Not described. Patients were selected after a multidisciplinary meeting among clinicians. Selection criteria were related to aneurysm and aneurysm neck size, aneurysm location, and whether a neurosurgical option was available. Aneurysms suitable for standard coiling or clipping were excluded, unless the patient refused the surgical option.
Technique	3 types of WEB device (Sequent Medical, US) were used: WEB-DL, WEB-SL and WEB-SLS. The procedure was elective in 83.5% (91/109) of patients and acute in 16.5% (18/109). There was no consistent antiplatelet regimen used across the different centres.
Follow up	**Minimum 3 months (range 3 to 16 months)**
Conflict of interest/source of funding	Sequent Medical funded Axiom Fusion eClinical Suite to build the WEB UK study database and provided funding for the statistical analysis. Five authors are consultants for Sequent Medical. Two are also consultants for other companies, including Covidien, Medtronic, Stryker and Pulsar Vascular.

Analysis

Follow-up issues: Follow-up results were available for 92% (100/109) of patients.

Study design issues: Data were collected retrospectively until March 2014 and prospectively after this date. Two independent interventional neuroradiologists classified all reported adverse events into 5 categories: device related, procedure related, aneurysm-disease related, ancillary device related, or related to another incidental condition. Clinical outcome was assessed using the modified Rankin Scale (mRS).

Study population issues: 7% (8/109) of patients had partial thrombosis of the aneurysm. Basilar aneurysms were the most common at 40% (44/109), followed by middle cerebral artery (36%), internal carotid artery (8%), anterior communicating artery (7%), posterior communicating artery (4%), posterior cerebral artery (1%), and anterior cerebral artery (4%). All patients had difficult to treat aneurysms that would not be suitable for unassisted coiling. 86% (84/109) had a wide neck, 45% (49/109) were bifurcation aneurysms, and 19% (21/109) of patients were not surgical candidates. Aneurysms were incidental in 59% (64/109) of patients, 17% (18/109) of patients had acute subarachnoid haemorrhage, and 18% (20/109) of patients were symptomatic. 6% (7/109) of patients had recurrent aneurysms. The maximum aneurysm diameter ranged from 3.8 to 18.4 mm (mean 8.2 mm) and the maximum diameter of the aneurysm neck ranged from 2.4 to 11.4 mm (mean 6.2 mm).

Other issues: Study is included in systematic review by Tau et al. (study 1).

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: 109
Successful device placement=95% (103/109)
1 patient had 2 successful procedures on separate occasions.
8 procedures were abandoned because of access issues.

Modified Rankin Scale score
<table>
<tr><th rowspan="2">Follow up</th><th colspan="7">mRS score</th></tr>
<tr><th>0</th><th>1</th><th>2</th><th>3</th><th>4</th><th>5</th><th>6</th></tr>
<tr><td>Preoperative, n=109</td><td>73.4%</td><td>10.1%</td><td>4.6%</td><td>3.7%</td><td>3.7%</td><td>4.6%</td><td>0%</td></tr>
<tr><td>At discharge, n=109</td><td>78.9%</td><td>8.2%</td><td>6.4%</td><td>5.5%</td><td>0.9%</td><td>0%</td><td>0%</td></tr>
<tr><td>>3-month follow up, n=100</td><td>77.0%</td><td>8.0%</td><td>6.0%</td><td>4.0%</td><td>0%</td><td>0%</td><td>5.0%</td></tr>
</table>
</td><td>
Overall morbidity at discharge=1.8% (2/109) (increase in mRS score to >2)
1 patient had thromboembolism secondary to the procedure and vasospasm from an acute subarachnoid haemorrhage. The other patient developed right cerebellar infarcts and cerebellar ataxia 5 days after the procedure.

Overall morbidity at follow up=6.0% (6/100)
In addition to the patient with cerebella ataxia described above, there were 5 patients who died.
No morbidity was associated with complications specific to the WEB device.

Mortality before discharge=0%

Mortality at follow up=5.0% (5/100)
None of the deaths was considered to be device related. 2 patients had delayed rupture, 1 of a different aneurysm (at 300 and 336 days after the procedure respectively), 1 patient had hydrocephalus, subarachnoid haemorrhage and died 259 days after the procedure, 1 patient had a delayed thromboembolic event 279 days after the procedure and 1 patient died because of comorbidities 306 days after the procedure (no association with the procedure or device).

Total adverse events=36.7% (40/109)
• Procedural, n=14
• Device related, n=17
• Ancillary device related, n=5
• Disease related, n=6
• ‘other’, n=2

Thromboembolism=15.6% (17/109) (7 symptomatic and 10 asymptomatic)

10.1% (11/109) of patients had persistent clinical sequelae related to an adverse event.

Incorrect sizing of device was recorded as an adverse event in 4 patients.
</td></tr>
<tr><td colspan="2">Abbreviations used: DL, double layer; mRS, modified Rankin Scale; SL single layer; SLS, single-layer sphere; WEB, Woven EndoBridge</td></tr>
</table>

Study 6 Herbreteau D (2016)

Details

Study type	**Case series**
Country	France
Recruitment period	2012 to 2015
Study population and number	**n=39** Patients with intracranial aneurysms
Age and sex	Mean 59 years; 59% (23/39) female
Patient selection criteria	Not described. The decision for treatment and its technique was decided by a multidisciplinary team that included neurosurgeons and interventional neuroradiologists. The decision for treatment with the WEB device was made on the basis of aneurysm characteristics (location, size, and neck size).
Technique	The WEB-DL device (Sequent Medical, US) was initially used, but was later replaced by WEB-SL and WEB-SLS. All procedures were done under general anaesthesia with intraoperative heparin, and a single femoral approach. Antiplatelet therapy regimens before, during and after procedure varied.
Follow up	**6 to 18+ months**
Conflict of interest/source of funding	One author received payment from Sequent Medical for writing or reviewing the manuscript.

Analysis

Follow-up issues: 1 patient was lost to follow up at the short-term follow up (3 to 6 months). Mid-term and long-term follow-up data were available for 62% (24/39) of aneurysms.

Study design issues: Retrospective analysis of prospectively collected data from a single centre. The aim of the study was to analyse the safety and efficacy of the WEB device in long-term follow up in relation to WEB shape modification. Morbidity was defined as an mRS score >1 when the preoperative mRS was 1 or lower (or in ruptured aneurysms) and as an increase of 1 point when the preoperative mRS score was higher than 1. Aneurysm occlusion was evaluated using the 3-grade scale (complete occlusion, neck remnant, aneurysm remnant) immediately at the end of the procedure and at follow up. Adequate occlusion was defined as complete occlusion or neck remnant. Modifications of the WEB device were evaluated by comparing angiographic views of the distance between the distal and proximal markers of the device and evaluating the concavity of the distal and proximal surfaces.

Study population issues: 90% (35/39) of aneurysms were unruptured. No aneurysm had been previously treated. Aneurysms were located at the middle cerebral artery bifurcation (54%), the anterior communicating artery (23%), the basilar tip (13%), the internal carotid artery terminus (5%), the pericallosal artery (3%) and the posterior communicating artery (3%). Aneurysm mean diameter ranged from 4.3 to 9.5 mm (72% were ≥5 mm). Neck size was <4 mm in 18% of aneurysms and ≥4 mm in 82% (32/39) of aneurysms. All except 1 met the definition of wide-neck bifurcation aneurysms.

Other issues: 14 patients were also included in the case series described by Pierot L et al., 2018 (study 2).

Key efficacy and safety findings

Efficacy

Number of patients analysed: **39**
Technical success=100% (39/39)
Adjunctive stent placement=5.1% (2/39) (because of WEB protrusion)

Aneurysm occlusion by follow-up period

	3 to 6 months n=38	1 year n=24	≥18 months n=24
Complete occlusion	60.5% (23/38)	50.0% (12/24)	54.2% (13/24)
Neck remnants	26.3% (10/38)	33.3% (8/24)	33.3% (8/24)
Aneurysm remnants	13.2% (5/38)	16.7% (4/24)	12.5% (3/24)
Adequate occlusion	86.8% (33/38)	83.3% (20/24)	87.5% (21/24)

Retreatment=5.1% (2/39) (1 patient had an unruptured aneurysm treated with an undersized WEB, retreated at 8 months with stent placement and coiling. The other patient had an unruptured aneurysm treated with an appropriately sized WEB, and was retreated at 14 months for an aneurysm remnant.)

Device sizing and shape medication
The WEB device was undersized (according to the rule of +1 mm/-1 mm) in 28.2% (11/39) of patients. Among the 38 patients with short-term angiographic follow up, 10 (26.3%) had an undersized device and 28 (73.7%) had an appropriately sized device.

Occlusion rates according to device sizing – short-term follow up

	Undersized device	Appropriately sized device	p value
Complete occlusion	50.0% (5/10)	64.3% (18/28)	0.67
Neck remnants	20.0% (2/10)	28.6% (8/28)	Not reported
Aneurysm remnants	30.0% (3/10)	7.1% (2/28)	Not reported
Adequate occlusion	70.0% (7/10)	92.9% (26/28)	0.10

WEB shape modification=31.6% (12/38) of patients at short-term follow up. At long-term follow up, 1 additional patient had WEB shape modification.

