NuMED
Summary of Safety and Clinical Performance
SSCP – Aortic PTV

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)	NuMED Aortic PTV Family Z-MED Z-MED II NuCLEUS NuCLEUS-X	
Model Number	NuMED Aortic PTV Family – Model 1150 Z-MED – Model 302.1 Z-MED II – Model 305.1 NuCLEUS – Model 230 NuCLEUS-X – Model 230X	
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	08877141150SQ	
Medical device nomenclature description / text	EMDN – C019014 – CARDIAC VALULOPLASTY CATHETERS	
Class of device	III	
Year when first certificate (CE) was issued	NuCLEUS – Aortic / Mitral (1998)	Z-MED – Pulmonary (1999) Z-MED – Aortic / Mitral (2013)
	NuCLEUS-X – Aortic / Mitral (2008)	Z-MED II – Pulmonary (1999) Z-MED II – Aortic / Mitral (2013)
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	Recommended for Percutaneous Transluminal Valvuloplasty (PTV) of aortic positions. The use of this catheter is particularly indicated in stenosis where difficulty in balloon positioning during inflation is experienced.
Contraindications and/or limitations	In addition to the standard risks associated with insertion of a cardiovascular catheter, the below contraindications apply: Contraindications for Aortic Balloon Valvuloplasty: • Aortic Stenosis • Moderate to Severe Aortic Valve Regurgitation The patient's medical condition could affect successful use of this catheter.

3. Device description	
Description of the device	The NuMED PTV Catheters are coaxial in construction. The inner and outer shafts are constructed of polyamide tubing. The x-line versions inner tubing is comprised of a multi-layer extrusion of polyamide that surrounds a braid of 304 LV Stainless Steel. All catheters feature a proximal end bifurcate with two distinct luminal passages. The inflation lumen terminates into a distally mounted balloon. This balloon is non-compliant. The balloon is designed to inflate to the diameter and length listed on the label at a specific pressure. Thus, it is recommended that the device be used in conjunction with a mechanism to monitor pressure, an inflation device with pressure gauge. The balloon size is ± 10 % at Nominal Pressure (NP) or Rated Burst Pressure (RBP) and the Rated Burst Pressure (RBP) is not to be exceeded. Catheters with NuCLEUS in the name feature a balloon with a waist. The balloon is designed with a waist formed into the middle of the balloon to allow accurate balloon placement and stability. Upon reaching a specified pressure, the waist will expand to the rated balloon diameter and dilate the valve to the rated diameter. The through lumen terminates at the tip of the catheter and will accept the passage of the appropriate guidewire. All catheter sizes will have radiopaque platinum marker band(s), centered or under the balloon shoulders to aid during placement. These devices are also designed to be used with an appropriately sized introducer and guidewire. The catheters are supplied sterile, by ethylene oxide gas, and are intended for single use only. The catheters are invasive and intended for transient use (continuous use of <60 minutes) on patients.
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, introducer, and an inflation device with pressure gauge.

