NuMED
Summary of Safety and Clinical Performance
SSCP – Delivery System

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device.

The SSCP is not intended to replace the Instructions for Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following information is intended for users/healthcare professionals.

1. Device identification and general information	
Device trade name(s)	NuDEL
Model Number	NuMED Delivery System Family – Model 1675 NuDEL – Model 423.1
Manufacturer's name and address	NuMED, Inc. 2880 Main Street Hopkinton, NY 12965 USA
Manufacturer's single registration number (SRN)	US-MF-000010948
Basic UDI-DI	08877141675TZ
Medical device nomenclature description / text	EMDN – P070401020199 - PTFE VASCULAR ENDOPROSTHESES, STRAIGHT - OTHER
Class of device	III
Year when first certificate (CE) was issued	2015
Authorised Representative (AR)	G. van Wageningen B.V. Hallenweg 40, 5683 CT Best, The Netherlands
AR SRN	NL-AR-000010437
Notified Body	SGS Belgium NV
Notified Body ID number	1639

2. Intended use of the device	
Indications for use	Coarctation of the Aorta (CoA) Indicated for implantation in the native and/or recurrent coarctation of the aorta on patients with the following clinical conditions: • Stenosis of the aorta resulting in significant anatomic narrowing as determined by angiography or non-invasive imaging, i.e. echocardiography, magnetic resonance imaging (MRI), CT scan; • Stenosis of the aorta resulting in hemodynamic alterations, resulting in systolic pressure gradient, systemic hypertension or altered left ventricular function; • Stenosis of the aorta where balloon angioplasty is ineffective or contraindicated; • Stenosis diameter <20% of adjacent vessel diameter. Stenosis that would present increased risk of vascular damage or disruption; or aneurysm associated with coarctation of the aorta.

	Right Ventricular Outflow Tract (RVOT) Indicated for treatment of right ventricle to pulmonary artery (right ventricular outflow tract) conduit disruptions that are identified during conduit pre-dilatation procedures performed in preparation for transcatheter pulmonary valve replacement.
Contraindications and/or limitations	Contraindications include: • Patients too small to allow safe delivery of the stent without compromise to the systemic artery used for delivery; • Unfavorable aortic anatomy that does not dilate with high pressure balloon angioplasty (CoA only); • Occlusion or obstruction of systemic artery precluding delivery of the stent (CoA only); • Clinical or biological signs of infection; • Active endocarditis; • Known allergy to aspirin, other antiplatelet agents, or heparin (CoA only); • Pregnancy.

3. Device description	
Description of the device	The NuDEL Delivery System is a balloon catheter system used for the delivery of a Covered CP Stent. The delivery system consists of a balloon-in-balloon (BIB) catheter housed in a braided pebax sheath with an obturator tip at the distal end, and three extensions with luer fittings on the proximal end. The catheter is designed to accommodate a 0.035" guidewire through its inner lumen. The braided pebax sheath is either 12F or 14F in size. The Covered CP Stent is crimped onto the BIB catheter and covered by the retractable sheath. The sheath houses both the balloon catheter and the Covered CP Stent. The sheath has a hemostasis valve at the proximal end that minimize blood loss around the inner catheter. The hemostasis valve has a flush port attached that allows for flushing of the system. The obturator tip is approximately 1.5cm in length and has a conical shape for easy introduction into the skin , and tracking to the delivery site. The proximal diameter of the obturator is sized to create a smooth transition from the sheath to the obturator. There are three extensions; one lumen for inflation of the inner balloon, one lumen for inflation of the outer balloon, and one lumen for the guidewire. The system is navigated through the venous from a femoral venous puncture to the delivery site over a guidewire. Once positioned, the sheath is retracted to expose the Covered CP Stent. The BIB balloons are inflated (inner first, outer last) to expand the Covered CP Stent. The balloons are deflated and the delivery system is removed from the patient. The Covered CP Stent is balloon expandable and intended for permanent implant. The Covered CP Stent is composed of heat treated 90% platinum/10% iridium wire that is arranged in laser welded rows with a "zig" pattern. The number of zigs in a row can be varied and will impact the strength of the stent as well as the eventual expanded diameter and percent stent shortening, while the number of rows will determine the unexpanded length of the stent. The Covered CP Stent has an ePTFE covering attached to the stent framework. This covering acts as a fluid barrier creating a fluid tight conduit through the stent length. The devices are supplied sterile, by ethylene oxide gas, and are intended for single use only. The stents are invasive and intended for permanent implant by an adequately trained/experienced healthcare professional. The delivery system is invasive and intended for transient use (continuous use of <60 minutes).
Reference to previous generation(s) or variants	N/A
Accessories which are intended to be used in combination with the device	There are no accessories that are intended to be used with this device.
Description of any other devices and products which are intended to be used in combination with the device	This device is designed to be used with a guidewire and an inflation device with pressure gauge.

4. Risks and Warning	
Residual risks and undesirable effects	All significant risks were considered, mitigated as far as possible (AFAP), and are acceptable in regard to the clinical benefit of the device. The clinical investigations performed on the Stent family of devices reported the following side effects: COAST: aortic aneurysm, stent fracture COAST II: iliac artery dissection PARCS: stent malposition, stent embolization The literature reported the following side effects: Acute wall rupture / dissection, aortic aneurysm / pseudoaneurysm, balloon rupture, death, stroke, stent embolization, groin hematoma, late lumen loss, left hemothorax, stent displacement, stent fracture, stent malposition, transitory arrhythmia, and cardiogenic / septic shock. Known and foreseeable clinical risks have been considered in accordance with risk management (RM) procedure AP-346 and through the RM files and mitigated as far as possible (AFAP). **POTENTIAL COMPLICATIONS/ADVERSE EFFECTS** NOTE: Circumferential tear of the delivery balloon catheter prior to complete expansion of the stent may cause the balloon to become tethered to the stent, requiring surgical removal. In case of rupture of an adequately sized balloon after stent expansion, it can be withdrawn and a new balloon catheter exchanged over a guidewire to complete expansion of the stent. Cardiac catheterization carries certain risks. Potential complications & adverse effects associated with device use and indication include: - Femoral artery injury, thrombosis or psuedoaneurysm - Stent Migration - Aortic Rupture/Tear - Thrombosis/Thromboembolism - Endocarditis - Stent Stenosis - Stent Malposition - AV fistula formation - Bleeding - Stent Fracture - Hematoma - Death - Cell necrosis at the site of implant - Aortic Aneurysm / Pseudoaneurysm - Sepsis/infection - Transitory arrhythmia - Cerebrovascular Incident
Warning and Precautions	The following Warnings and Precautions have been identified and are called out in the Instruction for Use: **WARNINGS** • The sheath must be flushed with heparinised saline via the proximal side port prior to introducing the delivering system in the body. • As with any type of implant, infection secondary to contamination of the stent may lead to aortitis, or abscess. • The platinum/iridium stent may migrate from the site of implant. • Over-stretching of the artery may result in rupture or aneurysm formation. • The inflated diameter of the stent should at least equal the diameter of the intended implant site. • Retracting the covered stent back in to the sheath may cause the covering to catch and tear off of the stent. • Do not exceed the RBP. An inflation device with a pressure gauge is recommended to monitor pressure. Pressure in excess of the RBP can cause balloon rupture and potential inability to withdraw the catheter into the sheath. • Confirm that the distal end of the outer sheath is at least 2.5 cm back from the proximal image marker before inflating the outer balloon. Failure to do so may stretch the outer tubing and severely hinder inner balloon deflation. • It is recommended to use two appropriate size inflation devices with pressure gauges for inflation. • Do not advance the guidewire, the combined balloon catheter in the sheath, or any other component if resistance is encountered, without first determining the cause and taking remedial action. • This catheter is not recommended for pressure measurement.

	• Do not remove the guidewire from the sheath-catheter at any time during the procedure except when the procedure has been completed. • Do not fully expose the Covered Stent before introduction into the body. • This device is intended for single use only. Do not resterilize and/or reuse it, as this can potentially compromise device integrity and performance, and increased risk of cross contamination and infection. **PRECAUTIONS** • Use of an inflation device with pressure gauge is highly recommended during this procedure. • Sheath-catheter manipulation and stent deployment must be conducted under fluoroscopic guidance with appropriate radiographic equipment. • Stents are delicate devices. Exercise caution when handling the stent to prevent breakage. • Guidewires should be handled with care to avoid kinking or breaking. When advancing the NuDEL system over the wire, the tip of the wire must be controlled at all times. • The NuDEL system, especially at the stent, is rigid and may make negotiation through vessels difficult. • Maintain tight catheter connections at all times. • De-air the sheath with heparanised saline prior to insertion in the patient. Apply repeated negative pressure cycles to the balloons to replace the air in the balloons with fluid: this enhances the efficiency of inflation and avoids air introduction into the circulation in the unusual case of balloon rupture. • The inflation diameter of the balloon used during stent delivery should approximate the diameter of the obstructive vessel and the intended implant site. • Under no circumstances should any portion of the sheath-catheter system be advanced or removed against resistance. Use fluoroscopy to identify and resolve the resistance. • If resistance is encountered upon removal, the whole system (balloon, guidewire and sheath) should be removed as a single unit, particularly if balloon rupture or leakage is known or suspected. This may be accomplished by firmly grasping and withdrawing the sheath and catheter, using a gentle anticlockwise twisting motion with traction. • The balloons must be completely deflated before retracting into the sheath. • Proper functioning of the sheath-catheter depends on its integrity. Exercise caution when handling the catheter. Damage may result from kinking, stretching, or forceful wiping of the catheter.
Other relevant aspects of safety, including a summary of any field safety corrective actions (FSCA including FSN) if applicable	There have not been any Field Safety Corrective Actions or Field Safety Notices on the devices in the Delivery System Family.

5. Summary of clinical evaluation and post-market clinical follow-up (PMCF)

Summary of clinical data related to equivalent device:

An equivalent device was not used for the clinical evaluation.

Summary of clinical data from conducted investigations of the device:

1. Study name: COAST

Purpose: to provide information that will support labeling of both the CP bare metal and covered stents to treat native and recurrent CoA in selected children, adolescents and adult.

Clinical Study Methodology: Single arm interventional study (open label). The COAST is a prospective, multicenter, single-arm clinical study involving 19 pediatric cardiology centers in the United States. The study includes patients with native or recurrent CoA treated by physicians at the participating institutions. A total of 105 patients underwent attempted implantation, with 104 successes.
Reference to the clinical study plan (and amendment) n°: NCT00552812
Investigation site: 19 pediatric **Ethics Committee Approval:** Institutional **Regulatory Authority Approvals:**

cardiology centers in United States	Review Board approvals from all participating institutions	Investigational Device Exemption from US FDA (August 3, 2007)

Patient Population: Patients with native or recurrent CoA. A total of 105 patients underwent attempted implantation, median age 16 years (range from 8 to 52 years) and with 69.5% male.

Clinical Study Results: Results held on file by Sponsor

Purpose	Criteria	Results
Performance	Blood pressure gradient and coarctation minimum diameter: cardiac catheterization before and after CP Stent placement	Average systolic blood pressure difference (mmHg) changed from 29±14 mmHg at baseline to -3±15 mmHg at 24 months follow-up. The Coarctation minimum diameter reported at 7.9 ± 2.7mm at baseline to 14±3 mm after implantation.
Safety	Adverse events	No serious adverse events reported, 7% of the patients experienced somewhat serious events. Aortic aneurysms (n=6): 5 were successfully treated with covered stent placement, and 1 resolved without intervention. Stent fractures were seen in 2 patients after one year, 11 patients at two years and 12 additional fractures above 2 years.

Reference to the Clinical Study Report n°: NCT00552812

Device Used: Bare CP Stent and BIB catheter; covered stents were available in case of aortic wall injury.

Conclusion: The CP stent is safe and associated with persistent relief of aortic obstruction. Stent fracture and progression of fracture occur but have not resulted in clinically important sequelae. Reintervention is common and related to early and late aortic wall injury and need for re-expansion of small-diameter stents.

2. Study name: COAST II

Purpose: To evaluate safety and short-term efficacy of the CP Stent in treating or preventing aortic wall injury in patients with aortic coarctation

Clinical Study Methodology: Single arm interventional study. Patients were enrolled if they had a history of CoA with pre-existing aortic wall injury (Treatment group) or with increased risk of aortic wall injury (Prevention group). Pre/post-implant hemodynamics and angiography were reported. A core laboratory performed standardized review of all angiograms. One month follow-up was reported.

Reference to the clinical study plan (and amendment) n°: NCT01278303

Investigation site: 19 pediatric cardiac centers in United States	**Ethics Committee Approval:** Johns Hopkins Institutional Review Board and Institutional review boards of all participating centers.	**Regulatory Authority Approvals:** Investigational Device Exemption from US FDA

Patient Population: Patients with aortic coarctation at risk of aortic wall injury or with existing aortic wall injury. A total of 158 patients (83 treatment cohort and 75 prevention cohort, median age 19 years (range from 5 to 70 years) and with 103 males and 55 females.

Clinical Study Results: Results held on file by Sponsor

Purpose	Criteria	Results
Short term efficacy	Blood pressure gradient (at 1 month)	All: from 24 ± 26 mmHg to -1 ± 15 mmHg Treatment group: from 14 ± 24 to -2 ± 14 Prevention group: from 35 ± 23 to 1 ± 15
Safety	Adverse events	17 adverse events; 2 serious (dissection of the iliac artery) and 15 somewhat serious. No deaths. Device related AEs included local stent migration (n=1) and stent malposition (n=1).