Occlusion rates according to WEB shape modification – short-term follow up

	WEB shape modification	No WEB shape modification	p value
Complete occlusion	25.0% (3/12)	76.9% (20/26)	0.004
Neck remnants	58.3% (7/12)	11.5% (3/26)	0.004
Aneurysm remnants	16.7% (2/12)	11.5% (3/26)	Not reported
Adequate occlusion	83.3% (10/12)	92.3% (24/26)	0.64

Safety

Adverse events
- Intraoperative aneurysm rupture=0% (0/39)
- Thromboembolic events=7.7% (3/39) (2 patients had no clinical deficit and 1 patient had a permanent deficit related to stent placement)

There were no delayed adverse events.

Procedure and device-related morbidity (mRS 2)=2.6%
Procedure and device-related mortality=0%

Abbreviations used: DL, double layer; mRS, modified Rankin Scale; SL single layer; SLS, single-layer sphere; WEB, Woven EndoBridge

Study 7 Khalid Z (2018)

Details

Study type	**Case series**
Country	Norway
Recruitment period	2012 to 2015
Study population and number	**n=16** Patients with ruptured or unruptured intracranial aneurysms
Age and sex	Median 59 years (range 39 to 71); 56% (9/16) female
Patient selection criteria	Not described. Mode of treatment was decided by a vascular team consisting of neurosurgeons and neurointerventionists.
Technique	A single WEB device was implanted in all procedures: 3 WEB-DL, 11 WEB-SL and 2 WEB-SLS
Follow up	**Median 36 months (range 13 to 49)**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: 1 patient was lost to follow up.

Study design issues: Retrospective analysis of prospectively collected data in a single centre cohort study. Data were obtained from the institutional prospective quality registry. Follow-up imaging was routinely done by CT angiography within a few days of the procedure and after 3 months. MR angiography was also done for all but 1 patient shortly after device insertion. Conventional angiography was only done on selected patients. Changes in size and shape of the device were assessed qualitatively on follow-up imaging, together with measurements of the distance between markers at the poles of the device.

Study population issues: At the time of intervention, 81% (13/16) of the aneurysms were unruptured (6 were symptomatic and 7 were incidental). Aneurysms were located at the basilar artery bifurcation (56%), anterior communicating artery (38%), and the middle cerebral artery (6%). Most of the aneurysms were ≥10 mm and the smallest aneurysm was 8.1 mm. 93.8% of the aneurysms were wide necked with a neck diameter ≥4 mm. Eleven aneurysms had an aspect ratio lower than 1.6 and 5 had an aspect ratio lower than 1.2. One aneurysm had previously been treated with coils. The authors noted that the population included a high number of aneurysms with circulated blebs or irregular configurations, which make it more difficult to obtain complete occlusion.

Other issues: the authors noted that the sizing recommendations from the device producer have been revised after gathering more experience into oversizing at the level of the neck. They stated that a large fraction of the failures in this study may be attributed to not oversizing the WEB device.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **16** **Occlusion immediately after device insertion** • Total occlusion=75.0% (12/16) • Neck remnants=18.8% (3/16) • Aneurysm remnant=6.2% (1/16) **Occlusion at follow up (median 36 months) excluding patients who had retreatment** • Total occlusion=4/8 • Neck remnants=3/8 • Aneurysm remnant=1/8 **Retreatment=46.7% (7/15)** All retreatments were for increasing circulation inside the aneurysm sac. In 3 of the retreated aneurysms, there were signs of shortening/retraction of the WEB device over time (1 of which also had compaction of coils from initial coiling treatment). In 2 aneurysms, there were signs of distal dislocation of the WEB without shortening. There were also signs of shortening in 3 WEB devices in aneurysms that were not retreated. Of the 7 patients who had retreatment, 5 had total occlusion at the end of follow up and 1 had an aneurysm remnant (for 1 patient, only the immediate status of retreatment was available, which showed complete occlusion). **WEB size evolvement** In the aneurysms that ruptured at 3 years and 10 months after initial treatment, the WEB device had increased by 25%. 26.6% (4/15) of WEB devices collapsed over time and had decreased in size by an average of 44.5% (range 35.9 to 59.1%). All of them had developed significant new circulation and needed retreatment. In the 9 aneurysms that were completely occluded at follow up, there was a successive slight decrease in WEB device size with an average of 13.2% (0 to 22.9%) at latest follow up.	There were no procedural or postprocedural thromboembolic events. 1 patient developed an inflammatory response around the WEB device. This was seen on MRI as perianeurysmal oedema from 10 months after the procedure and constantly increased thereafter. The patient also had an increasing neck remnant, which needed clipping. **Mortality** 1 patient died during follow up from aneurysm rupture, 3 years and 10 months after the original WEB device treatment. There was progressive aneurysm growth with increasing slow circulation between the WEB device and the aneurysm wall. This patient had the largest aneurysm of the series, originating from the basilar tip. Retreatment procedures led to complications in 2 patients: 1 patient had a subdural haematoma after craniotomy that could be managed conservatively, and 1 patient had a right-sided infarction of the A2 territory after aneurysm clipping (the same patient who developed an inflammatory response around the WEB device).
Abbreviations: DL, double layer; SL single layer; SLS, single-layer sphere; WEB, Woven EndoBridge	

Study 8 Fiorella D (2017)

Details

Study type	**Case series (WEB-IT)**
Country	US, UK, Hungary, Turkey (31 centres)
Recruitment period	2014 to 2016
Study population and number	**n=150** Patients with intracranial wide-necked bifurcation aneurysms
Age and sex	Mean 59 years (range 29 to 79); 73% (110/150) female
Patient selection criteria	Ruptured or unruptured saccular aneurysms, located at the basilar apex, middle cerebral artery bifurcation, internal carotid artery terminus, anterior communicating artery complex, dome-to-neck ratio≥1, wide-necked intracranial aneurysm with neck sized ≥4 mm or dome-to-neck ratio <2, diameter appropriate for treatment with the WEB device per instructions for use. Patients with ruptured aneurysms were required to be neurologically stable with a Hunt & Hess score of 1 or 2. Key exclusion criteria included: vascular tortuosity or morphology which could preclude safe access and support during treatment with WEB, and modified Rankin Scale (mRS) score ≥2 at baseline or prior to rupture.
Technique	A WEB device was implanted in all procedures: 19 WEB-DL, 107 WEB-SL and 22 WEB-SLS
Follow up	**30 days**
Conflict of interest/source of funding	Study was funded by Sequent Medical Inc. The primary investigators for the WEB-IT trial received institutional salary support for study related activities. Investigators in the WEB-IT trial also received payment for proctoring cases within the context of the trial.

Analysis

Follow-up issues: Follow up for safety data was only to 30 days.

Study design issues: Prospective multicentre single-arm study. The aim of the study was to report adverse events within the first 30 days after the procedure.

Study population issues: At the time of intervention, 9 of the aneurysms were ruptured. With respect to aneurysm characteristics, 91 (61%) were in the anterior circulation and 59 (39%) in the posterior circulation. The mean dome width was 6.4 mm (range 3.6 to 11.4), mean dome height was 6.1 mm (range 3.1 to 10.3), mean neck size was 4.8 mm (range 2.0 to 8.2), and mean dome-to-neck ratio was 1.3 (range 1.0 to 2.0).

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **150** **Technical success=98.7% (148/150)** Device insertion was unsuccessful in 2 patients; 1 because of anatomic tortuosity and 1 because of improper device size availability. Adjunctive stenting was done in 2 patients where the WEB device appeared to impinge upon the parent artery or adjacent branch. Adjunctive balloons were used to assist WEB positioning in 5 patients.	**Technical events related to device** • Failure to open or twisted on deployment, n=3 • Device detachment system failure, n=3 • Kinked pusher, n=2 • Multiple attempts needed for detachment, n=2 There were no patient sequelae and a device was successfully implanted in all of these patients. **Primary safety events=0.7% (1/150)** A delayed ipsilateral parenchymal haemorrhage unrelated to the treated aneurysm, happened on day 22 after the procedure. The event was adjudicated as a major stroke, most likely related to antiplatelet medication and underlying cerebrovascular disease. At last follow up the patient's mRS score was 4. **Additional safety outcomes** • Minor ischaemic stroke=4.7% (7/150) (5 resolved without sequelae and 2 were mRS 1 at 30 days. Of these, 1 was device related, 4 were procedure related and 2 were neither) • Transient ischaemic attack=2.7% (5/150) • Arterial thrombosis in parent or branch vessels near the WEB device=2.0% (3/150) • Intraprocedural subarachnoid haemorrhage=1.3% (2/150) (both patients were discharged without neurological symptoms) There were 136 adverse events in 65 patients, of which 24 were categorised as serious (9 device related, 68 procedure related). 125 of these resolved without sequelae, 8 remain ongoing and 3 incurred sequelae. Other common events in the 30 day follow up included headache (n=21, 15.4%), nausea (n=7, 5.1%) and vessel puncture site pain (n=5, 3.7%).
Abbreviations: DL, double layer; SL single layer; SLS, single-layer sphere; WEB, Woven EndoBridge	