4. Risks and Warning

Residual risks and undesirable effects	The clinical data, availability of guidelines from expert groups, established use of the device technology and the large numbers of devices sold demonstrate that there is high quality data of sufficient amounts to detect undesirable side-effects associated with the use of the PTV Catheters. Known and foreseeable clinical risks have been considered for the PTV Catheters in accordance with risk management (RM) procedure AP-346 and through the RM files for PTV Pulmonary Catheters and mitigated as far as possible (AFAP). Identified clinical residual risks/undesirable side-effects for the PTV Catheters are: Potential balloon separation following balloon rupture or abuse and the subsequent need to use a snare or other medical interventional techniques to retrieve the pieces. NOTE: There have been infrequent reports of larger diameter balloons bursting circumferentially, possibly due to the combination of tight focal strictures in large vessels. In any instance of a balloon rupture while in use, it is recommended that a sheath be placed over the ruptured balloon prior to withdrawal through the entry site. This can be accomplished by cutting off the proximal end of the catheter and slipping an appropriately sized sheath over the catheter into the entry site. For specific technique, refer to : tegtmeyer, Charles J., M.D. & Bezirdijan Diran R., M.D. "Removing the Stuck, Ruptured Angioplasty Balloon Catheter." Radiology, Volume 139, 231-232, April 1981. Potential complications and related adverse effects associated with the valvuloplasty catheter use include, but are not limited to: - Perforation - Conduction System Injury - Thromboembolic Events - Cardiovascular Injury - Balloon Rupture - Arrythmia Development - Valvular Tearing or Trauma - Restenosis Development - Inflammation - Infection - Cardiac Tamponade - Death - Valvular Regurgitation - Access Site Complications
Warning and Precautions	The following Warnings and Precautions have been identified and are called out in the Instruction for Use: **Warnings** • CAUTION: Do not exceed the RBP. An inflation device with pressure gauge is recommended to monitor pressure. Pressure in excess of the RBP can cause balloon rupture and potential inability to withdraw the catheter through the introducer sheath. • Catheter balloon inflation diameter must be carefully considered in selecting a particular size for any patient. The inflated balloon diameter should not be significantly greater than valvular diameter. The choice of the balloon size to be used for valve stenosis has been established by the VACA Registry to be approximately 0.9 to 1.0 times the valve annulus. It is important to perform an angiogram prior to valvuloplasty to measure the size of the valve in the lateral projection. • Balloons longer than 4cm are not recommended for children ≤ 10 years old. • Use only appropriate balloon inflation medium. Do not use air or gaseous medium to inflate the balloon. • This catheter is not recommended for pressure measurement or fluid injection. • Do not remove the guidewire from the catheter at any time during the procedure. • This device is intended for single use only. Do not resterilize and/or reuse it, as this can potentially result in compromised device performance and increased risk of cross-contamination.

	• The catheter should be used prior to the 'Use Before' date noted on the package label. • The catheter is intended for valvuloplasty applications only, and is not intended for angioplasty. • **THE CATHETER IS NOT INTENDED FOR USE WITH STENTS.** **Precautions** • Dilatation procedure should be conducted under fluoroscopic guidance with appropriate x-ray equipment. • Guidewires are delicate instruments. Care should be exercised while handling to help prevent the possibility of breakage. • Careful attention must be paid to the maintenance of tight catheter connections and aspiration before proceeding to avoid air introduction into the system. • Under no circumstances should any portion of the catheter system be advanced against resistance. The cause of the resistance should be identified with fluoroscopy and action taken to remedy the problem. • If resistance is felt upon removal, then the balloon, guidewire, and the sheath should be removed together as a unit, particularly if balloon rupture or leakage is known or suspected. This may be accomplished by firmly grasping the balloon catheter and sheath as a unit and withdrawing both together, using a gentle twisting motion combined with traction. • Before removing the catheter from the sheath it is very important that the balloon is completely deflated. • Proper functioning of the catheter depends upon its integrity. Care should be used 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 been (2) FSCAs for devices in the Aortic PTV Family. Both FSCAs were from the NuMED Canada, Inc. manufacturing location and both were for labeling issues. Both of these FSCAs were in 2011. No adverse events were reported for either of the FSCAs.

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

Summary of clinical data related to equivalent device:

NuMED has elected not to use the clinical data from an equivalent (clinical, technical, and biological characteristics) device(s). In the event there are devices considered equivalent, their data will be considered as similar devices.