Reference to the Clinical Study Report n°: NCT01278303

Device Used: Covered CP Stent by NuMED, pre-mounted on BIB stent delivery catheter.

Conclusion: The CP Stent can effectively treat and potentially prevent aortic wall injury associated with aortic coarctation. Access site arterial injury is the most common important complication. Longer-term follow up is necessary to define mid- and late-term outcomes.

3. Study name: PARCS

Purpose: Evaluation of the Covered CP Stent for repair of tears that occur in the pulmonary artery during dilation (enlargement) of a conduit (passageway) connecting the right ventricle of the heart to the pulmonary arteries.

Clinical Study Methodology: Single arm prospective study. The PARCS trial was a prospective, multicenter, single-arm pivotal clinical trial. Forty US centers participated in either the pivotal trial (22 centers) or the continued access protocol, which immediately followed the pivotal trial during Food and Drug Administration submission. If no conduit wall injury occurred during the procedure, the patient was considered a screen failure. If at any point during the procedure, including before intervention, the implanting physician identified an area of wall injury, a CCPS could then be selected and implanted.

Reference to the clinical study plan (and amendment) n°: NCT01824160

Patient Population: Participants receiving a Covered CP stent for repair of pulmonary artery injury. In the pivotal trial, fifty patients met the inclusion criteria, mean age 17 years (range from 6 to 44 years) and 56% of male patients. In the continued access, seventy patients with mean age of 16 years (range from 7 to 49 years) and 57% of male patients.

Clinical Study Results: Results held on file by Sponsor

Purpose	Criteria	Results
Pivotal (n=50): Severity of illness	Median improvement by at least 1 level from baseline to post-procedure	Median improvement of 1 level in Severity of Illness Score
Pivotal (n=50): Procedure success	≥ 75% patients, based on both device success and lesion success	Procedure success achieved in 68% of patients
Pivotal (n=50): Successful implantation of the Melody TPV	Coverage of conduit disruption defined as either no residual disruption or contained disruption, followed by successful implantation of Melody valve in ≥ 80% patients	Successful implantation achieved in 83% of patients
Pivotal (n=50): Adverse events attributed to covered CP Stent within 30 days	≥ 80% patients free of adverse events attributed to the covered CP Stent within 30 days	At least 80% were free of an adverse event attributed to the covered CP Stent. There was 1 report of stent malposition where the stent became dislodged and migrated into the pulmonary arteries
All patients (n=120): Performance	Covered CP Stent Implant success	CCPS implants successfully treated 95% of conduit injuries with either no or minimal residual conduit wall injury. Melody TPVR was successfully performed in 94% of the enrolled cohort, and TPV function was not adversely affected by placement within the CCPS substrate, with 6-month follow-up data comparing favorably with other previously published cohorts.
All patients (n=120): Safety	Stent-related AEs	AEs that specifically related to the CCPS and its implantation were uncommon. One serious (stent malposition) and one somewhat serious (stent embolization) AE occurred (both in the same patient who is described above). A device usage issue was identified whereby the expanded poly tetrafluoroethylene covering separated from the stent during attempts to load the CCPS device into the delivery sheath. This was identified before deployment; the stent was removed and replaced with a new CCPS without consequence to the patient.

Reference to the Clinical Study Report n°: NCT01824160

Device Used: Covered CP Stent pre-mounted on BIB

Conclusion: The study results demonstrate the safety and efficacy of use of the covered CP Stent when used for pre-stenting in the RVOT prior to Melody TPV implantation.

Summary of clinical data from other sources:

First Author (Year)	Appraisal/Results
1. Delaney et al. (2018)	**Safety & Performance** This publication presents the results from the PARCS trial – Covered CP Stent for Treatment of Right Ventricular Conduit Injury During Melody Transcatheter Pulmonary Valve Replacement (NCT01824160). Please refer information presented in **Table G-1** for safety and performance of the subject devices, Study no. 3. The state of the art information is presented below. **State of the Art** **Appraisal**

Medical condition		Alternatives		Risk/benefit		Side-effects		Equivalence		Surrogate endpoints	
Yes 1	No 2	**Yes 1**	No 2	**Yes 1**	No 2	**Yes 1**	No 2	Yes 1	**No 2**	Yes 1	**No 2**

Overall SOA Appraisal and Disposition

SOA Grade (Range 6-12)	8	Disposition (select)	**Accepted, < 12** Excluded, 12

Relevant SOA Results

Contribution	
S&P	x
SOA	x

SOA data

- Current knowledge:
  - Important conduit injury can occur during ultrahigh pressure angioplasty. Ultra-high pressure angioplasty is often required to dilate conduits effectively for TPVR. Conduit injury, once identified, could preclude further dilation of the conduit out of concern for extension of the area of injury.
  - Stenting of the conduit before valve implantation improves the durability of the implanted valve.
  - Covered stents have been used in the vascular space to isolate areas of injury.
- RVOT reconstruction:
  - RVOT reconstruction with a valved conduit or bioprosthetic pulmonary valve placement is necessary during surgical repair of a substantial subset of patients with congenital heart disease.
  - All valved RVOT substrates, regardless of type, have been associated with functional deterioration, with between 50% and 80% requiring replacement by 10 years.
  - RVOT dysfunction may be associated with substantial patient morbidity and even mortality.
  - Transcatheter RVOT conduit rehabilitation using high-pressure angioplasty with or without stent placement has been utilized to delay or defer the need for surgical pulmonary valve replacement. An injury within the wall of the conduit is likely to occur with any successful conduit dilation, although minor injuries may not be clinically relevant or recognized with angiography.
  - Successful RVOT conduit angioplasty often requires the use of ultrahigh pressure noncompliant balloons to effectively relieve the stenosis but with a higher rate of recognized conduit injury (≤33%). The vast majority of these injuries was not associated with hemodynamic compromise.
- Melody transcatheter pulmonary valve:
  - Introduction of the Melody transcatheter pulmonary valve (TPV; Medtronic) led to more frequent percutaneous conduit rehabilitation because cardiologists could effectively treat both stenosis and insufficiency, without the need for open-heart surgery.

	○ Melody TPV implants, without stent reinforcement of the conduit before valve implant, have been associated with a high rate of progressive valve deformity and stent fracture leading to valvular dysfunction. ○ Conduit wall injury is a known complication of isolated or serial balloon angioplasty of the RVOT conduit. Although bare metal stents may provide some reinforcement of a damaged conduit wall, they are not likely to allow for safe, continued dilation of an injured RVOT conduit that has not been fully prepared (e.g., left with hemodynamically important residual stenosis) for TPVR, and they are not anticipated to be effective in treating catastrophic conduit injuries. ○ Covered CP Stent (NuMED) is a balloon-expandable, large-diameter, covered stent whose construction and applications for vascular wall injury, tears, or leak have been reported previously. Experience with the Covered CP Stent outside of the United States is extensive and has included its routine use in the pre-stenting process for valve implantation. The European experience has suggested that this practice may reduce the clinical impact of conduit injury. ○ Some US centers did have access to the Covered CP Stent as participants in the COAST (Coarctation of the Aorta Stent Trial) and could apply for emergency use if an unexpected RVOT wall injury occurred. Non-COAST centers could apply for a single-patient compassionate use exemption if they felt a patient was at high risk for conduit injury.
Comments	- High-pressure balloon and stent angioplasty are frequently necessary to prepare the dysfunctional RVOT conduit before transcatheter pulmonary valve replacement (TPVR). Conduit injury can result, which may be catastrophic to the patient or prevent successful TPVR. Severe conduit injury was found to be rare but unpredictable. The covered stent was effective in either treating or mitigating this problem. The vast majority of patients, even with identified conduit injury, was able to complete the valve replacement procedure. The covered stent did not interfere with Melody valve function at short-term, 6-month follow-up.

2. Baykan et al. (2018)

Contribution	
S&P	X (S only)
SOA	-

Safety & Performance (for safety only)

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Control study. Study group was composed of 20 CoA patients who were treated with CP Stent between the dates October 2008 and February 2015, and control group was composed of 20 healthy children with age and sex matched.	To address the presence of hypertension and risk for cardiovascular diseases in patients with CoA who were treated with endovascular stent placement.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- CP Stents (Bare and Covered) - Unknown whether pre-mounted on BIB	**D1**	D2	D3
Application	- CoA	**A1**	A2	A3
Patient	- Patients who had undergone stent placement for CoA compared with control group (healthy children with age and sex matched).	**P1**	P2	P3

	- Sampling: n=20 CoA and n=20 healthy children
	- Mean age:
	  - CoA group: 14.2 (SD: 3.9) years
	  - Control group: 13.7 (SD: 2.7) years
	- Sex:
	  - CoA group: 16M; 4F
	  - Control group: 15M; 5F			

Report	- High quality	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Ambulatory blood pressure	**Yes 1**	No 2
Follow-up	- 6 months and 6 years	**Yes 1**	No 2
Statistical analysis	- Student t-test was used if the two independent group comparisons were normal and the Mann-Whitney U test was used if the normal distribution was not present. Pearson chi-square analysis was performed to determine whether there was a difference in categorical variables between the case and control groups.	**Yes 1**	No 2
Clinical significance	- It was shown that hypertension incidence as demonstrated by ambulatory blood pressure monitorization and risk for cardiovascular diseases as indicated by carotid intima media thickness and pulse wave velocity were higher than those in healthy population even after CoA is corrected. - CoA should be carefully monitored for hypertension, even if it has been completely corrected by any method. This study suggests that CoA is a part of generalized vasculopathy rather than being a localized narrowing.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (3) + Suitability (4) + Data Contribution (4) = 11	Disposition and Weighting (select)	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	- Hypertensive:
	  - Daytime: 5% were hypertensive and 20% were pre-hypertensive in the study group compared to 0% in the control group.
	  - Night: 15% were hypertensive and 15% were pre-hypertensive in the study group compared to 0% in the control group.

Benefits/claims data	- N/A
Strengths	- N/A
Weaknesses/ Potential bias	- Patients were treated only with “NuMED brand Bare and Covered Stent” types. In the future the authors can do more extensive studies with more cases and different types of stents.

	- Same methodology (blood pressure monitoring with Holter device) in pre-operative period could not be used because at that time they did not have a blood pressure Holter device.

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective data collected of the first NuDEL delivery systems used in patients from three centers (UK and Ireland).	To evaluate the first-in-man use of a new system (NuDEL) for implantation of CP Stent (Covered) in patients with complex structural and CHD.	1	2	3	**4**	5

3. Morgan et al. (2017)

Contribution	
S&P	x
SOA	x

Suitability	Relevant Data	Grading		
Device	- NuDEL Delivery System	**D1**	D2	D3
Application	- CoA and RVOT	**A1**	A2	A3
Patient	- Patients with COA and RVOT - Sampling: n=12 (13 CP Stents, Covered, delivered via 12 NuDELs); with 6 CoA, 5 RVOT, and 1 with severe stenosis of a Mustard systemic venous baffle. Note: "P2" due to one with severe stenosis of a Mustard systemic venous baffle. - Age: 10-43 years - Sex: Not reported	P1	**P2**	P3
Report	- High quality with minor deficiency as device performance is based on descriptive information.	R1	**R2**	R3
	Suitability Grade (Range 4-12)	6		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Procedure complications. - Ease of use.	**Yes 1**	No 2
Follow-up	- Not reported.	Yes 1	**No 2**
Statistical analysis	- Not reported.	Yes 1	**No 2**
Clinical significance	- NuDEL system is a safe and effective means of covered stent deployment in challenging anatomy.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	**6**	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (4) + Suitability (6) + Data Contribution (6) = 16	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- No procedural complications and no reports of equipment failure or dysfunction.
Performance data	- The system required minimal preparation – flushing only; therefore, despite a lack of familiarity, it was ready for deployment in each case in under two minutes after removing the packaging. - Key positive feedback and observations were that the assembly tracked well through the access site and through tortuous and narrowed anatomy in either the outflow tract or the descending aorta.