Study 9 Tikka J (2018)

Details

Study type	**Case report**
Country	Finland
Recruitment period	Not reported
Study population and number	**n=1** Patient with ruptured aneurysm of the anterior cerebral artery.
Age and sex	'woman in her 70s'
Patient selection criteria	N/A
Technique	The WEB-SL device (Sequent Medical, US) was used.
Follow up	**None**
Conflict of interest/source of funding	None

Key efficacy and safety findings

Case report: left cerebral hemisphere hydrophilic polymer embolism
The device insertion procedure was uneventful, but the patient remained unconscious. A CT scan 6 hours after the procedure showed rebleeding and ischaemic changes in the brain tissue surrounding the aneurysm with compression of the lateral ventricles. A ventriculostomy was done the next day. The patient then developed status epilepticus and pneumonia and died 24 days after admission.
Tissue samples from the left cerebral hemisphere showed foreign particles surrounded by multinucleated cells, suggesting a foreign-body reaction. The findings were consistent with 3-day to 2-month old polymer emboli.
The cause of death was certified as 'intracerebral and subarachnoidal haemorrhage from ruptured aneurysm of the left anterior cerebral artery'.
The authors noted that the precise role of hydrophilic polymer embolism in the sequence of events leading to death remain a matter for speculation.
Abbreviation: SL single layer; WEB, Woven EndoBridge

Study 10 Arthur AS (2019)

Details

Study type	**Case series (WEB-IT study)**
Country	US, Canada, Denmark, Germany, Hungary, Turkey
Recruitment period	2014 to 2016
Study population and number	**n=150** Patients with wide-neck bifurcation aneurysms of the anterior or posterior intracranial circulations
Age and sex	See Fiorella D et al. (2017)
Patient selection criteria	See Fiorella D et al. (2017)
Technique	See Fiorella D et al. (2017)
Follow up	**12 months**
Conflict of interest/source of funding	See Fiorella D et al. (2017)

Analysis

Follow-up issues: Of the 148 patients eligible at 6 months, 142 (96%) completed the visit. One patient refused further follow up after the 6-month window and was withdrawn from the study. All 147 patients who were eligible at 1 year were followed up clinically and 143 (97%) had follow-up imaging.

Study design issues: Prospective multicentre single-arm study. The primary effectiveness endpoint was defined as the proportion of patients with complete aneurysm occlusion without retreatment, recurrent subarachnoid haemorrhage, and without significant parent artery stenosis at 1 year after treatment in the intention-to-treat population.

Study population issues: See Fiorella D et al. (2017)

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **150** **Primary effectiveness endpoint with prespecified imputations done for patients without angiographic follow up=54.8%** **Complete occlusion in patients in whom the procedure was completed and follow-up imaging was done=53.8% (77/143)** **Adequate occlusion=84.6% (121/143)** The analyses of subgroups, including gender, race, ethnicity, sac width, aneurysm rupture status, aneurysm location, site experience and diameter of the device used, suggested no difference in the rate of complete or adequate occlusion. **Progression and stability of aneurysm occlusion** At 6 months: • 5.0% (7/141) were worse • 3.5% (5/141) were the same • 91.5% (129/141) were better At 12 months (compared with 6 months): • 11.5% (15/131) were worse • 79.4% (104/131) were the same • 9.2% (12/131) were better Most patients who had recanalisation or regrowth between 6 and 12 months declined by only a few percentage points. Ten patients who went from 100% occlusion at 6 months declined to 98% (n=3), 95% (n=5) and 90% (n=2) at 12 months. **Planned target aneurysm retreatment within 12 months=5.6% (8/143)** (1 coils alone, 4 stent-assisted coiling, 3 flow diversion) An additional 6 patients had electively scheduled retreatments within the ensuing 6 months. **Overall retreatment=9.8% (14/143)** There were no recurrent subarachnoid haemorrhages among the 9 patients who had ruptured aneurysms at baseline.	**Primary safety events** (including death from any non-accidental cause or any major stroke within the first 30 days after treatment, or a major ipsilateral stroke or neurological death from day 31 to 1 year after treatment). • There was 1 delayed ipsilateral parenchymal haemorrhage on postoperative day 22. There were no primary safety events between 30 days and 1 year after the procedure. **Other serious neurological events after 30 days** There were no deaths. 6 patients had unrelated serious neurological events after 30 days: 1 ischaemic stroke, 1 intracranial haemorrhage, 1 seizure and 3 transient ischaemic attacks. In 4 of these patients, the events resolved without any sequelae. One patient who had a reintervention with a Pipeline embolisation device on day 203 subsequently developed recurrent transient ischaemic attacks, which were described as 'ongoing' at the 12-month clinical follow up. One patient had 2 ischaemic stroke events (on day 12 and day 72) related to pre-existing cerebrovascular disease and had persistent right leg weakness and gait instability at the 12-month follow up.

Study 11 Goertz L (2019)

Details

Study type	**Case series**
Country	Germany (3 centres)
Recruitment period	2011 to 2018
Study population and number	**n=120** Patients with ruptured or unruptured intracranial aneurysms
Age and sex	Mean 58.5 years; 67% (80/120) female
Patient selection criteria	All treatment indications were made within an interdisciplinary team consisting of neurointerventionalists and neurosurgeons and after discussion with the patient. The procedure was typically used for wide-necked and bifurcation aneurysms as an alternative treatment option for stent-assisted procedures or microsurgical clipping in aneurysms, which were not deemed suitable for conventional coiling. Patients with multiple aneurysms treated during a single session were excluded from analysis.
Technique	The Woven EndoBridge (WEB; Sequent Medical, US) device was used: single layer (SL), double layer (DL) or single-layer sphere (SLS). All procedures were done under general anaesthesia, using a transfemoral approach. The use of adjunctive endovascular techniques was left to the neurointerventionalist's discretion.
Follow up	**6 months**
Conflict of interest/source of funding	One author serves as proctor for MicroVention Inc./Sequent Medical, US. Two authors serve as consultants for Acandis GmbH, Germany.

Analysis

Follow-up issues: No losses to follow up were described.

Study design issues: Retrospective, multicentre case series of consecutive patients. The objective of the study was to analyse the incidence and clinical relevance of complications related to the procedure.

Study population issues: Of the 120 patients, 38 (32%) presented with aneurysmal subarachnoid haemorrhage. The most common aneurysm locations were the basilar artery (33%), the anterior communicating artery (29%) and the middle cerebral artery (14%). The mean aneurysm size was 8.5±4.5 mm and the mean neck width was 4.5±1.7 mm. 91% (109/120) of aneurysms were classified as wide necked. A total of 11 patients (9%) were treated for a previously treated and recurrent aneurysm, 7 aneurysms (6%) had intrasaccular partial thrombus formation and 14 (12%) had a lobular shape.

Other issues: There is some patient overlap with Kabbasch C et al., 2018 (study 3)

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **120** Technical success=93.3% (112/120) The procedure was used in combination with other endovascular techniques in 23.2% (26/112) of patients. **Favourable outcome** *Overall population* • At discharge=80.0% (96/120) • At 6-month follow up=83.3% (100/120) *Non-subarachnoid haemorrhage patients* • At discharge=97.6% (80/82) • At 6-month follow up=97.6% (80/82) *Subarachnoid haemorrhage patients* • At discharge=42.1% (16/38) • At 6-month follow up=52.6% (20/38)	Overall complication rate=11.7% (14/120) • Symptomatic complications=5.0% (6/120) • Transient neurological deficits=3.3% (4/120) • Permanent neurological deficits=1.7% (2/120) • Thromboembolic events=9.2% (11/120) • Cerebral infarction=4.2% (5/120) • Symptomatic infarction=2.5% (3/120) (1 patient was moderately disabled at discharge) • Haemorrhagic events=1.7% (2/120) (1 intraoperative aneurysm rupture happened because of misplacement of the WEB device and resulted in subarachnoid haemorrhage; the patient died from brain oedema. In the second patient, a peri-interventional aneurysmal rupture resulted in intraventricular haemorrhage; the patient developed a hemiparesis and was discharged with a modified Rankin Scale score of 5). • Seizure=0.8% (1/120) • Mild postoperative brain oedema, associated with a transient hemiparesis=0.8% (1/120) Procedure-related mortality=0.8% In univariate analysis, a lower aspect ratio (p=0.04) and an increased width-to-height ratio (p=0.03) were statistically significant risk factors for procedural complications.