Summary of clinical data from conducted investigations of the device :

1.	**Study name:**	
	Purpose: To establish the safety and effectiveness of the Tyshak and Z-MED models of the NuMED PTV Catheters, utilized for pulmonary valvuloplasty.	
	Clinical Study Methodology: Prospective study of 130 subjects (100 patients for the Tyshak model and 30 patients for the Z-MED model). ***Reference to the clinical study plan (and amendment) n°: IDE # G890030***	
	Investigation Sites: Dr Hugh Allen, Children's Hospital of Columbus Dr Ziyad Hijazi, New England Medical Center Dr Thomas Jones, Children's Hospital and Medical Center Dr Larry Latson, The Cleveland Clinic Foundation Dr Robert Morrow, Arkansas Children's Hospital Dr Michael Kuhn, Loma Linda University Children's Hospital Dr Donald Hagler, The Mayo Clinic Foundation Dr John Moore, Dupont Children's Hospital Dr Daphne Hsu, Columbia-Presbyterian Medical Center Dr Paul Seib, Arkansas Children's Hospital	***Reference to Document n°: IDE # G890030***

Dr John Cheatham, Children's Hospital of Omaha	

Patient Population: Patients with >50mmHg gradient resting state or >35mmHg gradient resting state with right ventricular hypertrophy on ECG and/or echo.

Inclusion Criteria:

- Any patient with a pulmonary valve gradient of >50mmHg, resting state
- Any patient with a pulmonary valve gradient of >35mmHg, resting state with right ventricular hypertrophy on ECG and/or echo
- Patients with isolated pulmonary valve stenosis
- Patients with pulmonary valve stenosis with other minor congenital heart disease that does not require surgical intervention

Exclusion Criteria:

- Patients with pulmonary valve gradient of <35mmHg, with normal ECG
- Other significant cardiac abnormalities (such as tetralogy of Fallot, supravalve pulmonary stenosis, or infundibular pulmonary stenosis) where dilatation may be achieved but will not result in a significant change in the gradient and therefore be of no value to the patient
- Patients with pulmonary valvar stenosis with major congenital heart defects that require open heart surgery
- Patients enrolled in any other study for investigational devices or drugs should not be enrolled in this study.

Clinical Study Results:

Purpose	Criteria	Results
Procedural Success	Valvular pressure difference reduced by ≥ 50% or reduced to ≤ 30 mmHg.	97% success rate (n=103); No deaths

Devices Used: Tyshak indicated for patients with non-dysplastic valves and Z-MED indicated for patients with dysplastic and/or calcified valves.

Conclusion: The devices were found to be safe and effective for use in valvuloplasty.

This study was conducted on the Z-MED catheter for Pulmonary Valvuloplasty. This device previously held this indication in the EU until the switch from the MDD to the MDR. At that point the pulmonary indication was dropped in the EU. The pulmonary indication is still applicable to both the U.S. and Canada.

Summary of clinical data from other sources:

The following is a summary of clinical data found during the literature review of the PTV Catheter Device Family:

<table>
<tr><th>Author</th><th>Results/Outcome</th><th>Clinical Application</th></tr>
<tr><td>Rodés-Cabau et al. 2008</td><td>

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

Safety & Performance Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective Registry	To evaluate the results of such a multidisciplinary PAVI program, focusing on patient and approach selection criteria, procedural results, and complications, as well as mid-term follow-up.	1	2	3	4	**5**

Suitability	Relevant Data	Grading		
Device	Z-MED (NuMED Canada, Inc.)	**D1**	D2	D3
Application	PAVI	A1	**A2**	A3
Patient	Patients with symptomatic severe aortic stenosis Sampling: n=22 Mean age: 84 ± 7 years Sex: 10 M; 12 F	**P1**	P2	P3
Report	High quality	**R1**	R2	R3
Suitability Grade (Range 4-12)		**5**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Procedural success	**Yes 1**	No 2
Follow-up	6 months	**Yes 1**	No 2
Statistical analysis	Qualitative variables are expressed as percentages and quantitative variables as mean ± SD or median (range). Comparisons of numerical variables were performed using Student's t test or Wilcoxon's rank-sum test depending on variable distribution. Differences were considered statistically significant at p values <0.05.	**Yes 1**	No 2
Clinical significance	Procedural success was defined as the implantation of a functioning prosthetic valve within the aortic annulus at the end of the procedure without in-laboratory mortality.	**Yes 1**	No 2
Data Contribution Grade (Range 4-8)		**4**	