	- Stent was easy to uncover, and the markers on the system provided added re-assurance to this process.
Benefits/claims data	- Most difficult part of the catherization procedure is getting the stent into the required anatomical position before deploying it. To this end, the NuDEL system has been developed. - NuDEL reported to require minimal preparation and tracked well through the access site and tortuous and narrowed anatomy.
Strengths	- Our initial series suggests that the NuDEL system provides a safe, efficient method of deploying a covered stent in patients with complex outflow tract stenosis and those with CoA. Using this system avoids some of the pitfalls associated with stent mounting and management of the stent–balloon–delivery system complex. - Stent was easy to uncover and markers on the system provided added re-assurance of the process.
Weaknesses/ Potential bias	- Conflict of interest: None - Financial support: Research received no specific grant from any funding agency or from commercial or not-for-profit sectors

State of the Art

Appraisal

Medical condition		Alternatives		Risk/benefit		Side-effects		Equivalence		Surrogate endpoints	
Yes 1	No 2	Yes 1	**No 2**	**Yes 1**	No 2	Yes 1	**No 2**	Yes 1	**No 2**	Yes 1	**No 2**

Overall SOA Appraisal and Disposition

SOA Grade (Range 6-12)	10	Disposition (select)	**Accepted, < 12** Excluded, 12

Relevant SOA Results

SOA data	- Conduit rupture is an anxiety-provoking potential complication; the availability of a "ready-to-go" covered stent system may provide an attractive emergency backup. This may be of benefit to operators who perform a low volume of large-caliber stent procedures and are not conversant with the techniques involved, even in the elective setting. - The range of stents available for these therapies has developed well over the last 10–15 years, allowing authors to make semi-quantitative decisions about stent choice for each individual case. - Safety and accuracy of deployment are at least partially dependent on the precise mounting of the stent on its delivery balloon and passing it into and along the delivery sheath to its required position. The most difficult part of the catherization procedure is getting the stent into the required anatomical position before deploying it. A lot of time is taken in getting these essential steps right, and there is potential for safety, efficiency, and efficacy problems at every step. Slipping of the stents off balloons leading to migration of the stent before or during deployment and damage to the balloon or stent during mounting are some of the problems encountered, which may require re-crossing of the target areas, lead to vascular risk of removing and re-inserting a long, large-caliber sheath, and at worst can have major safety consequences.
Comments	- Stent implantation in the RVOT and for the treatment of CoA has become standard practice for congenital interventional cardiologists.

4. Bishnoi et al. (2015)

Contribution	
S&P	x
SOA	x

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective review of incidence and potential predictors of conduit disruption.	To assesses the frequency of RVOT conduit disruption during transcatheter pulmonary valve replacement (TPVR) and the effectiveness and safety of NuMED Covered Mounted CP Stentsfor its prevention or treatment.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- Covered Mounted CP Stents (12 to 22mm)	**D1**	D2	D3
Application	- NuMED CP Stents (Covered) for prevention or treatment of RVOT conduit disruption during TPVR	**A1**	A2	A3
Patient	- Population: Patients undergoing TPVR requiring treatment of RVOT conduit disruption (patients with pre-existing tears, patients developed tears after performing conduit dilation, and patients developed tears after transcatheter pulmonary valve implantation, or prophylactically placed in patients of perceived high risk related to degree of calcification and/or severity of homograft stenosis). - Sampling: 50 patients receiving 69 Covered CP Stents during TPVR/PPVI procedures (comparative cohort: 251 implants US Melody transcatheter pulmonary valve IDE Trial, planned for bare metal stenting of supported conduit) Note: overall incidence of conduit disruption requiring intervention was 6% in the study. - Mean Age: 21.4 (SD 3.7) years (5.5 to 56 years) - Sex: not reported	**P1**	P2	P3
Report	- High quality	**R1**	R2	R3
	Suitability Grade (Range 4-12)	**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Peak-to-peak RVOT gradient - Mean Doppler RVOT Gradient at 6 months - Valve competence with no or trivial pulmonary regurgitation - Safety	**Yes 1**	No 2
Follow-up	- 6 months	Yes 1	**No 2**
Statistical analysis	- Not provided	Yes 1	**No 2**
Clinical significance	- Covered Mounted CP Stent implantation can successfully treat RVOT conduit disruption without negative impact on the transcatheter pulmonary valve function	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	6	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade	LOE (3) + Suitability (4) +	Disposition and Weighting (select)	Accepted and Pivotal 9-12

(Range 9-25)	Data Contribution (6) = 13		**Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- Stent fracture: 1/50 patients with 2 CP Stents (Covered) developed multiple stent fracture 3 years following implantation. Patient was successfully treated with implantation of a stainless steel stent to support remaining portions of the CP Stent (Covered). - No Covered CP Stent-related acute complications were reported.
Performance data	- Peak-to-peak RVOT gradient: Decreased from 45.5 ± 17.5 mm Hg to 10.6 ± 6.3 mm Hg - Mean Doppler RVOT Gradient at 6 months: 12.86 ± 5.0 mmHg compared to 20.0 ± 8.6 mmHg from the Melody TPV IDE trial. - Valve competence with no or trivial pulmonary regurgitation: At follow-up 94% in study group and 93% in comparator group. - Conduit tears: prevented or repaired in 49/50 patients.
Benefits/claims data	- N/A
Strengths	- CCPS implantation can successfully treat RVOT conduit disruption without negative impact on the TPV function. - This retrospective analysis suggests high RVOT conduit systolic pressure gradient is a risk factor for conduit tears during PPVI.

Weaknesses/ Potential bias	- Retrospective analysis of prospectively collected data for other purposes and thus, suffers the biases of such investigations.
	- Sample size is small and in most cases the follow-up period is short. Long term results are unknown.
	- Conflict of interest reported:
	  - Bishnoi RN: none
	  - Jones T: research grant and consultant for Medtronic; research grant support from NuMED.
	  - Kreutzer J: research grant support from Medtronic and St. Jude Medical; consultant for Medtronic, Inc.
	  - Ringel RE: research grant support from Medtronic, Inc. and NuMED.

State of the Art

Appraisal

Medical condition		Alternatives		Risk/benefit		Side-effects		Equivalence		Surrogate endpoints	
Yes 1	No 2	**Yes 1**	No 2	**Yes 1**	No 2	Yes 1	**No 2**	Yes 1	**No 2**	Yes 1	**No 2**

Overall SOA Appraisal and Disposition

SOA Grade (Range 6-12)	9	Disposition (select)	**Accepted, < 12** Excluded, 12

Relevant SOA Results

SOA data	- Surgical management of patients with CHD such as tetralogy of Fallot, pulmonary atresia, transposition of the great arteries, truncus arteriosus, and those undergoing Ross procedure for treatment of aortic valve disease, often includes implantation of a bioprosthetic valve or RVOT conduit. - The lifespan of bioprosthetic valves or RVOT conduits is limited by progressive obstruction and/or regurgitation due to

	variety of factors including mechanical fatigue, immunologic reaction to the surgical implant, extrinsic conduit compression and somatic outgrowth on growing children. - Endovascular treatment using balloon dilatation and bare stent implantation has been shown to extend conduit lifespan and reduce a patient's need for repeated open heart surgeries. - While resolving the problem of conduit obstruction, bare stent placement leads to creation or exacerbation of pulmonary regurgitation.
Comments	- No further comment

5. Sohrabi et al. (2014)

Contribution	
S&P	x
SOA	-

Safety & Performance
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective randomized controlled trial.	To evaluate outcomes of treatment with Covered versus Bare NuMED CP Stents.	1	**2**	3	4	5

Suitability	Relevant Data	Grading		
Device	- NuMED CP Stent (Bare and Covered) - Stent was hand-crimped down onto BIB	**D1**	D2	D3
Application	- Severe native CoA	**A1**	A2	A3
Patient	- Patients with severe native CoA - Sampling: n=120 (60 CP Stents versus 60 CP Stents, Covered) - Mean age: 23.6±10.99 (range 12 to 58) years - Sex: 79 M; 41 F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Procedural success - Reduction in systolic blood pressure gradient - Reduction in mean diameter of coarctation segment - Adverse effects	**Yes 1**	No 2
Follow-up	- 31.1 ± 19.2 months	**Yes 1**	No 2
Statistical analysis	- A p-value <0.05 was considered significant.	**Yes 1**	No 2
Clinical significance	- Implanting CP Stent (Bare) and CP Stent (Covered) have very high success rates with remarkable hemodynamic effects in severe native CoA patients, with no significant complication during the procedure and hospitalization. - Patients undergoing CP Stent (Covered) implantation experienced a non-significantly lower re-coarctation rate and a higher occurrence of pseudoaneurysm formation with respect to CP Stent (Bare) stenting during follow-up. - In both groups, blood pressure was significantly reduced after intervention.	**Yes 1**	No 2

	- These findings indicate that CoA stenting is a safe procedure.		
	Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (2) + Suitability (4) + Data Contribution (4) = 10	Disposition and Weighting (select)	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	- Pseudoaneurysms: 0 (CP Stent, Bare) versus 2 (CP Stent, Covered) - Mortality: 1 (CP Stent, Bare) versus 0 (CP Stent, Covered)
Performance data	- Successful placement: successful in all patients - Mean systolic blood pressure gradient reduction: from 54.61 (CP Stent, Bare) and 54.42 (CP Stent, Covered) to 3.47 and 3.36 mmHg respectively; no significant difference between the two types of stent, P<0.001 - Mean diameter of coarctation segment reduction: From 3.34 (CP Stent, Bare) and 3.30 (CP Stent, Covered) to 16.07 and 15.82 mm respectively; no significant difference between the two types of stent, P<0.001 - Recurring coarctation: 4 (CP Stent, Bare) versus 0 (CP Stent, Covered), non-significant
Benefits/claims data	- Reduction in mean systolic blood pressure gradient - Reduction in diameter of coarctation segment
Strengths	- The CP Stent was hand-crimped down onto a balloon-in-balloon catheter (NuMED), which allows a precise and safe stent delivery
Weaknesses/ Potential bias	- Although the first randomized clinical trial in this respect, study was limited in some aspects. First, during follow-up, patients did not undergo 24-hour ambulatory blood pressure monitoring, which could have diagnosed the normotensive state more accurately. Second, evaluation of the blood pressure response during exercise testing could have been more valuable in defining the procedure outcome.

6. Vanagt et al. (2014)

Contribution	
S&P	x
SOA	-

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Single-center retrospective study (CHD database of all CP Stent, Covered, during 2003-2012)	To evaluate possibilities and safety of CP Stent (Covered) in CHD.	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	- Covered CP Stent - The stent was hand-crimped on BIB	**D1**	D2	D3
Application	- CoA and RVOT pre-stenting for percutaneous revalvulation	**A1**	A2	A3
Patient	- Patients with CoA and RVOT pre-stenting for percutaneous revalvulation. For the RVOT group, CP Stent (Covered) was chosen for delivery balloon protection after rupture of the pre-dilation balloon in 7/37 patients (19%) and 30 (81%) because tear, rupture, or fracture of the conduit	**P1**	P2	P3

	was expected, or further stent expansion following somatic growth was anticipated.
	- Sampling: n= 51 (CoA group), n=37 (RVOT group)
	- Mean age:
	  - CoA group: 19 (range from 8 to 69) years
	  - RVOT group: 16 (range from 6 to 43) years
	- Sex:
	  - CoA group: 38M; 13F
	  - RVOT group: 26M; 11F			

Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Increase in diameter at coarctation (CoA group) - Decrease in peak to peak gradient (CoA group) - Number of procedures for pre-stenting and pulmonary valve delivery (RVOT Group) - increase in graft diameter (RVOT Group) - Adverse effects	**Yes 1**	No 2
Follow-up	- Not specified.	Yes 1	**No 2**
Statistical analysis	- Two-sided p<0.05 was considered significant.	**Yes 1**	No 2
Clinical significance	- CP Stents (Covered) can safely be applied in CHD patients. The covering allows adequate sealing of existing or expected tears, thereby increasing the safety margin with more complete dilation.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	5	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (4) + Suitability (4) + Data Contribution (5) = 13	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- CoA Group:
	  - No acute bleeding, aneurysm formation or life-threatening complications.
	  - Mild procedure related-complications included groin hematoma (n = 3), transient nodal rhythm (n = 1, no wire present in left ventricle), and transient atrioventricular block with nodal escape rhythm (n = 1, while wire was present in left ventricle).
	  - During follow-up: no stent fractures, nor stent recompression occurred, and none of the patients had limb ischemia or signs of vessel occlusion at the puncture site.
	- RVOT group:
	  - No procedure-related complications and no extravasation.
	  - No embolization nor fracture of CP Stent (Covered) found on annual chest X-ray follow-up.

Performance data	- Diameter at coarctation (CoA group):

	- Increased from 6 (0-15) to 14 (7-20) mm, P<0.001. - Peak to peak gradient (CoA group): - Reduced from 23 (0-86) to 2 (0-25) mm Hg, P<0.001. - Number of procedures for pre-stenting and pulmonary valve delivery (RVOT Group): - 22/37 single procedure and 15/37 in a second procedure. - Graft diameter (RVOT Group) - Increased from graft stenosis diameter of 13 (5-22) mm to 22 (16-26) mm at pre-revalvulation, P<0.001.
Benefits/claims data	- Increase in luminal diameter in CoA patients.
Strengths	- CP Stent (Covered) frame is made from 90% platinum and 10% iridium 0.013" wire, welded in a zig pattern with additional gold soldering. The strut thickness is slightly larger than most other stents, but makes the stent edges relatively atraumatic. - CP Stent (Covered) was hand-crimped on a balloon-in-balloon (BIB, Numed). Hand-inflation of the balloon was performed with a 10 ml syringe on the inner balloon and 20 ml syringe on the outer balloon, automatically limiting inflation pressures to 4–6 atmospheres.
Weaknesses/ Potential bias	- In this retrospective study, there are no control groups with bare stents, the lack of which is inherently related to the fact that some of these procedures would have been impossible, or significantly less safe, if bare stents were used.