Study 12 Kabbasch C (2019a)

Details

Study type	**Non-randomised comparative study**
Country	Germany (3 centres)
Recruitment period	2011 to 2018
Study population and number	**n=132 (66 Woven EndoBridge [WEB] device and 66 stent-assisted coiling)** Patients with ruptured or unruptured intracranial aneurysms
Age and sex	• WEB device: mean age 57.5 years; 68% (45/66) female • Stent-assisted coiling: mean age 55 years; 77% (51/66) female
Patient selection criteria	Inclusion criteria: successful aneurysm treatment by WEB or stent-assisted coiling, aneurysm size 3 to 11 mm, location at the anterior communicating artery, middle cerebral artery, internal carotid artery, or basilar artery, patient age >18 years, unruptured or ruptured aneurysm status, at least 1 available angiographic follow up. Exclusion criteria: partially thrombosed aneurysms, fusiform aneurysms, dissecting aneurysms, multiple aneurysms treated during 1 session, combined treatment by WEB and stent implantation.
Technique	The Woven EndoBridge (WEB; Sequent Medical, US) device was used. All procedures were done under general anaesthesia, using a transfemoral approach. Adjunctive coiling was used in selected patients to provide optimal aneurysm occlusion.
Follow up	**6 months**
Conflict of interest/source of funding	One author serves as proctor for MicroVention Inc./Sequent Medical, US. Two authors serve as consultants for Acandis GmbH, Germany.

Analysis

Follow-up issues: No losses to follow up were described.

Study design issues: Retrospective, multicentre, matched case-control study. Patients who had treatment by WEB were matched with patients who had stent-assisted coiling on the basis of aneurysm location and unruptured or ruptured status. To avoid a potential selection bias, an Inverse Probability Treatment Weighting approach based on the propensity score model was used. Propensity scores were calculated using a multivariate logistic regression model with treatment as the response and the following covariates: patient age, sex, ruptured/unruptured status, aneurysm location, aneurysm size, and neck width. All angiographic images were assessed blinded and independently by 3 experienced consultant neurointerventionalists. Discrepancies were resolved by consensus.

Study population issues: There were no significant differences in baseline patient and aneurysm characteristics between the 2 groups. In both groups, 24 aneurysms were initially ruptured, 16 were at the anterior communicating artery, 9 at the middle cerebral artery, 13 at the internal carotid artery and 28 at the basilar artery.

Other issues: There may be some patient overlap with other studies reported from the same centres.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **132 (66 WEB, 66 stent-assisted coiling [SAC])**

98.5% (65/66) of patients in the WEB group had WEB treatment alone; 1 patient had adjunctive coils.

Immediate complete aneurysm occlusion

- WEB=59.1% (39/66)
- SAC=92.4% (61/66)

Functional outcome at 6-month follow up

	Overall			Unruptured aneurysms			Ruptured aneurysms		
	WEB n=66	SAC n=66	p	WEB n=42	SAC n=42	p	WEB n=24	SAC n=24	p
mRS score			0.1			0.2			0.1
0	45	41		37	32		8	9	
1	5	13		3	7		2	6	
2	7	3		2	3		5	0	
3	2	0		0	0		2	0	
4	1	3		0	0		1	3	
5	5	5		0	0		5	5	
6	1	1		0	0		1	1	

Proportion of patients with favourable outcome

- WEB=86.4% (57/66)
- SAC=86.4% (57/66), p=1.0

In the weighted analysis, a favourable outcome was achieved by a similar proportion in both groups (OR 1.3, 95% CI 0.7 to 2.5)

Angiographic outcome

	WEB (n=66)	SAC (n=66)	p value
Follow-up period (months)	5.7±5.0	6.0±5.6	0.6
Complete occlusion	55 (83.3%)	56 (84.8%)	1.0
Neck remnant	7 (10.6%)	6 (9.1%)	
Aneurysm remnant	4 (6.1%)	4 (6.1%)	
Adequate occlusion	62 (93.9%)	62 (93.9%)	1.0
Retreatment	7 (10.6%)	8 (12.1%)	1.0

In the weighted analysis, adequate occlusion rates (OR 1.1, 95% CI 0.4 to 3.2, p=0.8) and retreatment rates (OR 0.9, 95% CI 0.4 to 1.8, p=0.7) were not statistically significantly different between the 2 groups.

Safety

Procedure-related complications

	WEB (n=66)	SAC (n=66)	p value
Complications	8 (12.1%)	14 (21.2%)	0.16
Thromboembolic complications	8 (12.1%)	12 (18.2%)	0.3
Haemorrhagic complications	0 (0%)	2 (3.0%)	0.5
Neurological complications	1 (1.5%)	5 (7.6%)	0.2
Ischaemic stroke	1 (1.5%)	4 (6.1%)	0.4

There was no procedure-related mortality.

After Inverse Probability Treatment Weighting adjustment, SAC was associated with a higher risk for both overall (OR 2.2, 95% CI 1.08 to 4.4, p=0.03) and neurological complications (OR 5.4, 95% 1.2 to 25.2, p=0.02) compared with WEB treatment.

Abbreviations used: CI, confidence interval; mRS, modified Rankin Scale; OR, odds ratio; SAC, stent-assisted coiling; WEB, Woven EndoBridge

Study 13 Kabbasch C (2019b)

Details

Study type	**Non-randomised comparative study**
Country	Germany (3 centres)
Recruitment period	2011 to 2018
Study population and number	**n=123 (56 Woven EndoBridge [WEB] device and 67 coiling)** Patients with unruptured intracranial aneurysms
Age and sex	• WEB device: mean age 59.5 years; 64% (36/56) female • Coiling: mean age 55 years; 75% (50/67) female
Patient selection criteria	Inclusion criteria: successful treatment of an unruptured aneurysm by stand-alone coiling or by WEB implantation with or without adjunctive coils; maximum aneurysm diameter ranging from 3 to 11 mm; patient older than 18 years. Exclusion criteria: previous aneurysm rupture; stent-assisted coiling or WEB placement with additional stent implantation; fusiform aneurysms; dissecting aneurysms; partial intrasaccular thrombosis; multiple aneurysms treated during 1 session. Generally, the WEB was used for wide-necked and bifurcation aneurysms with an unfavourable configuration for conventional coiling as a treatment alternative for stent-assisted coiling or surgery.
Technique	The Woven EndoBridge (WEB; Sequent Medical, US) device was used: single layer (SL), double layer (DL) or single-layer sphere (SLS). All procedures were done under general anaesthesia, using a transfemoral approach. In some patients, additional coiling was done to provide optimal aneurysm occlusion.
Follow up	**6 months**
Conflict of interest/source of funding	One author serves as proctor for MicroVention Inc./Sequent Medical, US. Two authors serve as consultants for Acandis GmbH, Germany.

Analysis

Follow-up issues: Angiographic outcomes were available for 84% (47/56) of patients in the WEB group and 76% (51/67) of patients in the coiling group.

Study design issues: Non-randomised, retrospective, multicentre, comparative study. A propensity score matching was done on the basis of aneurysm location, aneurysm size, dome-to-neck ratio, neck width, and aneurysm shape. Following propensity score adjustment, 38 aneurysms treated by WEB were matched with 38 coiled aneurysms. Procedure-related complications, clinical outcomes and angiographic results were retrospectively evaluated and compared. Functional outcome was evaluated by the modified Rankin Scale (mRS) at discharge and at 6-month follow up. Unfavourable outcome was defined as mRS greater than 2.

Study population issues: Patients in the WEB group were statistically significantly older than those in the coil group (p=0.048) and there were statistically significant differences in the frequency of posterior circulation aneurysms (37.5% in the WEB group and 10% in the coil group, p<0.01), aneurysm size (6.7±2.0 mm compared with 5.9±2.5 mm, p=0.02), and neck width (4.2±1.3 mm compared with 3.4±1.3 mm, p<0.01). There were no statistically significant differences in baseline characteristics in the matched groups.

Other issues: There may be some patient overlap with other studies reported from the same centres.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **123 (56 WEB, 67 coiling)**

Functional outcome – all patients

	WEB (n=56)	Coiling (n=67)	p value
mRS at discharge			
≤2	55 (98.2%)	66 (98.5%)	1.0
>2	1 (1.8%)	1 (1.5%)	
mRS at 6-month follow up			
≤2	55 (98.2%)	66 (98.5%)	1.0
>2	1 (1.8%)	1 (1.5%)	

Functional outcome – after propensity score matching

	WEB (n=38)	Coiling (n=38)	p value
mRS at discharge			
≤2	38 (100%)	37 (97.4%)	1.0
>2	0 (0%)	1 (2.6%)	
mRS at 6-month follow up			
≤2	38 (100%)	37 (97.4%)	1.0
>2	0 (0%)	1 (2.6%)	

Angiographic results and retreatment rates – all patients

	WEB	Coiling	p value
Number of patients	47 (83.9%)	51 (76.1%)	
Mean follow up (months)	11.1±6.5	15.0±11.4	0.01
Complete occlusion	41 (87.2%)	31 (60.8%)	<0.01
Neck remnant	3 (6.4%)	14 (27.5%)	
Aneurysm remnant	3 (6.4%)	6 (11.8%)	
Retreatment	2 (4.3%)	9 (17.6%)	0.05

Angiographic results and retreatment rates – after propensity score matching

	WEB	Coiling	p value
Number of patients	32 (84.2%)	29 (76.3%)	
Mean follow up (months)	10.8±5.9	17.7±12.6	0.01
Complete occlusion	28 (87.5%)	20 (69.0%)	0.08
Neck remnant	2 (6.3%)	6 (20.7%)	
Aneurysm remnant	2 (6.3%)	3 (10.3%)	
Retreatment	1 (3.1%)	4 (13.8%)	0.13