</td><td>

Population: Patients with symptomatic severe aortic stenosis

Sampling: n=22

Mean age: 84 years

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Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	**LOE (5) + Suitability (5) + Data Contribution (4) = 14**	**Disposition and Weighting (select)**	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Objective: Evaluate the feasibility and initial results of a multidisciplinary percutaneous aortic valve implantation program.
Method: Patients identified for percutaneous aortic valve implantation underwent BAV prior to valve implantation.
Relevant Results:

Criteria	Results	P value
Procedural success	91%	NA
Procedural and 30 day mortality	4.3% and 8.7% respectively	NA
Mean aortic gradient	Reduced from 34±10mmHg to 9±3mmHg	P<0.001
Mean aortic valve area at follow up	Increase from 0.63±0.18 cm^2 to 1.45±10 cm^2	NA

Safety concern:

Criteria	Results	P value
Adverse Events	3 significant procedural complications reported; n=1 severe aortic regurgitation rectified with a second valve implantation, n=1 periprocedural cardiac tamponade treated with pericardiocentesis, n=1 myocardial apical tear and severe bleeding after left ventricular sheath removal requiring surgical repair of ventricular apex under femoral-femoral cardiopulmonary bypass. One patient died on day 29 due to pneumonia. Paravalvular aortic regurgitation was present in 13 patients (1+ in 9 patients, 2+ in 4 patients).	NA

Conclusion: The study demonstrates safety and efficacy of the Z-Med catheter when used for BAV of severe aortic stenosis prior to aortic valve implantation.
Device used: Z-Med

Mentias et al. 2016

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

Safety & Performance Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective cohort study	To determine the outcomes in patients with high-risk symptomatic AS with sever or very severe COPD referred for multispecialty evaluation by a high-risk	1	2	3	**4**	5

Population: Patients with severe aortic stenosis and severe chronic obstructive pulmonary disease

Sampling: n= 131; patients treated with balloon aortic valvuloplasty n=29

Mean age (BAV Group): 76.2 years

		AVR team and who ultimately decided to undergo TAVR, SAVR, BAV, or continued medical therapy.					

Suitability	Relevant Data	Grading		
Device	Z-med II	**D1**	D2	D3
Application	BAV	**A1**	A2	A3
Patient	Patients with severe aortic stenosis and severe chronic obstructive pulmonary disease Sampling: n=131; n=29 (BAV group) Mean age: 78.8 ± 7.4 years (BAV group) Sex: 44.8% M (BAV group)	**P1**	P2	P3
Report	High quality	**R1**	R2	R3
Suitability Grade (Range 4-12)		**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	All-cause mortality	**Yes 1**	No 2
Follow-up	Median 3.0 ± 1.5 years	**Yes 1**	No 2
Statistical analysis	Continuous variables are expressed as mean ± standard deviation, or median and interquartiles for skewed distributions, and compared using the Student t test or ANOVA (for normally distributed variables) or the Wilcoxon test (for nonnormally distributed variables). Categorical data are expressed as a percentage and compared using Fisher exact or chi-square test. To assess outcomes, Cox proportional hazards analysis was performed to assess independent predictors of outcome (using $P < 0.05$ for statistical significance). Hazard ratios (HRs) with 95% confidence intervals were calculated and reported. Cumulative proportion of events as a function over time was obtained by the Kaplan-Meier method to do the survival analysis.	**Yes 1**	No 2
Clinical significance	Cardiavascular death	**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

Objective: Determines the outcomes in patients with high-risk symptomatic AS with severe or very severe chronic obstructive pulmonary disease (COPD) referred for multispecialty evaluation by a high-risk aortic valve replacement team and who ultimately were decided to undergo TAVR, SAVR, BAV, or continued medical therapy.
Method: Patients were evaluated and were divided retrospectively into 4 groups: 1—medical management, 2—balloon aortic valvuloplasty, 3—SAVR, and 4—TAVR. Baseline, clinical, and echo data were recorded. Primary outcome was cardiovascular death. Patients who were deemed inoperable or high risk
and did not undergo TAVR due to peripheral arterial disease, annulus size, unclear contribution of AS to functional decline owing to comorbid conditions, or patient desire underwent BAV.