7. Alcibar et al. (2013)

Contribution	
S&P	x
SOA	-

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective and observational study.	To investigate reduction in aortic wall rupture and dissection, as well as aneurysms by implanting covered stents.	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	- Covered CP Stent - BIB or Z-Med balloons (NuMED) – 9 of the 17 patients had BIB - Hand crimped	**D1**	D2	D3
Application	- CoA and re-coarctation	**A1**	A2	A3
Patient	- Patients treated for CoA and re-coarctation (2 adolescents and 15 adults treated between November 2005 and January 2012). - Sampling: n=17 (11 native CoA and 6 re-coarctation) - Mean age: 35 (range 14-65) years - Sex: 4 M; 13 F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Reduction in blood pressure	**Yes 1**	No 2

	- Reduction in lumen diameter - Reduction of hypertensive medications at follow-up - Adverse effects		
Follow-up	- 2.5 years	**Yes 1**	No 2
Statistical analysis	- Significance was considered as P<0.05.	**Yes 1**	No 2
Clinical significance	- CP Stents (Covered) are effective in treating CoA and re-coarctation in adolescents and adults, are the treatment of choice in patients with complex anatomy, and must be available in the operating room as a rescue device when implanting a conventional stent.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (4) + Suitability (4) + Data Contribution (4) = 12	Disposition and Weighting (select)	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	- One death: patient died two days post-op due to massive hematemesis as a result of the combination of an extreme increase in blood pressure and an existing aneurysm. - No local complications occurred, except one hematoma that resolved spontaneously. - No patient had any complication at the iliac-femoral level that required stenting.

Performance data	- Blood pressure gradient: Reduced from 40 to 2 mmHg (P<0.001)
	- Lumen diameter: Increased from 4 to 15 mm (P<0.001)
	- At follow-up (2.5 years):
	  - All good initial outcome persisted without any signs of re-obstruction.
	  - 13/17 patients underwent imaging study; no aneurysms, dissections, and/or obstructive processes were observed.
	  - Medication for hypertension was reduced in 5 patients and in 2 patients could not be discontinued.

Benefits/claims data	- Increased in luminal diameter - Decreased in antihypertensive medication use
Strengths	- Having observed the case of aortic rupture, and with the aim of reducing these complications in patients who have had CoA and re-coarctation since their youth, the authors decided to electively implant a NuMED (Hopkinton, New York, United States) ePTFE CP Stent (Covered). This stent is mounted on a balloon catheter and protects the vascular wall when expanded.
Weaknesses/ Potential bias	- Retrospective and observational study with no control group of patients receiving conventional stents. Although all patients underwent clinical follow-up, this did not include an imaging study in all cases, and so authors cannot determine with certainty the incidence of potential aneurysms.

8. Chang et al. (2012)

Contribution	
S&P	x
SOA	-

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Single arm interventional study.	To evaluate the use of CP Stent (Covered) as the primary modality in the treatment for native CoA.	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	- CP Stent (Covered and Bare) 25 covered stents and 2 bare stents in 25 patients (one patient had 3 stents (2 bare, one covered) for native CoA with aortic arch hypoplasia (combination covered + stents = a new approach) - The covered CP stent was hand-crimped down onto BIB	**D1**	D2	D3
Application	- Native CoA	**A1**	A2	A3
Patient	- Patients with native CoA without previous treatment - Sampling: n=25 - Mean age: 22.5 (range 14-46) years - Sex: 16 M; 9 F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Decrease in systolic gradient - Increase in stenotic segment diameter	**Yes 1**	No 2
Follow-up	- 32 (7-72) months	**Yes 1**	No 2
Statistical analysis	- P<0.05 was set as statistically significant.	**Yes 1**	No 2
Clinical significance	- Implantation of CP Stent (Covered) as the primary modality is safe and effective in the treatment for native CoA in adolescents and adults. - Treatment modality of native CoA in adolescents and adults acquired excellent results, such as significant reduction in peak systolic gradient across CoA, successful relief of anatomic stenosis, and reduction of systemic hypertension. - Above all, no adverse events were encountered during the procedure or during the follow-up period of up to 72 months.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (4) + Suitability (4) + Data Contribution (4) = 12	Disposition and Weighting (select)	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	- No acute complications were observed. - During a follow-up period of up to 72 months (median, 32 months and quartile range, 51 months), no adverse effects

	(e.g., dissection, aneurysm formation, stent migration, stent fracture) were encountered. - In the patient with the implantation of three CP stents, the aneurysm formation related to the bare CP stent was not encountered, the left subclavian artery crossed by the bare CP stent presented patent without thrombosis, and the left arm ischemia was not detected.

Performance data	- Peak systolic gradient across the lesion:
	  - Decreased from median 67.5 mmHg to median 2 mmHg (P<0.0001)
	- Stenotic segment diameter
	  - Increased from median 5.0mm to median 17.9mm (P<0.0001)
	- At follow-up (up to 72 months):
	  - Most patients (21/25) were normotensive; except from 4/25 patients still required antihypertensive medication during follow-up

Benefits/claims data	- Reduced in peak systolic gradient. - Reduced in luminal diameter. - BIB offered precise and safe control over the stent implantation without any stent migration
Strengths	- Use of covered CP stents as the primary treatment modality may reduce the risk of significant complications related to stent implantation.
Weaknesses/ Potential bias	- Conflict of interest: not reported.

9. Erdem et al. (2011)

Contribution	
S&P	X (S only)
SOA	-

Safety & Performance (for safety only)

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Single arm interventional study.	To present author's institutional experience of endovascular CP Stent implantation in children and adults with native and recurrent CoA.	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	- CP Stent (16 Covered or 31 Bare) – n=47 - BIB (n=29) (not subject device) or single balloon catheter (n=18) (not subject device), Z-med (not subject device); manually crimped	D1	**D2**	D3
Application	- Patients with native or recurrent CoA	**A1**	A2	A3
Patient	- Patients with native CoA (Group 1); recurrent CoA and/or aneurysm developed after either surgery or balloon angioplasty (Group 2) - Sampling: n=45 (47 CP Stents, Covered or Bare) - Median age: 11 (range: 5-33) years - Sex: 34M; 11F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	5		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Decrease in invasive and echocardiographic gradients - Increase in lesion diameter - Adverse effects	**Yes 1**	No 2
Follow-up	- 12.1±7.1 months; median 11 month (range 2-29)	**Yes 1**	No 2
Statistical analysis	- A p value <0.05 was considered statistically significant.	**Yes 1**	No 2
Clinical significance	- Early and short- term follow-up results indicate that stent implantation is safe and very effective in reducing coarctation gradient and increasing lesion diameter both in native and recurrent CoA. - Some serious complications do occur and hypertension remains in some patients. - Aortic disruption and stent displacement are potentially catastrophic complications of stenting but implanting a second covered stent can seal the ruptured wall and parking in a safe area or replacement of displaced stent carried by half-inflated balloon could solve the problem.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (4) + Suitability (5) + Data Contribution (4) = 13	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- No procedure related death.
	- Two immediate complications relating to stenting:
	  - One an acute wall rupture, successfully managed immediately in the same session with implantation of a second covered stent
	  - One stent was displaced before it was completely opened. It was carried with support of partially inflated balloon and long sheath, and repositioned into the correct place.
	- No femoral arterial complications
	- No difficulty in catheter manipulation.
	- None of the patients required intensive care following the procedure, and all were discharged home the following day except the patient with aortic rupture and after stenting with covered stent this patient was followed two days in intensive care unit.

Benefits/claims data	- Increase in luminal/lesion diameter.
Strengths	- CP stent is the one of the most commonly used stent in pediatric cardiology - This stent has excellent radial strength even at larger diameters and also has brilliant visibility on fluoroscopy.

Weaknesses/ Potential bias	- Some limitations have to be noted about this study:
	  - Firstly, there is a need a greater number of patients have undergone stent implantation and their long-term results.
	  - Secondly, population included both children and adult.
	  - Thirdly, this was a single-center report and patients were not compared with surgery or balloon angioplasty

	alone. - Fourthly, 24-hour ambulatory blood pressure monitoring before stenting was not performed in any patients. - Finally, radiologic imaging for aneurysm was done in limited number of patients after procedure. - Conflict of interest: None declared.

10. Butera et al. (2011)

Contribution	
S&P	x
SOA	-

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective single arm interventional study.	To evaluate the management of aneurysms associated with CoA by covered stent deployment.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- Covered CP Stent - BIB or Crystal balloon (not subject device) (manually crimped)	D1	**D2**	D3
Application	- Patients with native CoA associated with aortic wall aneurysm	**A1**	A2	A3
Patient	- Patients with CoA associated with aortic wall aneurysm - Sampling: n=11 (3 native CoA, 3 with previous surgical repair, 3 with previous balloon angioplasty, and 2 with previous bare stent implantation) - Median age: 13 (range: 6-66) years - Sex: Not reported	P1	**P2**	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	6		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Systolic pressure gradient reduction - Increase in aortic diameter - Adverse effects	**Yes 1**	No 2
Follow-up	- Median follow-up 50 (16-61) months	**Yes 1**	No 2
Statistical analysis	- P-value less than 0.05 was considered to be statistically significant	**Yes 1**	No 2
Clinical significance	- CP Stent (Covered) are a safe and effective treatment with low risk of complication for the treatment of CoA associated with aortic wall aneurysm. - CP Stents (Covered, e-PTFE) may be considered the treatment of choice for native CoA associated with aortic wall aneurysm.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (3) + Suitability (6) + Data Contribution (4) = 13	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- No early complications observed.
Performance data	- Successful device deployment: Achieved in all patients. - Successful relief of stenoses and complete sealing of all aneurysms. - Systolic pressure gradient reduction: From median 30 (25-50) to 5 (0-20) mmHg, P<0.01 - Increase of aortic diameter: From median 6 (0.5 – 11) to 12 (10-22) mm, P<0.001 - Re-dilatation required at follow-up: four patients developed systemic hypertension (one intrastent restenosis secondary to significant endothelial growth, three showed restenosis secondary to somatic growth). Re-dilatation with a larger balloon was performed without complication in all cases.
Benefits/claims data	- Increase in luminal diameter - Reduce systolic pressure gradient - Reduce/prevent aortic wall injury (patients associated with aortic wall aneurysm)
Strengths	- Covered CP stents are manufactured with an alloy of 90% platinum and 10% iridium. Theoretically, this combination is more malleable and with good radial strength, which is enhanced by being designed in a ''zig'' pattern. The CP stent has rounded edges, decreasing the risk of balloon rupture or injury to the vessel wall and, in addition, the platinum component makes it more radio-opaque. Furthermore, the e-PTFE protects the stenotic and diseased segment.
Weaknesses/ Potential bias	- No conflict of interest reported.

11. Tanous et al. (2010)

Contribution	
S&P	x
SOA	-

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Single arm interventional study.	To determine the safety and efficacy of the CP Stent (Covered) in adults with CoA.	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	- Covered CP Stent hand-crimped on Z-Med II (NuMED) or Covered Mounted CP Stent	D1	**D2**	D3
Application	- Native CoA (n=14) and previous treatment (n=8)	**A1**	A2	A3
Patient	- Patients with native CoA and CoA with previous treatment - Sampling: 14 native CoA; 8 CoA (with previous treatment) - Mean age: 39±14 (range 19 to 67) years - Sex: 11 M; 11 F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	5		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Reduction in peak systolic gradient across coarctation site - Adverse effects	**Yes 1**	No 2

Follow-up	- 12 (9-15) months	**Yes 1**	No 2
Statistical analysis	- A P-value <0.05 was considered significant.	**Yes 1**	No 2
Clinical significance	- Covered stents are safe, durable, and efficacious in the management of CoA.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (4) + Suitability (5) + Data Contribution (4) = 13	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- One pseudoaneurysm. Patient was treated successfully. Note: this problem may have been caused because the stent was hand crimped. When pre-mounted stents were used the problem did not reoccur.
Performance data	- Reduction in peak systolic gradient across coarctation site: From average 29 ± 17 to 3 ± 5 mmHg immediately post intervention and 6 ± 9 mmHg at follow up, P<0.001
Benefits/claims data	- Reduction in peak systolic gradient
Strengths	- N/A
Weaknesses/ Potential bias	- This review is limited by the small sample size and lack of a randomized comparison group. - This study was not intended to demonstrate the efficacy of percutaneous therapy, or the superiority of covered stents, but rather to document a single-center experience as an alternative and safe treatment option in a broad spectrum of patients with aortic coarctation.

12. Moltzer et al. (2010)

Contribution	
S&P	X (S only)
SOA	-

Safety & Performance (for safety only)

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective observational study.	To evaluate the intermediate-term outcome of stent implantation for CoA in adults.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- CP Stent (Bare and Covered) – 6 of the 24 patients had covered stents - BIB (manually crimped)	**D1**	D2	D3
Application	- Native CoA and re-coarctation	**A1**	A2	A3
Patient	- Patients with native CoA and re-coarctation - Sampling: n=24 - Mean age: 36 (18-60) years - Sex: 12 M; 12 F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Decrease in systolic gradient - Increase in minimum aortic diameter - Adverse effects	**Yes 1**	No 2
Follow-up	- 24 hours post intervention and 33 (8-77) months	**Yes 1**	No 2
Statistical analysis	- All statistical tests were two-sided and a p-value <0.05 was considered statistically significant	**Yes 1**	No 2
Clinical significance	- Stenting in adults results in significant blood pressure gradient decrease and increase in vessel diameter. However, serious complications do occur and hypertension remains in the majority of patients.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (3) + Suitability (4) + Data Contribution (4) = 11	Disposition and Weighting (select)	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	- One death due to aorta ruptured. - Two groin hematoma post-op.
Benefits/claims data	- Reduced in systolic gradient - Increased in minimum aortic diameter
Strengths	- N/A
Weaknesses/ Potential bias	- Only a small number of patients have undergone stent implantation since the authors started this procedure in 2003. This was a single-center report and patients were not compared with surgery or balloon angioplasty alone. Finally, 24-hour blood pressure monitoring before stenting was not performed in the majority of the patients. Post-stent 24-hour ambulatory blood pressure monitoring is therefore difficult to translate in terms of blood pressure reduction.