Safety

Complications – all patients

	WEB (n=56)	Coiling (n=67)	p value
Procedural complications	5 (8.9%)	6 (9.0%)	1.0
Thromboembolic complications	4 (7.1%)	5 (7.5%)	1.0
Haemorrhagic complications	1 (1.8%)	1 (1.5%)	1.0
Neurological complications	1 (1.8%)	3 (4.5%)	0.8

Complications – after propensity score matching

	WEB (n=38)	Coiling (n=38)	p value
Procedural complications	2 (5.3%)	3 (7.9%)	1.0
Thromboembolic complications	2 (5.3%)	2 (5.3%)	1.0
Haemorrhagic complications	0 (0%)	1 (2.6%)	1.0
Neurological complications	0 (0%)	3 (7.9%)	0.2

Abbreviations used: mRS, modified Rankin Scale; WEB, Woven EndoBridge

Validity and generalisability of the studies

- No randomised controlled trials were identified.
- Most studies were retrospective.
- There are different devices used for the procedure, which may have different safety and efficacy profiles.
- The patient populations are heterogenous for size and location of the aneurysms, although most aneurysms were classified as wide necked.
- The evidence includes both ruptured and unruptured aneurysms.
- Antiplatelet regimens vary within and between studies.
- Patient selection criteria were not described in detail in several studies.
- Some of the studies include the first patients to have treatment with the procedure.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Supraorbital minicraniotomy for intracranial aneurysm. NICE interventional procedures guidance 84 (2004). Available from http://www.nice.org.uk/guidance/IPG84
- Coil embolisation of ruptured intracranial aneurysms. NICE interventional procedures guidance 106 (2005). Available from http://www.nice.org.uk/guidance/IPG106

- Coil embolisation of unruptured intracranial aneurysms. NICE interventional procedures guidance 105 (2005). Available from http://www.nice.org.uk/guidance/IPG105

Medical technologies

- Pipeline Flex embolisation device with Shield Technology for the treatment of complex intracranial aneurysms. NICE Medical technologies guidance 10 (2012, updated 2019). Available from http://www.nice.org.uk/guidance/mtg10

Additional information considered by IPAC

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by specialist advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Three Specialist Adviser Questionnaires for intrasaccular blood-flow disruption device insertion for intracranial aneurysm were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE received 8 completed questionnaires. The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the specialist advisers.

Company engagement

A structured information request was sent to 3 companies who manufacture a potentially relevant device for use in this procedure. NICE did not receive any completed submissions.

Issues for consideration by IPAC

Ongoing studies:

- WEB Clinical Assessment of IntraSaccular Aneurysm Therapy (WEBCAST); NCT01778322; Denmark, France, Germany, Hungary; prospective cohort study; n=100; estimated study completion date: June 2020

- The WEB-IT Clinical Study (WEB-IT); NCT02191618; US, Canada, Denmark, Germany, Hungary, Turkey; prospective cohort study; n=150; estimated study completion date: March 2021

- The WEB®-IT China Clinical Study (WEB-IT China); NCT03207087; China; single group assignment; n=60; estimated study completion date: March 2021

- CLARYS: CLinical Assessment of WEB® Device in Ruptured aneurYSms (CLARYS); NCT02687607; France; observational (registry); n=50; estimated study completion date: June 2018

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2. Pierot L, Moret J, Barreau X et al. (2018) Safety and efficacy of aneurysm treatment with WEB in the cumulative population of three prospective, multicenter series. Journal of Neurointerventional Surgery 10: 553–9
3. Kabbasch C, Goertz L, Siebert E et al. (2018) Factors that determine aneurysm occlusion after embolization with the Woven EndoBridge (WEB). Journal of Neurointerventional Surgery 24
4. Mine B, Goutte A, Brisbois D et al. (2018) Endovascular treatment of intracranial aneurysms with the Woven EndoBridge device: mid term and long term results. Journal of Neurointerventional Surgery 10: 127–32
5. Lawson A, Molyneux A, Sellar R et al. (2018) Safety results from the treatment of 109 cerebral aneurysms using the Woven EndoBridge technique: preliminary results in the United Kingdom. Journal of Neurosurgery 128: 144–53
6. Herbreteau D, Bibi R, Narata AP et al. (2016) Are anatomic results influenced by WEB shape modification? Analysis in a prospective, single-center series of 39 patients with aneurysms treated with the WEB. American Journal of Neuroradiology 37: 2280–6
7. Khalid Z, Sorteberg W, Nedregaard B et al. (2018) Efficiency and complications of Woven EndoBridge (WEB) devices for treatment of larger, complex intracranial aneurysms-a single-center experience. Acta Neurochirurgica 13: Dec 13
8. Fiorella D, Molyneux A, Coon A et al. (2017) Demographic, procedural and 30-day safety results from the WEB Intra-saccular Therapy Study (WEB-IT). Journal of Neurointerventional Surgery 9: 1191–6
9. Tikka J, Gardberg M, Rautio R et al. (2018) Left cerebral hemisphere hydrophilic polymer embolism associated with endovascular WEB treatment of a ruptured aneurysm of the anterior cerebral artery. Legal Medicine 35: 66–8
10. Arthur AS, Molyneux A, Coon AL et al. (2019) The safety and effectiveness of the Woven EndoBridge (WEB) system for the treatment of wide necked bifurcation aneurysms: final 12-month results of the pivotal WEB Intrasaccular Therapy (WEBIT) Study. J NeuroIntervent Surg 0:1–7. doi:10.1136/neurintsurg-2019-014815

11. Goertz L, Liebig T, Siebert E et al. (2019) Risk factors of procedural complications related to Woven EndoBridge (WEB) embolization of intracranial aneurysms. Clinical Neuroradiology https://doi.org/10.1007/s00062-019-00762-8

12. Kabbasch C, Goertz L, Siebert E et al. (2019) WEB embolization versus stent-assisted coiling: Comparison of complication rates and angiographic outcomes. Journal of NeuroInterventional Surgery Published Online First: 23 January 2019. doi: 10.1136/neurintsurg-2018-014555

13. Kabbasch C, Goertz L, Siebert E et al. (2019) Comparison of WEB embolization and coiling in unruptured intracranial aneurysms: safety and efficacy based on a propensity score analysis. World Neurosurgery 126: e937–e943

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	30/04/2019	Issue 4 of 12, April 2019
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	30/04/2019	Issue 4 of 12, April 2019
HTA database (CRD website)	30/04/2019	-
MEDLINE (Ovid)	30/04/2019	1946 to April 29, 2019
MEDLINE In-Process (Ovid) & Medline ePub ahead (Ovid)	30/04/2019	1946 to April 29, 2019
EMBASE (Ovid)	30/04/2019	1974 to 2019 Week 17

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1 Intracranial Aneurysm/
2 ((intracranial or brain* or cerebral or wide-neck or 'basilar artery' or berry) adj4 aneurysm*).tw.

3	((intracranial or brain* or cerebral or wide-neck or 'basilar artery' or berry) adj4 (unrupt* or thin* or bulg* or weak* or balloon* or bubbl* or dilat* or puls* or swell*)).tw.
4	1 or 2 or 3
5	((intrasaccular or endosaccular) adj4 flow* adj4 (disrupt* or divert* or diversion or alter* or redirect* or change*)).tw.
6	'woven endobridge'.tw.
7	((intrasaccular or endosaccular or embolization or embolisation) adj4 (system* or device* or therap* or technique*)).tw.
8	(WEB or WEB-IT or Luna or artisse).tw.
9	or/5-8
10	4 and 9
11	Animals/ not Humans/
12	10 not 11

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in table 2
Anil G, Goddard AJ, Ross SM et al. (2016) WEB in Partially Thrombosed Intracranial Aneurysms: A Word of Caution. American Journal of Neuroradiology 37: 892–6	Case series n=4	This small, select case series shows that WEB placement with adjunctive stent placement may be an effective treatment in the management of partially thrombosed intracranial aneurysms, which merits further validation. However, exclusive intrasaccular flow disruption may have an adverse influence on the natural history of this disease.	Larger studies are included.
Armoiry X, Turjman F, Hartmann DJ et al. (2016) Endovascular Treatment of Intracranial Aneurysms with the WEB Device: A Systematic Review of Clinical Outcomes. American Journal of Neuroradiology 37: 868-72	Systematic review n=7 articles	Endovascular treatment of bifurcation wide-neck aneurysms with the WEB device is feasible and allows an acceptably adequate aneurysm occlusion rate; however, the rate of neck remnants is not negligible. The WEB device needs further clinical and anatomic evaluation with long-term prospective studies, especially of the risk of WEB compression. Prospective controlled studies should be encouraged.	A recent update of the review is included (Tau et al, 2018)
Asnafi S, Rouchaud A, Pierot L et al. (2016) Efficacy and Safety of the Woven EndoBridge (WEB) Device for the Treatment of Intracranial Aneurysms: A Systematic Review and Meta-Analysis. American Journal of Neuroradiology 37: 2287-2292	Systematic review n=565 (15 studies)	Early evidence derived from uncontrolled studies suggests that Woven EndoBridge treatment has a good safety profile and promising rates of adequate occlusion, especially given the complexity of aneurysms treated. Further prospective clinical trials are needed to confirm these results and better define the risks and benefits of use of the Woven EndoBridge device in treating wide-neck and wide-neck bifurcation aneurysms.	A more recent systematic review is included (Tau et al, 2018)
Behme D, Berlis A and Weber W (2015) Woven EndoBridge Intrasaccular Flow Disrupter for the Treatment of Ruptured and	Case series n=55 FU=3 months	A favourable angiographic result at 3 months was achieved in 29/44 (66%) cases, whereas the percentage of good anatomic	Studies with more patients or longer follow up are included.