13. Agnoletti et al. (2009)

Contribution	
S&P	X (S only)
SOA	-

Safety & Performance (for safety only)

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Two arms comparative interventional study.	To compare the CP Stent and the Palmaz stent for treatment of native and postoperative lesions of CHD patients.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- CP Stent (Bare & Covered), crimped on BIB in 77 cases - 96 CP Stents (34 covered), 77 Palma Stents - Palmaz stent, crimped on BIB and simple balloons	**D1**	D2	D3
Application	- Patients with CHD (including CoA/re-coarctation, RVOT)	A1	**A2**	A3
Patient	- Patients with CHD (including CoA/re-coarctation, RVOT and other CHD conditions, such as	P1	**P2**	P3

	transposition of the great arteries, ventricular septal defect, single ventricle, etc.)
	- Sampling: n= 153
	  - 89 patients with CP Stents (crimped on 77 BIB & 12 other balloons)
	  - 64 patients with Palmaz Stents (crimped on 23 BIB and 41 simple balloons)
	- Mean age:
	  - CP Stents: 15.4 (SD: 9.2) years
	  - Palmaz Stents: 11.6 (SD: 8.1) years
	- Sex: Not reported			

Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	6		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Blood pressure gradient reduction - Vessel diameter reduction - Adverse effects	**Yes 1**	No 2
Follow-up	- Not reported.	Yes 1	**No 2**
Statistical analysis	- A P-value less than 0.05 was considered statistically significant for stent group comparison.	**Yes 1**	No 2
Clinical significance	- The use of the CP Stents to treat stenotic lesions of CHD is effective and relatively safe. The overall efficacy of CP Stents for the treatment of stenotic lesions is superior to that of the Palmaz stent. - CP Stents' overall safety is higher than that of the Palmaz stent; but Palmaz stents have a lower profile when inserted.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	5	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (3) + Suitability (6) + Data Contribution (5) = 14	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- Stent-related complications:
	  - CP Stents (n=89 patients): 4 mild, 1 moderate, 1 severe.
	  - Palmaz (n=64 patients): 10 mild, 2 moderate, 2 severe.
	- Stent migration:
	  - CP Stents: 7.
	  - Palmaz: 4.
	- Non stent related complications:
	  - CP Stents: 1 mild, 2 moderate.
	  - Palmaz: 1 mild, 2 moderate, 5 severe.
	- Urgent surgery:
	  - CP Stents: 2 due to homograft rupture and stent migration.

	- Palmaz: 1 for aortic dissection. - Balloon related complications: Balloon burst - CP Stents: 0. - Palmaz: 7 (3 in BIB, 3 with simple balloons, and 1 on pre-mounted stent).
Benefits/claims data	- Decreased in blood pressure gradient. - Increased in vessel diameter.
Strengths	- Efficacy of CP Stents was similar to that of Palmaz stent for stenting of the right ventricular outflow, and higher than that of Palmaz for the stenting of aorta, but the difference was not statistically.
Weaknesses/ Potential bias	- Study presented retrospective results obtained in 153 consecutive patients. - CP stents were used for patients weighing more than 15 kg; and thus two populations were different concerning age, weight, indication for stenting; however, none of these differences were related to occurrence of complications. - Subgroup analyses were not performed.

14. Bruckheimer et al. (2009)

Contribution	
S&P	x
SOA	-

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective interventional single arm study to evaluate placement of CP Stent (Covered) with smallest possible balloon sizes, then dilation with larger diameter balloons until pressure gradient was <20 mmHg and the stent was opposed to the aortic wall.	To report on the early results of treatment of native CoA by implantation and serial dilations of covered stents.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- Covered CP Stents - Manually crimped on a balloon	**D1**	D2	D3
Application	- Native CoA	**A1**	A2	A3
Patient	- Patients with native CoA - Sampling: n=22 - Mean age: 15.5 (7.8 – 38.6) years - Sex: 14 M; 8 F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Increase of coarctation diameter - Reduction of peak pressure gradient - Adverse effects	**Yes 1**	No 2
Follow-up	- Median 18.5 (1.6-31.4) months	**Yes 1**	No 2

Statistical analysis	-	P-values reported.	**Yes 1**	No 2
Clinical significance	-	Serial dilation of CP Stents (Covered) is feasible, safe and an effective percutaneous method for the treatment of native CoA.	**Yes 1**	No 2
		Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (3) + Suitability (4) + Data Contribution (4) = 11	Disposition and Weighting (select)	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	- One small tear at the distal stent edge - One femoral pseudoaneurysm which spontaneously resolved

Performance data	- Increase of coarctation diameter:
	  - From 3.6 ± 1.9 mm pre-intervention to 12.6 ±1.9 mm post-intervention, P=0.001
	- Reduction of peak pressure gradient:
	  - From 29.4 ± 8.5 to 6.7 ± 5.7 mmHg, P=0.001

Benefits/claims data	- Increase of coarctation diameter - Reduction of peak pressure gradient
Strengths	- N/A
Weaknesses/ Potential bias	- No conflict of interest reported.

15. Tzifa et al. (2006)

Contribution	
S&P	x
SOA	-

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Single arm interventional study.	To evaluate the use of Covered CP Stents in treatment of CoA.	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	- Covered CP Stent - BIB (hand-crimped)	**D1**	D2	D3
Application	- CoA	**A1**	A2	A3
Patient	- Patients with CoA (fully grown patients) - Sampling: n=30 - Mean age: 28±17.5 (range 8 to 65) years - Sex: not reported	**P1**	P2	P3
Report	- High quality.	R1	**R2**	R3
	Suitability Grade (Range 4-12)	5		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Reduction in blood pressure gradient - Reduction in coarctation diameter	**Yes 1**	No 2
Follow-up	- 11 months	**Yes 1**	No 2
Statistical analysis	- Statistical significance was defined as P<0.05.	**Yes 1**	No 2
Clinical significance	- CP Stents (Covered) may be used as the therapy of choice in patients with complications after CoA repairs, whereas they provide a safe alternative to conventional stenting in patients with severe and complex CoA lesions or advanced age.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (4) + Suitability (5) + Data Contribution (4) = 13	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- Two stent fractures in the "old" design of the stent, no fractures in the "new" stent design Note: Since May 2002, the CP Stents (Covered) have been produced with reinforced golden soldering joints as the "new" stent design
Performance data	- Blood pressure gradient: From 36 + 20 mmHg to 4 + 4 mmHg, P<0.0001 - Diameter at coarctation: From 6.4 +3.8 mm to 17.1 + 3.1 mm, P<0.0001
Benefits/claims data	- Reduction in blood pressure gradient - Reduction in coarctation diameter - BIB allows readjustment of position after inflation of the inner balloon.
Strengths	- Covered stents were chosen: 1) as a rescue treatment in patients with CoA aneurysms or previous stent-related complications; and 2) in patients at risk of complications because of complex CoA anatomy or advanced age (defined as >65 years) - Covered CP stents are made of a framework of platinum iridium wire welded in a zig pattern. The addition of a gold soldering to each weld spot fills any voids caused by the welding and transfers the stresses to a larger area of the stent. The gold also serves to encapsulate the welded area, once again adding to the total strength of the weld. The stent is then fitted with a covering of ePTFE to achieve a solid tubular structure that retains fluid. The ePTFE covering is initially approximately 7 mm in diameter and will stretch over the range of diameters of expansion (usually from 12 to 24 mm diameter), and will always be taut over the stent when expanded. When the covering is mounted, it is folded over the crimped stent and expands uniformly when the balloon is inflated. - The BIB allows for readjustment of position after inflation of the inner balloon.
Weaknesses/ Potential bias	- Not reported.

16. Meadows et al. (2015)

Contribution	
S&P	X (S only)
SOA	-

Safety & Performance (for safety only)
This publication presents the results from the COAST trial for CP Stent (Bare and Covered) to treat native and recurrent CoA in selected children, adolescents and adult (NCT00552812). Please refer information presented in **Table G-1** for safety and performance of the subject devices, Study no. 1.

17. Taggart et al. (2016)

Contribution	
S&P	x
SOA	-

Safety & Performance
This publication presents the results from the COAST II trial to evaluate the safety and short-term efficacy of the CP Stent in treating or preventing aortic wall injury in patients with CoA (NCT01278303). Please refer information presented in **Table G-1** for safety and performance of the subject devices, Study no. 2.

18. Sasikumar et al. (2020)

Contribution	
S&P	X (S only)
SOA	x

Safety & Performance (for safety only)
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective study.	To study the early and late outcomes after stenting of native and recurrent CoA with uncovered and covered stents.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- CP Stent (Bare and Covered) – "D1" for subject devices - Unknown if pre-mounted on BIB - Other devices, including Advanta V12 stent (covered), Andra XL and XXL stents, Palmaz XL	**D1**	D2	D3
Application	- CoA (native and recurrent)	**A1**	A2	A3

Patient	- Patients with CoA (native and recurrent)
	- Sampling: n=45 (20 covered stents, 25 non-covered stents)
	  - Covered stents used were covered 7 CP Stent; 13 Advanta V12 Stent
	  - Non-covered stents used were 17 CP Stent, 6 Andra XL and XXL stents, and 2 Palmaz XL.
	- Mean age: 28±17.5 (range 8 to 65) years. Age per device group was not reported.
	- Sex: 32 M, 13 F. Sex per device group was not reported.
		P1	**P2**	P3

Report	- High quality with deficiencies	R1	**R2**	R3
	Suitability Grade (Range 4-12)	6		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Safety	**Yes 1**	No 2
Follow-up	- Covered stent group: 57 months	**Yes 1**	No 2

	- Non-covered stent group: 35 months		
Statistical analysis	- Statistical analysis was done by the Statistical Package for Social Sciences (version 21.0). Quantitative data were presented as mean ± SD or as median and range and qualitative data were presented as frequency (percentages). The categorical parameters were compared by chi-square test, and the continuous variables were compared by Student t test for independent continuous data and Manne Whitney U test for nonparametric data.	**Yes 1**	No 2
Clinical significance	- Not reported specifically for subject devices.	Yes 1	**No 2**
	Data Contribution Grade (Range 4-8)	5	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (3) + Suitability (6) + Data Contribution (5) = 14	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	**Outcomes**	**Covered (n=18)**	**Uncovered (bare metal) (n=8)**
	Late lumen loss (no or mild)	2 (Advanta 1, CP 1)	4 (CP 3, Palmaz 1)
	Late lumen loss (moderate)	12 (Advanta 7, CP 4, Andra 1)	4 (CP3, Palmaz 1)
	Late lumen loss (severe)	4 (Advanta 3, CP 1)	0
	Fracture	1 Advanta	0
Performance data	- Not reported specially for subject devices.		
Benefits/claims data	- Not reported		
Strengths	- Not reported.		
Weaknesses/ Potential bias	- Not reported.		

State of the Art

Appraisal

Medical condition		Alternatives		Risk/benefit		Side-effects		Equivalence		Surrogate endpoints	
Yes 1	No 2	**Yes 1**	No 2	**Yes 1**	No 2	**Yes 1**	No 2	Yes 1	**No 2**	Yes 1	**No 2**

Overall SOA Appraisal and Disposition

SOA Grade (Range 6-12)	8	Disposition (select)	**Accepted, < 12** Excluded, 12

Relevant SOA Results

	SOA data	- Patients in the covered stent group were older and had greater basal pressure gradient. More patients in the covered stent group had residual gradient >10 mm Hg after the procedure. - No mortality or aortic wall injury in either group. - Mean number of anti-hypertensive was 1.38 ± 0.74 in the covered goup and 1+0.7 in the uncovered group - Greater incidence of severe late lumen loss (>30% lumen loss) in the covered stent group on follow-up. According to the authors, this phenomenon was brand specific (Advanta V12 stent). Single strut fracture which was not causing any lumen obstruction was also noted in one Advanta V12 stent. The stents have an open cell stent geometry with consequent less radial strength. - A previous study on Advanta stent implantation in 25 patients did not show any complications related to the stent. However, the median period of follow-up in that study was only 4.9 months and longer follow-up is needed to look for re-coarctation or aneurysm formation. - Another study described 2 patients with Advanta stent implantation who developed in-folding of the proximal edge of the stent on follow-up and both the cases were managed by re-stenting. The authors had a similar proximal stent collapse in a patient who had Advanta stent implantation, which was managed by balloon angioplasty. Though the residual gradient was 5 mm Hg immediately after the balloon angioplasty, the gradient increased to 25mmHg on follow-up and he underwent a repeat balloon angioplasty with good result.
	Comments	- Uncovered stents can be safely implanted with minimal risk of aortic wall injury in patients with low risk anatomic features. Covered stent implantation is associated with higher incidence of planned and unplanned re-intervention.

19. Stassen et al. (2021)

Contribution	
S&P	x
SOA	x

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Single center retrospective study.	The aim of this study was to investigate the impact and safety of covered stent placement for treatment of (re)CoA during a longer follow-up period.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- Only 8-zig covered Cheatham Platinum (CCP) stents (NuMED Inc. Hopkinton, NY, USA) were included in the study; 8z22 (1.1%), 8z28 (18.0%), 8z34 (25.8%), 8z39 (25.8%), 8z45 (28.1%) and 8z55 (1.1%). - Unknown if pre-mounted on BIB	**D1**	D2	D3
Application	- CoA (recurrent)	**A1**	A2	A3
Patient	- Patients with CoA who were treated with 102 covered stents from 2003 to 2017 - All patients with a covered stent implantation for a native CoA or reCoA after surgical or transcatheter repair were included. - 89 patients with 102 covered stents in 93 procedures - Mean age 23.9±15.8 years (5.1-71.6) - 35 patients <16 years and 54 patients ≥16 years - 60 (67.4%) male and 29 (32.6%) female	**P1**	P2	P3
Report	- High quality report	**R1**	R2	R3

Suitability Grade (Range 4-12)	4

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Short-term pre/post-implant hemodynamics and angiographic data were reported. Changes in blood pressure, the use of antihypertensive drugs and complications were recorded during follow-up.	**Yes 1**	No 2
Follow-up	- Mean follow-up time was 6.6±3.7 years (min max range 0.2-15.7 years).	**Yes 1**	No 2
Statistical analysis	- Continuous variables are presented as mean plus minus standard deviation (range minimum–maximum). In case of an asymmetric distribution of data, results are reported as median (interquartile range (IQR)). Proportions are noted as number and percentage. Comparison of individual parameters before and after stenting was performed using the two-tailed paired t test. Categorical data were compared with a McNemar. A p value of less than 0.05 was considered statistically significant. Statistical analysis was done using the SPSS software version 26 package (SPSS Inc., Chicago, IL USA).	**Yes 1**	No 2
Clinical significance	- The magnitude of the treatment effect observed was clinically significant.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (3) + Suitability (4) + Data Contribution (4) = 11	Disposition and Weighting (select)	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	- Long-term adverse events were found in 4.5% of patients (covered stent fracture (n=3), aneurysm formation (n=2)).
Performance data	- The procedural success rate was 100%. - The mean invasive ascending-to-descending aorta systolic gradient under general anaesthesia decreased from 25 ± 16mmHg to 4 ± 7mmHg (p<0.001). After a mean follow-up time of 6.6 ± 3.7 years, there was a persistent improvement of the mean systolic blood pressure gradient between right arm and leg (~7 ± 18 vs 38 ± 24mmHg; p<0.001). A larger proportion of patients required antihypertensive medication (33.7% vs 50.0%, p=0.017) and needed ≥ two drugs (20.2% vs 27.4%, p=0.066) to control blood pressure.
Benefits/claims data	- Covered stent implantation for CoA is highly successful, safe and results in a persistent hemodynamic improvement in the immediate and long-term outcome. Lifelong follow-up with additional antihypertensive drug treatment is mandatory to maintain favourable hemodynamic results after stenting.
Strengths	- Patients were followed for a mean period of 6.6±3.7 years (maximum follow-up time 15.7 years). To authors knowledge, this is the largest study with the longest follow-up of the use of covered stents in (re)CoA.
Weaknesses/ Potential bias	- Retrospective design - Single centre design - Incomplete follow-up achieved: 14 of the 89 patients had no follow-up data. Among the 75 remaining patients, 47 had 5 years follow-up (so with imaging).

State of the Art

Appraisal

Medical condition		Alternatives		Risk/benefit		Side-effects		Equivalence		Surrogate endpoints	
Yes 1	No 2	**Yes 1**	No 2	**Yes 1**	No 2	**Yes 1**	No 2	Yes 1	**No 2**	**Yes 1**	No 2

Overall SOA Appraisal and Disposition

SOA Grade (Range 6-12)	7	Disposition (select)	**Accepted, < 12** Excluded, 12

Relevant SOA Results

SOA data	CoA: - CoA is a congenital cardio-vascular malformation, characterised by a restriction of the lumen of the thoracic aorta. It occurs in approximately 4 of 10,000 live births and comprises 5% to 8% of CHD. - Mostly, CoA is detected in childhood and repaired surgically or by endovascular therapy. Occasionally it is diagnosed in adolescence or adulthood by investigations done for systemic hypertension. - The natural history of CoA carries a poor prognosis due to complications such as left ventricular failure, intracranial haemorrhage, aortic rupture or dissection, premature coronary artery disease and sudden death. - Smaller and younger infants are typically treated surgically but remain at risk for recurrent obstruction with up to 10% requiring further intervention during adulthood. - In older children and adults, the preferred treatment method depends on the individual anatomy and nature of the lesion, but endovascular therapy with either balloon angioplasty or stent implantation is commonly preferred over surgery. Although balloon angioplasty results in excellent acute hemodynamics, it is associated with a high rate of aortic wall injury and recurrent obstruction. Because of these concerns, stent implantation is usually favoured to avoid overdilation or the elastic recoil of the aorta. Bare stent implantation has become a worthy alternative to surgery and balloon angioplasty and seems to lead to better results and fewer complications. However, although interventions with bare stent implantation seem efficient and generally safe, major complications such as local aneurysm formation, aortic rupture, dissection and even death may occur. To prevent these aortic wall injuries (AWI) during the stent procedure, covered stents are increasingly used and their safety and efficacy for immediate and intermediate follow-up have been demonstrated. However, long-term results remain limited. Covered stents: - Covered stents are increasingly used in severe and complex coarctations of the aorta, mainly to avoid the risk of aortic wall injuries such as local aneurysm formation, dissection and aortic rupture. Nevertheless, the aorta can still rupture with a covered stent, but no unlimited bleeding will occur, unless there was insufficient sealing, the covering was torn or in case of vessel tear with retrograde bleeding from collaterals.
Comments	- Not reported

20. Holzer et al. (2021)

Safety & Performance (for safety only)

Appraisal

Contribution	
S&P	x (S

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Included in this report are the 5-year	To report the late-term follow-up data and to	1	2	**3**	4	5

	only)
SOA	x

	follow-up data from patients in these 2 trials and those treated through their Continued Access protocols. Data was prospectively collected during the 2 multi-center studies.	compare this to earlier follow-up data. For the purpose of this study, follow-up was defined as: - Immediate (1 month), - Early (12 months), - Late (48 or 60 months). To identify possible predictors of late-term outcome post-stent implantation.					

Suitability	Relevant Data	Grading		
Device	- CP Stent (Bare and Covered) - 52% received covered stents and 48% received bare stents. - No data if pre-mounted or not with BIB - The minimum stent diameter was 14.4mm (interquartile range (IQR), 12.6-16.0mm) with a minimum stent diameter to the aorta at diaphram ratio of 0.87 (IQR, 0.77-1.0).	**D1**	D2	D3
Application	- CoA (native or recurrent) - Native coarctation was present in 49%, postsurgical in 24% and postcatheterization in 27%. - The minimum coarctation diameter was 8.0mm (IQR, 5.4-10.5mm), and median aortic diameter at the diaphragm was 16.0mm (IQR, 14.0-19.0mm).	**A1**	A2	A3
Patient	- All patients enrolled in the COAST or COAST II trials and their Continued Access extensions were included. Patients without late follow-up data were excluded from analysis, except for analyzing the estimated cumulative incidence of stent fractures, aortic wall injury, and reinterventions. - Cohort of 248 patients - COAST: 105 patients enrolled in COAST with 16 Continued Access patients (n=121) - COAST II: 82 participants from COAST II with an additional 45 Continued access patients (n=127). - From the 180 patient cohort, the median age at implant was 17 years (IQR, 13-28 years), the median weight (66.3kg, IQR, 53.8-78.1kg).	**P1**	P2	P3
Report	- High quality report	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Parameters used to assess aortic stent outcomes: -Hemodynamic -Systemic systolic hypertension -Use of antihypertensive medication -Upper limb to lower limb blood pressure difference of ≥20mm Hg -Reinterventions -Stent fractures -Aortic wall injury	**Yes 1**	No 2

		- Predictor variables used to assess late-term results: -Demographics -Type of coarctation -Preimplantation clinical data -Baseline characterization data -Type of stent -Poststent catherization data -Postcatheterization data		
	Follow-up	- Follow-up data was collected at 1, 6, 12, 24, 36, 48 and 60 months and included MRI at 12 and 24 months, and fluoroscopy at 12, 24, 48 and 60 months. - 96% of patients returned for 1-month follow-up, 86% for 12-month follow-up, and 63% for 60-month. - A total of 180 patients (73%) had either 48- or 60-month follow-up data. - Out of the 180 patients with late follow-up, 177 (98%) had also immediate and 180 (100%) early follow-up data available for analysis. - Aortic imaging (either MRI, computed tomography, or angiography) was available for 180/180 (100%) at immediate follow-up, 177/180 (98%) at intermediate follow-up, and 41:180 (23%) at late follow-up. Fluoroscopy was available for 180/180 (100%) at immediate follow-up, 178/180 (99%) at intermediate follow-up, and 136/180 (76%) at late follow-up.	**Yes 1**	No 2
	Statistical analysis	- Categorical variables are summarized as frequencies and percentages, and continuous variables as either means and SDs or medians with interquartile range (IQR) as noted. For the entire cohort, the cumulative incidence of stents fractures, aortic wall injury, and reinterventions at immediate, early and late follow-up was estimated using the Kaplan-Meier method. Patients who did not have an outcome event were censored at time. Changes in hemodynamic measures over time were evaluated using tests of trend. For patients with late follow-up, associations between patient and procedure characteristics and 4 binary outcome variables – suboptimal hemodynamic outcome, stent fractur, catheter reintervention, and aortic wall injury – were assessed using Fisher exact test. Characteristics significant at the 0.20 level were considered for inclusion in multivariable logistic regression models. Forward selection was used, and P <0.05 was required for retention in the final model. To assess generalizability, characteristics of patients with and without late follow-up were compared using Fisher exact and Wilcoxon rank sum tests; no significant differences were found. All analytics were performed using SAS software version 9.4.	**Yes 1**	No 2
	Clinical significance	- Coarctation stenting is effective at maintaining obstruction relief up to 60 months postimplant with reduction in the number of patients requiring antihypertensive medication. However, an increase in-stent fractures and reinterventions were observed between medium and long-term follow-up. Covered stents appear to confer some protection from the development of stent fractures but do not provide complete protection from late aneurysm formation.	**Yes 1**	No 2
		Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (3) + Suitability (4) + Data Contribution (4) = 11	Disposition and Weighting (select)	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	Aortic Wall Injury: - 13 patients were identified as having aneurysms or pseudo-aneurysms (COAST: 6/121 [5%], COAST II: 7/127 [5.5%]. - No dissections were found. - The cumulative incidence was 1.2% by early and 6.3% by late follow-up. - In 3 patients, the aneurysm was proximal to the implanted stent, in one patient the location was not specified, and in the reminder, the aneurysm was within the borders of the implanted stent. - In 4 of 13 patients, aneurysms were identified on MRI or computed tomography before reintervention, while in 9 patients the aneurysms were diagnosed by angiography during catheterization performed for other reasons such as elective stent re-expansion. - 17 patients had covered stents implanted to treat the aneurysm; 2 did not. - By univariate analysis, coarctation minimum diameter <6mmm was the only factor significantly associated with aortic wall injury (12% versus 2%, P=0.007). - There was a borderline relationship between minimum stent to aortic diameter at the diaphragm <0.7 and aortic wall injury (19% versus 5%, M=0.059). - Aneurysms did not just occur in patients with bare metal stents, but equally in patients who had covered stents implanted. As such, the notion that covered stent implantation confers long-term protection from the development of aneurysm, may not be the case. Data are in contrast with Butera et al.[1] who did show a significant difference in the incidence of aneurysm formation when comparing patients bare versus covered stents, albeit in a much smaller cohort. Also, the median follow-up in that study was significantly longer for those with bare stents compared with covered stents (85 versus 35 months). This is important as the current study demonstrates that the majority of aneurysms were not identified until late follow-up. - Most aneurysms developed within the borders of the stent, including covered stents. One possible explanation is that pressure within the aorta distributes flow between the stent and the aortic wall, eventually leading to aneurysm formation. Another possibility is that the expanded polytetrafluoroethylene became damaged during initial implantation. - Current study did not investigate the benefit of a covered stent to reduce the risk of acute aortic wall injury during stent implantation because cases have not been randomly assigned and high-risk patients were excluded for bare stent implantation and received covered stents. Other Adverse Events: - Over the follow-up period, 2 patients had additional adverse events that were captured in the data set. One patient had a self-resolving neurological adverse event (possible transient ischemic attack) 2 weeks after the procedure without any clear relationship to the procedure itself. Another patient developed cardiogenic/sceptic chock 7 months after the procedure. No other serious adverse events were documented in any patients.

[1] Butera G, Manica JL, Marini D, Piazza L, Chessa M, Filho RI, Sarmento Leite RE, Carminati M. From bare to covered: 15-year single center experience and follow-up in trans-catheter stent implantation for aortic coarctation. Catheter Cardiovasc Interv. 2014 May 1;83(6):953-63. doi: 10.1002/ccd.25404. Epub 2014 Feb 4. PMID: 24459104.