Unruptured Wide-Neck Cerebral Aneurysms: Report of 55 Cases. American Journal of Neuroradiology 36: 1501-6		results increased from 40% in 2012 to 75% in 2014.	Study is included in systematic review by Tau et al, 2018.
Bhogal P, AlMatter M, Hellstern V et al. (2018) The Combined Use of Intraluminal and Intrasaccular Flow Diversion for the Treatment of Intracranial Aneurysms: Report of 25 Cases. Neurointervention 13: 20-31	Case series n=25 FU=mean 10 months	The Medina Embolic Device can be successfully used in combination with intraluminal flow diverter stents (FDS) and in selected aneurysms this may represent an alternative to FDS and adjunctive coiling.	Studies with more patients or longer follow up are included.
Bozzetto Ambrosi P, Gory B, Sivan-Hoffmann R et al. (2015) Endovascular treatment of bifurcation intracranial aneurysms with the WEB-SL/SLS: 6-month clinical and angiographic results. Interventional Neuroradiology 21: 462-9	Case series n=10 FU=6 months	From this preliminary study, treatment of bifurcation intracranial aneurysms using WEB-SL is feasible. WEB-SL treatment seems safe at 6 months; however, the rate of neck remnants is not negligible due to compression of the WEB-SL. Further technical improvements may be needed in order to ameliorate the occlusion in the WEB-SL treatment.	Studies with more patients or longer follow up are included.
Cagnazzo F, Dargazanli C, Lefevre PH et al. (2019) WEB-assisted microwire navigation for the treatment of complex wide-neck intracranial aneurysms: Technical note. Journal of Neuroradiology	Case series n=3	WEB-assisted microcatheterisation appears an alternative strategy for the treatment of complex aneurysms.	Larger studies are included.
Caroff J, Mihalea C, Da Ros V et al. (2017) A computational fluid dynamics (CFD) study of WEB-treated aneurysms: Can CFD predict WEB "compression" during follow up? Journal of Neuroradiology 44: 262-268	Case series n=22 FU=mean 17 months	The mechanisms underlying the worsening of aneurysm occlusion in patients who had a WEB because of device compression are most likely complex as well as multifactorial. However, it is apparent from our pilot study that a high arterial inflow is, at least, partially involved.	Studies with more patients or longer follow up are included.
Caroff J, Mihalea C, Dargento F et al. (2014) Woven Endobridge (WEB) Device for endovascular treatment of ruptured intracranial wide-neck aneurysms: a single-center experience. Neuroradiology 56: 755-61	Case series n=6 FU=3 months	From this preliminary study, the high feasibility rate and lack of need for systematic antiplatelet agents favour the WEB device providing a solution for endovascular treatment of ruptured wide-neck bifurcation aneurysms during the acute phase. However, further studies are needed to evaluate the complication rate and long-term efficiency.	Studies with more patients or longer follow up are included.
Caroff J, Mihalea C, Klisch J et al. (2015) Single-Layer WEBs: Intrasaccular Flow Disrupters for Aneurysm Treatment-	Case series n=95 FU=3 months	The feasibility and safety of the single-layer WEB device was comparable with that of the double layer. However, further	Studies with more patients or longer follow up are included.

Feasibility Results from a European Study. American Journal of Neuroradiology 36: 1942-6		studies are needed to evaluate long-term efficacies.	Study is included in systematic review by Tau et al, 2018.
Caroff J, Mihalea C, Neki H et al. (2014) Role of C-arm VasoCT in the use of endovascular WEB flow disruption in intracranial aneurysm treatment. American Journal of Neuroradiology 35: 1353-7	Case series n=12	High-resolution contrast-enhanced flat panel detector CT (VasoCT) allowed a precise evaluation of the WEB sizing and its relation to the parent vessel. Such information very likely enhances the ability to safely use this device, avoiding potential thromboembolic events in cases of protrusion in the parent arteries.	Study focuses on imaging technique.
Clajus C, Strasilla C, Fiebig T et al. (2017) Initial and mid-term results from 108 consecutive patients with cerebral aneurysms treated with the WEB device. Journal of Neurointerventional Surgery 9: 411-417	Case series n=108 FU=mean 13 months	Thromboembolic complications occurred in 10% (11/110) of interventions, with a new permanent deficit in 1 patient. Re-rupture after WEB treatment was detected in 2 aneurysms (4%), which had both initially presented with subarachnoid haemorrhage. Angiographic follow up revealed adequate occlusion in 76% (68/90) of aneurysms. Fifteen aneurysms required retreatment.	Studies with more patients or longer follow up are included. Study is included in systematic review by Tau et al, 2018.
Cognard C, Januel AC (2015) Remnants and recurrences after the use of the WEB intrasaccular device in large-neck bifurcation aneurysms. Neurosurgery 76: 522-30	Case series n=15	Compression of the WEB cage was seen at first follow up in 57% (8/14) and in an additional 43% (3/7) of cases at second control. Last angiography showed complete occlusion in 7% (1/14), neck remnant in 57% (8/14) and residual aneurysm in 36% (5/14) of cases.	Studies with more patients or longer follow up are included. Study is included in systematic review by Tau et al, 2018.
Colla R, Cirillo L, Princiotta C et al. (2013) Treatment of wide-neck basilar tip aneurysms using the Web II device. Neuroradiology Journal 26: 669-77	Case series n=4 up to 12 months	Preliminary results suggest that the WEB II is a suitable device for endovascular treatment of unruptured wide-necked basilar tip aneurysms.	Studies with more patients or longer follow up are included.
Da Ros V, Bozzi A, Comelli C et al. (2018) Ruptured Intracranial Aneurysms treated with Woven Endobridge Intrasaccular Flow Disruptor (WEB): a multi-center experience. World Neurosurgery 27	Case series n=33 FU=mean 14 months	Overall WEB-related complication was 27% (5 device protrusion; 2 sac-perforation; 2 thromboembolism) with a WEB-related mortality of 12% and 3% of permanent neurologic deficit. At follow up, no early or delayed aneurysm re-ruptured were seen; complete occlusion was obtained in 7/21 patients (33%), neck remnant in 8/21 (38%), residual aneurysm filling in 6/21 (29%) patients with an mRS 0-2 seen in 17/21 patients (80%).	Studies with more patients or longer follow up are included.

Gawlitza M, Soize S, Manceau PF et al. (2019) An update on intrasaccular flow disruption for the treatment of intracranial aneurysms. Expert Review of Medical Devices 16: 229-236	Review	Expert commentary: The tools for the endovascular management of intracranial aneurysms continue to evolve rapidly with intrasaccular flow disruption being the most recent innovation in the field. The WEB is currently the only device on the market. Compared to competing techniques, intrasaccular flow disruption offers several advantages and it is likely that given the technically straightforward nature of the procedure and the high-quality scientific evidence of its safety and efficacy, the device will see a progressive expansion of its indications and will replace standard coiling in an increasing number of cases.	No meta-analysis
Gawlitza M, Soize S, Januel AC et al. (2018) Treatment of recurrent aneurysms using the Woven EndoBridge (WEB): anatomical and clinical results. Journal of Neurointerventional Surgery 10: 629-633	Case series n=17 FU=12 months	Permanent morbidity due to a thromboembolic complication occurred in 1 patient. There was no mortality. Rates of complete occlusion, neck remnant, and aneurysm remnant were 33%, 40%, and 27%, respectively.	Studies with more patients or longer follow up are included.
Gherasim DN, Gory B, Sivan-Hoffmann R et al. (2015) Endovascular treatment of wide-neck anterior communicating artery aneurysms using WEB-DL and WEB-SL: short-term results in a multicenter study. American Journal of Neuroradiology 36: 1150-4	Case series n=10 FU=1 month	One patient developed a procedural thromboembolic event. Angiographic control was obtained in all patients, including 6 adequate aneurysm occlusions (3 complete occlusions and 3 neck remnants) at short-term follow up.	Studies with more patients or longer follow up are included.
Haffaf I, Clarencon F, Shotar E et al. (2018) Medina embolization device for the treatment of intracranial aneurysms: 18 months' angiographic results. Journal of Neurointerventional Surgery 24	Case series n=19 FU=18 months	Medina embolisation device is a hybrid device, combining properties of a conventional coil with those of an intrasaccular flow disrupter. Our series shows a satisfactory long-term occlusion rate. Larger series with longer angiographic follow-up times are warranted to confirm these preliminary results.	Studies with more patients or longer follow up are included.
Kabbasch C, Goertz L, Siebert E et al. (2019) Treatment strategies for recurrent and residual aneurysms after Woven Endobridge implantation. Journal of NeuroInterventional Surgery 11: 390-395	Case series n=15	This pilot study shows that endovascular retreatment of recurrent or residual aneurysms after WEB implantation can be done safely and can achieve adequate occlusion rates.	Small case series, focusing on retreatment after the procedure.
Kabbasch C, Mpotsaris A, Reiner M et al. (2016) WEB as	Case series	All 8 of the complex, large, wide-neck aneurysms were treated	Studies with more patients or longer