Benefits/claims data	- At late follow-up, freedom from surgical intervention was 100%, catheter reintervention 78.7%, stent fracture 75.6%, and freedom from aortic wall injury 93.7%. - 44% of patients had suboptimal long-term hemodynamic outcomes. - It has documented that hemodynamic results are generally maintained over the follow-up period. Stent fractures, catheterization reinterventions, and aortic wall injuries, all increase in frequency between medium and long-term follow-up. Overed stents appear to confer some protection from the development of stent fractures, but they do not provide complete protection from late aneurysm formation.
Strengths	- The largest study to date with comprehensive follow-up data up to 60 months post-procedure.
Weaknesses/ Potential bias	- Small sample size - Did not have the statistical power to evaluate all parameters contributing to long-term morbidity in these patients, such as aortic wall injury. - Once the COAST studies were closed, it was not permissible to contact centers for additional data regarding stent fractures, indications for reintervention and other clinical data elements. - There were inherent differences between COAST and COAST II enrollment indications and the way some of the data was collected. - While this study defined 48 to 60 months follow-up as long-term, this is still a relatively short time period. - This study only analyzed the outcome of stent implantation for coarctation using CP stents. Ot did not compare the outcome of stent implantation to other treatment modalities, as was done in the Congenital Cardiovascular Interventional Study Consortium Report.[2]

State of the Art
Appraisal

Medical condition		Alternatives		Risk/benefit		Side-effects		Equivalence		Surrogate endpoints	
Yes 1	No 2	**Yes 1**	No 2	**Yes 1**	No 2	**Yes 1**	No 2	Yes 1	**No 2**	**Yes 1**	No 2

Overall SOA Appraisal and Disposition

SOA Grade (Range 6-12)	7	Disposition (select)	**Accepted, < 12** Excluded, 12

Relevant SOA Results

SOA data	CoA: - CoA is repaired during the neonatal period and infancy by surgery. Beyond infancy, percutaneous treatment using either balloon angioplasty or stent implantation are more frequently employed to treat native or recurrent coarctation. - The Cheatham-Platinum (CP) Stent was developed by NuMED (Hopkinton, NY) specifically designed to treat aortic

[2] Forbes TJ, Kim DW, Du W, Turner DR, Holzer R, Amin Z, Hijazi Z, Ghasemi A, Rome JJ, Nykanen D, Zahn E, Cowley C, Hoyer M, Waight D, Gruenstein D, Javois A, Foerster S, Kreutzer J, Sullivan N, Khan A, Owada C, Hagler D, Lim S, Canter J, Zellers T; CCISC Investigators. Comparison of surgical, stent, and balloon angioplasty treatment of native coarctation of the aorta: an observational study by the CCISC (Congenital Cardiovascular Interventional Study Consortium). J Am Coll Cardiol. 2011 Dec 13;58(25):2664-74. doi: 10.1016/j.jacc.2011.08.053. PMID: 22152954.

		coarctation. It has rounded edges to reduce the incidence of aortic wall injury and can be expanded to 24mm diameter. - Stent implantation, balloon angioplasty, and surgery are all treatment options for coarctation in patients beyond infancy. - Treated coarctation is associated with long-term morbidity irrespective of treatment strategy. COAST Trials: - The FDA pivotal trials COAST (Coarctation of the Aorta Stent Trial; 2007-2016) and COAST II (Covered Cheatham-Platinum Stents for Prevention or Treatment of the Aorta; 2010-2016) demonstrated safety and efficacy of the bare and Covered CP Stents when used to treat aortic coarctation. Short- and medium-term results have been previously reported (Meadows et al. *(48)* and Taggart et al. *(49)*). - The Covered CP Stent is a CP stent covered by a 0.28'' sleeve of 0.005'' thick expanded polytetrafluoroethylene tubing and was available to centers participating in the COAST trial for compassionate and emergency use for aortic wall injury occurring during aortic interventions. - COAST II included patients who received a Covered CP stent as an emergency or compassionate use during the initial COAST trial (legacy arm) and prospectively enrolled patients between 2010 and 2011. - COAST II included higher-risk groups, such as patients with aortic wall injuries and those with nearly atretic descending aorta of 3mm or less diameter.
	Comments	Hemodynamic Outcome: - Study corroborates the results from the largest multi-center study of stenting for coarctation from the Congenital Cardiovascular Interventional Study Consortium, which reported 23% systolic hypertension at 12 to 60 months of follow-up, 9% arm-leg blood pressure gradient ≥20 mm Hg, 23% need for antihypertensive medication and the presence of any of these 3 in 37%.[3] Stent Fractures: - Previous studies of the bare metal CP stent documented stent fractures of 2% at 12 months, and 12% at 24 months (Meadows et al. *(48)*). While the design and metallic composition of the CP stent may contribute, stents fractures are not limited to CP stents.[4] Boe et al.[5] reported a 21% fracture rate for Palmaz Genesis XD stents when used for coarctation therapy in children < 20Kg at a mean follow-up of 75 months. - It is unclear whether somatic growth can add additional force and loading conditions to the implanted stent, or whether participation in contact sports might impact the incidence of stent fractures. - Bare metal stents have a s significantly higher fracture rate than covered CP stent. Possible explanations could be that the struts of a bare stent become more solidly embedded into the aortic wall, and that the expanded polytetrafluoroethylene covering more equally distributes the radial force to multiple struts or that it reduces the transmission of aortic pulsability to the struts.

[3] Holzer R, Qureshi S, Ghasemi A, Vincent J, Sievert H, Gruenstein D, Weber H, Alday L, Peirone A, Zellers T, Cheatham J, Slack M, Rome J. Stenting of aortic coarctation: acute, intermediate, and long-term results of a prospective multi-institutional registry--Congenital Cardiovascular Interventional Study Consortium (CCISC). Catheter Cardiovasc Interv. 2010 Oct 1;76(4):553-63. doi: 10.1002/ccd.22587. PMID: 20882661.

[4] McElhinney DB, Marshall AC, Schievano S. Fracture of cardiovascular stents in patients with congenital heart disease: theoretical and empirical considerations. Circ Cardiovasc Interv. 2013 Oct 1;6(5):575-85. doi: 10.1161/CIRCINTERVENTIONS.113.000148. PMID: 24129934.

[5] Boe BB, Loccoh E, Stockmaster K, Holzer RJ, Cheatham SL, Cheatham JP, Armstrong A, Berman DP. Median and long-term outcomes of stent implantation for coarctation of the aorta in small patients (<20 kg). [Abstract presented at PICS 2019]. *J Struct Heart Dis. 2018;4:140.*

		Reinterventions: - Previously reported data documented transcatheter reinterventions of about 5% by 24 months follow-up (Meadows et al. *(48)*). - There is no expert consensus defining when a reintervention should be performed. - Reinterventions in this patient population are not unexpected and do not represent a poor outcome. Aortic Wall Injury: - Aneurysms did not just occur in patients with bare metal stents, but equally in patients who had covered stents implanted. As such, the notion that covered stent implantation confers long-term protection from the development of aneurysm, may not be the case. Data are in contrast with Butera et al.[6] who did show a significant difference in the incidence of aneurysm formation when comparing patients bare versus covered stents, albeit in a much smaller cohort. Also, the median follow-up in that study was significantly longer for those with bare stents compared with covered stents (85 versus 35 months). This is important as the current study demonstrates that the majority of aneurysms were not identified until late follow-up. - Most aneurysms developed within the borders of the stent, including covered stents. One possible explanation is that pressure within the aorta distributes flow between the stent and the aortic wall, eventually leading to aneurysm formation. Another possibility is that the expanded polytetrafluoroethylene became damaged during initial implantation. - Current study did not investigate the benefit of a covered stent to reduce the risk of acute aortic wall injury during stent implantation because cases have not been randomly assigned and high-risk patients were excluded for bare stent implantation and received covered stents.

[6] Butera G, Manica JL, Marini D, Piazza L, Chessa M, Filho RI, Sarmento Leite RE, Carminati M. From bare to covered: 15-year single center experience and follow-up in trans-catheter stent implantation for aortic coarctation. Catheter Cardiovasc Interv. 2014 May 1;83(6):953-63. doi: 10.1002/ccd.25404. Epub 2014 Feb 4. PMID: 24459104.

An overall summary of the clinical performance and safety:

A comprehensive, systematic, and critical evaluation of the pertinent clinical data and pre-clinical study data in relation to the Covered Stents has been carried out and documented in this report. Based on the results of this evaluation, it is considered that:

a) Conformity with relevant general safety and performance requirements set out in MDR Annex I under the normal conditions of the intended use of the device has been confirmed.
b) Undesirable side-effects and acceptability of the benefit-risk ratio have been evaluated and are acceptable according to the current knowledge/the state of the art in the medical fields concerned and according to available medical alternatives.
c) The information materials supplied by NuMED, and the risk reduction measures are adequate taking into account the intended purpose of the device.
d) Usability aspects have been adequately considered and the Covered Stents and NuDEL including the IFUs, is suitable for the intended users.
e) The claims foreseen in the information materials provided with the CER are adequate taking into account the intended purpose of the device.
f) The information materials supplied and the RM documentation for the device under evaluation are consistent with the clinical data and pre-clinical study data presented in this CER and with the current knowledge/state of the art.

Overall, it is concluded that the risks associated with the use of the Covered Stents and NuDEL are acceptable when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art; that the intended clinical performances are achieved by the device; and that known and foreseeable risks and undesirable side-effects are considered acceptable when weighed against the benefits from performance achieved by the device.

Ongoing planned post-market clinical follow-up:

The Delivery System Family has been on the market since 2015 in the EU and in other markets. Since then, the devices are likely to have been used in a variety of patients and populations. The Covered Stents that are part of the Delivery System have been on the market since 2004 in the EU and 1999 in other markets. Over time variants of the stents have been introduced to these markets. Since then, the devices are likely to have been used in a variety of patients and populations. The stents have been subjected to several clinical investigations where efficacy and safety has been demonstrated.

A PMCF study was initiated in 2015 for the NuDEL device, and then updated in 2018 for the additional indication that was added to the product line to determine if there were any new complications which were previously not addressed through actual clinical use, or if any new risks are introduced. The target study size was 59 patients, based on a confidence level of 95%. The study was conducted by issuing a form to the treating physician and collecting data. The results of this study are included in the clinical data that is used for the clinical evaluation.

6. Possible diagnostic or therapeutic alternatives

Alternative treatments for CoA include surgery or balloon angioplasty.

Alternative treatments for RVOT include surgery, transcatheter pulmonary valve replacement, or balloon valvuloplasty / angioplasty (to delay the need for replacement only).

7. Suggested profile and training for users

The Delivery System Family is intended for use by a Cardiac surgeon and/or interventionalist.

8. Reference to any harmonised standards and CS applied

There are no Common Specifications for this type of device.

The following harmonised standards are followed for this device:

- EN ISO 10993-10: 2023 – Biological Evaluation of Medical Devices – Part 10: Tests for Skin Sensitization
- EN ISO 10993-23: 2021 – Biological Evaluation of Medical Devices – Part 23: Tests for Irritation
- EN ISO 11135: 2014 / A1:2019 – Sterilization of health-care products – Ethylene oxide – Requirements for the development, validation and routine control of a sterilization process for medical devices.

- EN ISO 11737-1: 2018 / A1:2021 – Sterilization of medical devices – Microbiological methods – Part 1: Determination of a population of microorganisms on products
- EN ISO 13485: 2016 / A11:2021 – Medical devices – Quality management systems – Requirements for regulatory purposes
- EN ISO 14971: 2019 / A11:2021 – Medical Devices – Application of Risk Management to Medical Devices
- EN ISO 15223-1: 2021 – Medical devices – Symbols to be used with medical device labels, labelling and information to be supplied – Part 1: General requirements

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10. Revision History

SSCP revision number	Date Issued	Change Description	Revision validated by Notified Body
00	22 June 2022	Initial implementation	☐ Yes Validation Language: English ☒ No
01	06 July 2023	Updated sections 5, 7, 8, and 9 for CER Update.	☐ Yes Validation Language: English ☒ No

NuMED
Summary of Safety and Clinical Performance
SSCP – Delivery System

Document Revision: 01
Date issued: 06 July 2023

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device. The information presented below is intended for patients or lay person. A more extensive summary of its safety and clinical performance prepared for healthcare professionals is found in the first part of this document.

The SSCP is not intended to give general advice on the treatment of a medical condition. Please contact your healthcare professional in case you have questions about your medical condition or about the use of the device in your situation. This SSCP is not intended to replace an Implant card or the Instructions for Use to provide information on the safe use of the device.

1. Device identification and general information	
Device trade name(s)	NuDEL
Manufacturer's name and address	NuMED, Inc. 2880 Main Street Hopkinton, NY 12965 USA
Year when first certificate (CE) was issued	2015
Basic UDI-DI	08877141675TZ
2. Intended use of the device	
Intended purpose	The Delivery System is intended for implantation in the native and/or recurrent coarctation of the aorta. An aortic coarctation is a partial blockage or narrowing in the aorta, the body's main blood vessel distributing blood to all parts of the body. This blockage of the aorta makes the heart work harder to pump blood to your body and can weaken the heart muscle. Furthermore, this blockage can cause severe upper body hypertension (high blood pressure), increasing the risk of stroke. This blockage is present from birth. The Delivery System is also intended for treatment of right ventricle to pulmonary artery (right ventricular outflow tract) conduit disruptions that are identified during conduit pre-dilatation procedures performed in preparation for transcatheter pulmonary valve replacement. A Right Ventricular Outflow Tract (RVOT) is also known as a pulmonary conduit, and it is a tube that connects the heart to the lungs. Placement of an RVOT is typically associated in patients that have one of the following conditions: Pulmonary Atresia, Tetralogy of Fallot, or Double Outlet Right Ventricle. These three conditions can lead to pulmonary conduit failure.
Indications and intended patient groups	The device is used to treat any patients that have an aortic coarctation or RVOT conduit disruptions as long as none of the below listed contraindications and/or limitations are applicable.
Contraindications and/or limitations	The following patients should NOT receive the Stent: • Patients who are too small to allow the stent to pass through their arteries without damaging the artery; • Patients with a stiff aorta that does not get larger with balloon dilation. (CoA only) • Patients with blocked leg arteries making it difficult or unsafe to move the catheter and stent to the narrowed aorta; (CoA only) • Patients with any signs of infection;

	• Patients with active infection in the heart or blood vessels (endocarditis); • Patients with a known allergy to aspirin, other antiplatelet agents, or heparin; (CoA only) • Pregnancy.

3. Device description	
Description of the device	The covered stent portion of the NuDEL device is balloon expandable and intended to permanently stay in your body. The Covered CP Stent is used for coarctation of the aorta or treatment of right ventricle to pulmonary artery (right ventricular outflow tract) conduit disruptions that are identified during conduit pre-dilatation procedures performed in preparation for transcatheter pulmonary valve replacement (TPVR). The covering acts as a fluid barrier creating a fluid tight conduit through the stent length. Blood cannot flow across the covering. The NuDEL Delivery System consists of a balloon-in-balloon (BIB) catheter housed in a braided pebax sheath with an obturator tip at the distal end, and three extensions with luer fittings on the proximal end. The catheter is designed to accommodate a 0.035" guidewire through its inner lumen. The braided pebax sheath is either 12F or 14F in size. The Covered CP Stent is crimped onto the BIB catheter and covered by the retractable sheath. The sheath houses both the balloon catheter and the Covered CP Stent. The sheath has a hemostasis valve at the proximal end that minimizes blood loss around the inner catheter. The hemostasis valve has a flush port attached that allows for flushing of the system. The obturator tip is approximately 1.5cm in length and has a conical shape for easy introduction into the skin , and tracking to the delivery site. The proximal diameter of the obturator is sized to create a smooth transition from the sheath to the obturator. There are three extensions; one lumen for inflation of the inner balloon, one lumen for inflation of the outer balloon, and one lumen for the guidewire. The system is navigated through the venous from a femoral venous puncture to the delivery site over a guidewire. Once positioned, the sheath is retracted to expose the Covered CP Stent. The BIB balloons are inflated (inner first, outer last) to expand the Covered CP Stent. The balloons are deflated and the delivery system is removed from the patient. The Covered CP Stent is composed of heat treated 90% platinum/10% iridium wire that is arranged in laser welded rows with a "zig" pattern. The number of zigs in a row can be varied and will impact the strength of the stent as well as the eventual expanded diameter and percent stent shortening, while the number of rows will determine the unexpanded length of the stent. The Covered CP Stent has an ePTFE covering attached to the stent framework. This covering acts as a fluid barrier creating a fluid tight conduit through the stent length.
Medicinal Substances	The Delivery System does not contain any medicinal substances.
Mode of Action	The Delivery System is navigated through the venous from a femoral venous puncture to the delivery site over a guidewire. Once positioned, the sheath is retracted to expose the Covered CP Stent. The BIB balloons are inflated (inner first, outer last) to expand the Covered CP Stent. The balloons are deflated and the delivery system is removed from the patient and the stent stays in place.
Description of Accessories	There are no accessories used with the Delivery System.

4. Risks and Warning	
Contact your healthcare professional if you believe that you are experiencing side effects related to the device or its use or if you are concerned about risks. This document is not intended to replace a consultation with your healthcare professional if needed.	
How potential risks have been controlled or managed	The Delivery System Family has been developed in accordance with documented processes to ensure that it is designed, manufactured, packaged, and labelled in accordance with the current state of the art and meets all requirements of the appropriate regulations. Design verification activities were performed and include pre-clinical testing and clinical investigations. A clinical literature review has

	also been performed on the Delivery System Family as well as the associated Stent Device Family. All risks identified during these activities were mitigated as far as possible and are considered acceptable in regards to the clinical benefit of the device. Continued review of all Post Market Surveillance and Post Market Clinical Follow-up Data is performed to identify any additional risks that may be identified after the device was placed on the market.
Remaining risks and undesirable effects	Cardiac catheterization and stent insertion carry certain risks. Potential complications & adverse effects associated with device use and indication include: • Femoral Artery Injury, Thrombosis or Psuedoaneurysm • Stent Migration – movement of the stent away from original implant site • Stent Stenosis – growth of tissue within the stent, leading to return of the blockage • Stent Fracture – break in the frame of the stent • Aortic Aneurysm/Pseudoaneurysm – weakening or injury of the aorta wall • Vessel Rupture/Tear – perforation or tearing of the aorta, causing internal bleeding • Stent Malposition – poor position of stent, requiring a 2nd stent • Hematoma - bruising at the site where the device is introduced into the body • Sepsis/infection - infection • Thrombosis/Thromboembolism - formation or presence of a blood clot • Femoral artery occlusion - injury to artery used for implant, possibly requiring surgical repair • AV fistula formation - abnormal passageway between an artery and a vein • Transitory arrhythmia - irregular heartbeat • Endocarditis - infection within the stent • Bleeding - at the site of where the device is introduced into the body • Cell necrosis at the site of implant - death of cells at the implant site • Cerebrovascular Incident - stroke • Death
Warning and Precautions	The majority of warnings and precautions listed for the Delivery System pertain to the placement and use of the device in the cath. lab by the physician. MRI Conditional information is applicable to the stent portion of the device after it is implanted. This information should be used by any MRI technician that is performing an MRI procedure on any patient with a NuMED Stent implanted. All patients will be provided with an Implant Card after their procedure. This Implant Card will give the location of where to find the most up to date MRI parameters to be used for patients that have a NuMED Stent implanted.
Summary of any field safety corrective actions (FSCA including FSN) if applicable	There have not been any Field Safety Corrective Actions or Field Safety Notices on the devices in the Delivery System Family.

5. Summary of clinical evaluation and post-market clinical follow-up	
Clinical background of the device	The Delivery System Family has been sold globally since 2015. The covered stent portion of the device has been sold globally since 1999. The covered stent was tested and found to be safe and effective to repair aortic wall injuries and to widen the narrow part of the aorta related to coarctation of the aorta. A study was conducted with 82 patients weighing more than 31 lbs at the time of implant. Most of the patients (89%) were treated with one Covered CP stent, 11% needed more than one to complete the repair. On average arm systolic blood pressure was 25 mmHg higher than the leg pressure before the procedure. A reduction of a gradient to 15mmHg or less following the procedure suggests that the

	blockage is reduced effectively. By one month after covered stent placement the average arm pressure was only 1 mmHg higher than the leg pressure. Two years after implant, 85% of patients had arm blood pressures less than 15 mmHg above their leg pressure, which suggests that most of the treated aortas did not re-narrow. Repair of aortic wall injury was successful in all of the 49 patients who received their Covered CP Stent to repair their weakened aortic wall. An overview of complications and additional treatments provided after the stenting procedure is shown below: • Serious complications related to the Covered CP Stent or implant procedure, such as: causing injury to the aortic wall or damage to the leg artery used for Stent insertion, were identified in 6 out of 100 (6%) of patients within the first month of implant. • No patients needed surgery to repair the aorta or to remove the stent. • One patient required stent repair of the leg artery damaged during insertion of the implant catheter. • One patient required surgical repair of the leg artery damaged during insertion of the implant catheter. • 1 out of 20 (5%) patients developed small aneurysms (weakened areas of the aorta) in the area of stent placement in the years following stent therapy, making CT or MRI imaging an important part of follow up care. However, none of the patients who developed aneurysms demonstrated symptoms or required surgery. All were successfully treated with additional covered stent placement. • Overall, 16% of patients required repeat cardiac catheterization for a second dilation of the stent, mostly to keep up with the size of the patient as he/she grew and for some to repair aortic wall injuries as noted above. The covered stent was tested and found to be safe and effective to use as a Treatment of right ventricle to pulmonary artery (right ventricular outflow tract) conduit disruptions that are identified during conduit pre-dilatation procedures performed in preparation for transcatheter pulmonary valve replacement (TPVR). A study was conducted with 50 patients weighing an average of 58 kg. at the time of implant. Most patients (80%) were treated with one Covered CP stent. Out of 49 patients treated with the Covered CP Stent (CCPS), 81.6% of them had device and lesion success with no adverse events attributed to the CCPS. Out of 49 patients treated with the CCPS, 93.9% of the patients had successful coverage of conduit disruption followed by successful implantation of an artificial valve. An overview of complications and additional treatments provided after the stenting procedure is shown below: • Serious complications related to the CCPS or stent implant procedure, such as: stent embolization was identified in 1 out of 50 (2%) patients. • 7 (14%) of the patients required a second CCPS, and (3) 6% of the patients required a third CCPS during the procedure. Of these 10 patients, 4 (40%) of them planned on having the second CCPS implanted before the procedure.
The clinical evidence for the CE marking	The CE marking was based on data from three clinical studies, a review of published literature, and a review of post market surveillance data provided by NuMED. Additional pre-clinical testing was performed as part of the development and design of the device. In vitro (on the bench) testing was performed on the devices as part of the Design History File. Biocompatibility testing was also performed on the materials used to manufacture this device to determine if it met the requirements for an implant in the human body. The device passed all tests.
Safety	The clinical data and pre-clinical study data demonstrated that the device performed as intended by NuMED in the clinical setting; the device does not pose unacceptable safety concerns in the clinical setting; and any risks associated with clinical use of the device are acceptable when weighed against the benefits to the patient.

6. Possible diagnostic or therapeutic alternatives

When considering alternative treatments, it is recommended to contact your healthcare professional who can take into account your individual situation.

Coarctation of the Aorta

Your cardiologist believes that relief of the blockage is important for your health and safety. There are three ways to relieve the blockage: by surgery, by stent implantation without surgery, or by balloon angioplasty.

Surgical Therapy

Surgical treatment of the blockage is usually performed through an incision on the side of the chest, approaching the aorta by spreading the ribs. The narrowed portion of the aorta is removed and then the aorta is sewn back together. For more complicated coarctation, surgery might be performed from the front of the chest, opening the breast bone and using heart lung bypass. For some patients a benefit of a surgical approach is that the repair can be performed without the use of man-made materials. However, for other (especially adult) patients a man-made tube graft or patch may be needed. Please consult with your surgeon regarding his or her approach. For younger patients, surgery results in a lower need for a second procedure to keep up with growth when compared to balloon or stent therapy.

Risks of surgery include: pain from the surgical incision, prolonged fluid drainage from the chest after surgery, chest or wound infection, longer recovery time compared to stent therapy, prolonged postoperative rib discomfort and increased risk of very high blood pressure occurring after immediately after surgery, requiring intravenous therapy in an ICU, compared to stent repair. There is a low risk, probably less than 5%, of developing an aneurysm (weakened areas of the aorta) in the area of surgery in the years following stent therapy, making CT or MRI imaging an important part of follow up care.

Stent Therapy (without surgery)

A stent is an expandable metal tube that is implanted into your aorta to keep it open. Surgery is not required for this procedure. The stent is implanted using a thin hollow tube (catheter) with a balloon on the end. The catheter with stent is inserted through the artery in the upper leg. The balloon and stent are then moved to the appropriate position to the narrowed part of your aorta. Once in place, the balloons are inflated to expand the stent against the aortic wall. The catheter is then removed from the body and the stent remains in place.

Balloon Angioplasty

A specially designed catheter with a tiny balloon is carefully guided through the artery to the blockage, then inflated to widen the opening and increase blood flow to the heart.

RVOT

There are three ways to treat pulmonary conduit failure. One is a surgical conduit replacement, one is Transcatheter Pulmonary Valve Replacement, and the last is Balloon Valvuloplasty / Angioplasty.

Surgical Replacement:

Surgical replacement of a pulmonary valve conduit involves a physician removing the narrow or leaking conduit and replacing it with an artificial valve.

Transcatheter Pulmonary Valve Replacement:

An artificial valve is mounted on a thin hollow tube (catheter) with a balloon on the end, and is inserted into the artery in your upper leg. It is then advanced to the pulmonary conduit and the balloon inflated to place the new artificial pulmonary valve. The catheter is then removed from the body.

Balloon Valvuloplasty / Angioplasty:

A thin hollow tube (catheter) with a balloon on the end is inserted into the artery in your upper leg and advanced to the pulmonary conduit. The balloon is then inflated to a specified pressure to open your conduit so that the blood will flow better. The catheter is then removed from the body.

7. Suggested profile and training for users

The Delivery System Family is intended for use by cardiology and surgical professionals undertaking stent implantation.