part of a multimodality treatment in complex, large, and partially thrombosed intracranial aneurysms: a single-center observational study of technical success, safety, and recurrence. Journal of Neurointerventional Surgery 8: 1235-1239	n=43	successfully and without periprocedural adverse events. At follow up, the 2 non-thrombosed aneurysms were completely occluded, but all 6 partially thrombosed aneurysms recurred and were retreated. There was no morbidity or mortality in these 8 patients.	follow up are included.
Klisch J, Sychra V, Strasilla C et al. (2011) The Woven EndoBridge cerebral aneurysm embolization device (WEB II): initial clinical experience. Neuroradiology 53: 599-607	Case series n=2 FU=8 weeks	In both cases, complete aneurysm occlusion was seen within minutes of device deployment. Short-term angiographic follow up confirmed stable complete occlusion at 8 weeks.	Studies with more patients or longer follow up are included.
Lawson A, Goddard T, Ross S et al. (2017) Endovascular treatment of cerebral aneurysms using the Woven EndoBridge technique in a single center: preliminary results. Journal of Neurosurgery 126: 17-28	Case series n=22	The technique is safe, and short-term results show effective occlusion of complex aneurysms with minimal complications associated with the procedure. Long-term efficacy, however, still needs to be assessed.	Studies with more patients or longer follow up are included.
Lescher S, du Mesnil de Rochemont R, Berkefeld J (2016) Woven Endobridge (WEB) device for endovascular treatment of complex unruptured aneurysms-a single-center experience. Neuroradiology 58: 383-90	Case series n=22	Follow-up angiographic imaging proved total or subtotal occlusion of the aneurysm in 19 of 22 cases. Two minor recurrences remained stable during a period of 15 months. One patient with a partially thrombosed giant middle cerebral artery aneurysm had a major recurrence and was retreated with a second WEB in combination with coiling.	Studies with more patients or longer follow up are included.
Liebig T, Kabbasch C, Strasilla C et al. (2015) Intrasaccular Flow Disruption in Acutely Ruptured Aneurysms: A Multicenter Retrospective Review of the Use of the WEB. American Journal of Neuroradiology 36: 1721-7	Case series n=47	This retrospective series showed good procedural safety, feasibility, and stability of mid-term occlusion in ruptured wide-neck bifurcation aneurysms.	Studies with more patients or longer follow up are included. Study is included in systematic review by Tau et al, 2018.
Limbucci N, Leone G, Rosi A et al. (2018) Endovascular Treatment of Unruptured Intracranial Aneurysms by the Woven EndoBridge Device (WEB): Are There Any Aspects Influencing Aneurysm Occlusion? World Neurosurgery 109: e183-e193	Case series n=24 FU=median 18 months	Endovascular treatment with WEB is a safe treatment for unruptured cerebral aneurysms, also resulting in a good adequate occlusion rate in aneurysms that would otherwise require complex assisted coiling techniques. However, results are less favourable in cases of very large aneurysmal neck.	Studies with more patients or longer follow up are included. Study is included in systematic review by Tau et al, 2018.
Lubicz B, Klisch J, Gauvrit JY et al. (2014) WEB-DL endovascular treatment of wide-	Case series n=45	The results suggest that the WEB endovascular treatment of wide-neck bifurcation	Studies with more patients or longer

neck bifurcation aneurysms: Short- and midterm results in a European study. American Journal of Neuroradiology 35: 432-438	FU=median 13 months	aneurysms offers stable occlusion in a class of aneurysms that are historically unstable.	follow up are included.
Lubicz B, Mine B, Collignon L et al. (2013) WEB device for endovascular treatment of wide-neck bifurcation aneurysms. American Journal of Neuroradiology 34: 1209-14	Case series n=19 FU=12 months	Angiographic controls were obtained in all patients (mean 6 months), and they showed stable or improved results in all except 4 cases, including 2 complete occlusions, 15 near-complete occlusions, and 2 incomplete occlusions.	Studies with more patients or longer follow up are included.
Lv X, Zhang Y, Jiang W (2018) Systematic Review of Woven EndoBridge for Wide-Necked Bifurcation Aneurysms: Complications, Adequate Occlusion Rate, Morbidity, and Mortality. World Neurosurgery 110: 20-25	Systematic review n=935 (19 studies)	The thromboembolic complication rate was 8% (95% CI, 6%-11%). The overall bleeding complication rate was 2% (95% CI, 1%-3%). The adequate occlusion rate was 81% (95% CI, 76%-85%). Morbidity during follow up was 3% (95% CI, 1%-4%) (I^2=30%), and mortality was 2% (95% CI, 1%-3%).	A review with a more recent search date is included (Tau et al, 2018).
Mihalea C, Caroff J, Pagiola I et al. (2019) Safety and efficiency of the fifth generation Woven EndoBridge device: Technical note. Journal of NeuroInterventional Surgery 11: 511–515	Case series n=25	The WEB 17 is safe and technically feasible, according to this retrospective single centre analysis. For very small bifurcation aneurysms, the WEB 17 seems to have lower complication rates than stent-assisted techniques. However, further studies are needed to evaluate the complication rate and long-term efficiency.	Studies with more patients or longer follow up are included.
Mihalea C, Escalard S, Caroff J et al. (2019) Balloon remodeling-assisted Woven EndoBridge technique: Description and feasibility for complex bifurcation aneurysms. Journal of NeuroInterventional Surgery 11: 386-389	Case series n=9	The balloon remodelling-assisted WEB technique seems to be a safe and effective solution for endovascular treatment of unruptured wide-neck bifurcation aneurysms with specific complex anatomy. However, further studies are needed to evaluate the rate of complications and long-term efficacy.	Studies with more patients or longer follow up are included.
Mine B, Tancredi I, Aljishi A et al. (2016) Follow-up of intracranial aneurysms treated by a WEB flow disrupter: a comparative study of DSA and contrast-enhanced MR angiography. Journal of Neurointerventional Surgery 8: 615-20	Case series n=15	Contrast-enhanced MRA is a useful tool for the follow up of intracranial aneurysms (IAs) treated with a WEB-DL. However, early follow up with digital subtraction angiography remains mandatory to detect inadequately occluded IAs.	Study focuses on imaging techniques.
Muskens IS, Senders JT, Dasenbrock HH et al. (2017)	Systematic review	Thromboembolic events were described in 71 patients (10% of	A review with a more recent

The Woven Endobridge Device for Treatment of Intracranial Aneurysms: A Systematic Review. World Neurosurgery 98: 809-817.e1	n=687 (19 papers)	all patients) and infarctions in 8 patients (1% of all patients). Despite initial promising results, the WEB device should be used with caution given its potentially large learning curve and because it has primarily been investigated only in wide-neck and bifurcation aneurysms.	search date is included (Tau et al, 2018).
Papagiannaki C, Spelle L, Januel AC et al. (2014) WEB intrasaccular flow disruptor-prospective, multicenter experience in 83 patients with 85 aneurysms. American Journal of Neuroradiology 35: 2106-11	Case series n=83 FU=mean 5 months	Periprocedural complications=11% (9/83), leading to permanent neurologic deficits in 3 (4%). Morbidity and mortality at 1 month were 1% and 0%, respectively. Complete aneurysm occlusion was seen in 37/65 aneurysms (57%); neck remnant, in 23/65 (35%); and aneurysm remnant, in 5/65 (8%).	Studies with more patients or longer follow up are included.
Pierot L, Costalat V, Moret J et al. (2016) Safety and efficacy of aneurysm treatment with WEB: results of the WEBCAST study. Journal of Neurosurgery 124: 1250-6	Case series n=51 FU=6 months	The WEBCAST study showed good procedural and short-term safety of aneurysm treatment with WEB and good 6-month anatomical results.	Results from this study are included in Pierot et al, 2018 (study 2)
Pierot L, Gubucz I, Buhk JH et al. (2017) Safety and Efficacy of Aneurysm Treatment with the WEB: Results of the WEBCAST 2 Study. American Journal of Neuroradiology 38: 1151-1155	Case series n=55 FU=1 year	WEBCAST 2 confirms the high safety and efficacy of WEB aneurysm treatment showed in the WEBCAST and French Observatory studies.	Results from this study are included in Pierot et al, 2018 (study 2)
Pierot L, Klisch J, Cognard C et al. (2013) Endovascular WEB flow disruption in middle cerebral artery aneurysms: preliminary feasibility, clinical, and anatomical results in a multicenter study. Neurosurgery 73: 27-34	Case series n=33 FU=2 to 12 months	Mortality of the treatment was 0% and morbidity was 3% (intraoperative rupture with modified Rankin Scale score of 3 at the 1-month follow up). In short-term follow up, adequate occlusion (total occlusion or neck remnant) was seen in 83% of aneurysms.	Studies with more patients or longer follow up are included.
Pierot L, Klisch J, Liebig T et al. (2015) WEB-DL Endovascular Treatment of Wide-Neck Bifurcation Aneurysms: Long-Term Results in a European Series. American Journal of Neuroradiology 36: 2314-9	Case series n=45 FU=median 27 months	Long-term aneurysm occlusion in the 19 patients had the WEB only and did not have retreatment during follow up was complete occlusion in 68% (13/19) of patients, including aneurysms with opacification of the proximal recess in 9/19 patients (47%), neck remnant in 3/19 patients (16%), and aneurysm remnant in 3/19 patients (16%).	Studies with more patients or longer follow up are included.
Pierot, L, Liebig T, Sychra V et al. (2012) Intrasaccular flow-disruption treatment of intracranial aneurysms:	Case series n=20	One patient (5%) experienced transient clinical worsening (mRS 1 at 1 month, mRS 0 at 3 months) related to a	Studies with more patients or longer follow up are included.

preliminary results of a multicenter clinical study. American Journal of Neuroradiology 33: 1232-8	FU=2 to 8 months	thromboembolic event. Inadvertent detachment of the WEB was seen, and the WEB was retrieved in 1 patient, without adverse effects. In the short-term follow up, adequate occlusion (total occlusion or neck remnant) was seen in 80% of aneurysms.	
Pierot L, Moret J, Turjman F et al. (2016) WEB Treatment of Intracranial Aneurysms: Clinical and Anatomic Results in the French Observatory. American Journal of Neuroradiology 37: 655-9	Case series n=62 FU=1 year	This prospective French Observatory study showed very good safety of aneurysm treatment with the WEB, with a high rate of adequate aneurysm occlusion at 1 year (79%).	Results from this study are included in Pierot et al, 2018 (study 2)
Pierot L, Moret J, Turjman F et al. (2015) WEB Treatment of Intracranial Aneurysms: Feasibility, Complications, and 1-Month Safety Results with the WEB-DL and WEB-SL/SLS in the French Observatory. American Journal of Neuroradiology 36: 922-7	Case series n=62	This comparative study shows increased use of WEB treatment in ruptured, small, and anterior communicating artery aneurysms when using WEB-SL/SLS. There was a trend toward fewer thromboembolic complications with the WEB-SL/SLS. With both the WEB-DL and WEB-SL/SLS, the treatment was safe, with low morbidity and no mortality.	Study focuses on comparison of different devices.
Pierot L, Spelle L, Molyneux A et al. (2016) Clinical and Anatomical Follow-up in Patients With Aneurysms Treated With the WEB Device: 1-Year Follow-up Report in the Cumulated Population of 2 Prospective, Multicenter Series (WEBCAST and French Observatory). Neurosurgery 78: 133-41	Case series n=113	The analysis in this large cumulated population of studies confirms favourable safety and efficacy of WEB treatment.	Results from these studies are included in Pierot et al, 2018 (study 2)
Piotin M, Biondi A, Sourour N et al. (2018) The LUNA aneurysm embolization system for intracranial aneurysm treatment: short-term, mid-term and long-term clinical and angiographic results. Journal of Neurointerventional Surgery 10: 12 e34	Case series n=63 FU=36 months	There was one instance of mortality (1/63, 2%). Morbidity was 0% (0/63) and 2% (1/63) at the 12-month and 36-month follow ups, respectively.	Studies with more patients or longer follow up are included.
Popielski J, Berlis A, Weber W et al. (2018) Two-Center Experience in the Endovascular Treatment of Ruptured and Unruptured Intracranial Aneurysms Using the WEB Device: A Retrospective Analysis. American Journal of Neuroradiology 39: 111-117	Case series n=101 FU=12 months	Procedural complications occurred in 5% (5/102). Of these, 4 were thromboembolic events and 1 was an intraprocedural rupture. Angiographic follow up showed a sufficient aneurysm occlusion in 81% (63/78) at 3 months and 78% (38/49) at 12 months.	Studies with more patients or longer follow up are included.

		Delayed aneurysm ruptures have not been seen during the follow-up period to date.	
Raj R, Rautio R, Pekkola J et al. (2019) Treatment of Ruptured Intracranial Aneurysms Using the Woven EndoBridge Device: A Two-Center Experience. World Neurosurgery 123: e709-e716	Case series n=33 FU=6 months	For anatomically suitable ruptured intracranial aneurysms, WEB device treatment seems to be safe and results in acceptable occlusion rates. Still, larger studies with long-term results are needed before recommendations can be made.	Studies with more patients or longer follow up are included.
Sivan-Hoffmann R, Gory B, Riva R et al. (2015) One-Year Angiographic Follow-Up after WEB-SL Endovascular Treatment of Wide-Neck Bifurcation Intracranial Aneurysms. American Journal of Neuroradiology 36: 2320-4	Case series n=8 FU=1 year	Endovascular therapy of intracranial aneurysms with the WEB-SL device allows treatment of wide-neck aneurysms with a high rate of neck remnant at 1 year, at least partially explained by WEB compression. Initial size selection and technologic improvements could be an option for optimisation of aneurysm occlusion in WEB-SL treatment.	Studies with more patients or longer follow up are included.
Sourour NA, Vande Perre S, Maria FD et al. (2018) Medina Embolization Device for the Treatment of Intracranial Aneurysms: Safety and Angiographic Effectiveness at 6 Months. Neurosurgery 82: 55-162	Case series n=12 FU=6 to 9 months	One case of thromboembolic complication was seen in a ruptured anterior communicating artery aneurysm, without any clinical consequence at follow up. Grade A occlusion rate was 83% at follow up. Two cases (17%) of recanalisation were documented angiographically.	Studies with more patients or longer follow up are included.
van Rooij SBT, van Rooij WJ, Sluzewski M et al. (2019) The Woven EndoBridge (WEB) for recurrent aneurysms: Clinical and imaging results. Interventional Neuroradiology 25: 21-26	Case series n=17	The WEB device for recurrent aneurysms may be a feasible and safe option, especially in wide-necked, shallow aneurysm recurrences. Results were poor in partially thrombosed recurrent aneurysms.	Small case series, focusing on treatment of recurrent aneurysms.
van Rooij SBT, Peluso JP, Sluzewski M et al. (2018) The New Low-Profile WEB 17 System for Treatment of Intracranial Aneurysms: First Clinical Experiences. American Journal of Neuroradiology 39: 859-863	Case series n=40 FU=3 months	The WEB 17 is safe and effective for both ruptured and unruptured aneurysms. The WEB 17 is a valuable addition to the existing WEB size range, especially for very small aneurysms.	Studies with more patients or longer follow up are included.
van Rooij SBT, van Rooij WJ, Peluso JP et al. (2017) WEB Treatment of Ruptured Intracranial Aneurysms: A Single-Center Cohort of 100 Patients. American Journal of Neuroradiology 38: 2282-2287	Case series n=100 FU=3 months	Treatment of small ruptured aneurysms with the Woven EndoBridge was safe and effective. The Woven EndoBridge proved to be a valuable alternative to coils without the need for stents or balloons.	Studies with more patients or longer follow up are included.

van Rooij SB, van Rooij WJ, Peluso JP et al. (2018) The Woven EndoBridge (WEB) as primary treatment for unruptured intracranial aneurysms. Interventional Neuroradiology 24: 475-481	Case series n=51 FU=3 months	WEB treatment is safe and effective in selected unruptured aneurysms suitable for the device, regardless of neck size or location.	Studies with more patients or longer follow up are included.
van Rooij S, Peluso JP, Sluzewski M et al. (2018) Mid-term 3T MRA follow-up of intracranial aneurysms treated with the Woven EndoBridge. Interventional Neuroradiology 24: 601-607	Case series n=52 FU=mean 20 months	WEB-treated aneurysms with adequate occlusion at three-month angiography remained stable during serial 3T MRA follow up of 18-36 months. One aneurysm reopened during the 6- to 18-month interval. Once the WEB-treated aneurysm is adequately occluded in the short term, later reopening is uncommon.	Studies with more patients or longer follow up are included.
van Rooij WJ, Peluso JP, Bechan RS et al. (2016) WEB Treatment of Ruptured Intracranial Aneurysms. American Journal of Neuroradiology 37: 1679-83	Case series n=32 FU=3 months	WEB treatment of small ruptured aneurysms was safe and effective without the need for anticoagulation, adjunctive stents, or balloons. Our preliminary experience indicates that the WEB may be a valuable alternative to coils in the treatment of acutely ruptured aneurysms.	Studies with more patients or longer follow up are included.