Relevant Results:

Criteria	Results	P value
Cardiovascular death at 3 year follow up	87%, 97%, 47.7% and 51.8% of patients in groups 1-4 respectively	P<0.0001

Safety concern:

Criteria	Results	P value
Adverse Events	Heart failure, respiratory failure, and COPD exacerbation leading to hospital readmissions within 30 days occurred in 43%, 42%, 9.6% and 14.8% of patients in groups 1-4, respectively.	P=0.016

Conclusion: TAVR is similar to S for patients with severe AS and severe or very severe COPD regarding long-term survival and offers shorter hospital stay with less postoperative respiratory complications.
Device used: Z-Med II

Pedersen et al. 2014

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

Safety & Performance Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective study with matched control group	To report initial experience with BAV using the V8 balloon compared to cylindrical balloons	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	Z-med and Z-Med II	**D1**	D2	D3
Application	BAV	**A1**	A2	A3
Patient	Patients with symptomatic severe AS. Sampling: n=40; n=20 using cylindrical balloons and n=20 using V8 balloon Mean age: 85.5 ± 6.8 years (for matched controls) Sex: 14 M; 6 F (for matched controls)	**P1**	P2	P3
Report	High quality	**R1**	R2	R3
Suitability Grade (Range 4-12)		**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Aortic Valve Area and Aortic insufficiency	**Yes 1**	No 2
Follow-up	1 month	**Yes 1**	No 2
Statistical analysis	Descriptive statistics are displayed as means and SDs for continuous variables; number and percentage with characteristics are given for categorical variables. Categorical variables were analyzed using Pearson's ch-square or Fisher's exact tests, continuous variables using Student's T-test. A value of P<0.05	**Yes 1**	No 2

Population: Patients with symptomatic severe AS.

Sampling: n=40; n=20 using cylindrical balloons and n=20 using V8 balloon

	was considered significant.		
Clinical significance	Change in AVA	**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

Objective: Reports experience with an hour glass shaped balloon compared to a cylindrical balloon when used for BAV. An hour glass shaped balloon was designed to better conform to the aortic valve anatomy, having proximal and distal bulbous segments separated by a persistently narrowed waist to permit enhanced fixation better leaflet opening without annular compromise.
Method: Patients undergoing BAV with a V8 balloon were compared to a propensity matched group which used cylindrical balloons for BAV. Transthoracic echocardiographic imaged were obtained within one month pre-operatively and 72 hours postoperatively. Change in aortic valve area and aortic insufficiency were obtained from echocardiographic studies.
Relevant Results:

Criteria	Results	P value
Aortic valve area	Echocardiographic increase from baseline to post-procedure tended strongly in favor of the V8 balloon over cylindrical group Mean 0.30 ± 0.23 cm^2 vs. 0.17 ± 0.21 cm^2	P=0.063
Clinical outcomes	No significant increase in aortic insufficiency in either group.	N/A

Safety concern:

Criteria	Results	P value
Adverse Events	One patient in each group required a temporary pacemaker for transient AV block at time of transfer from cardiac catheterization lab to the floor. Procedural mortality occurred in 1 patient in the cylindrical balloon group.	NA

Conclusion: The study suggests that larger AVAs may be obtained using the novel hour glass balloon in comparison to the standard cylindrical balloons in patients with calcific AS. The authors did not see a greater incidence of atrioventricular conduction disorder, need for permanent pacemaker, change in aortic insufficiency or major adverse event.
Device used: Z-Med and Z-Med II

Olasinska-Wisniewska et al. 2016

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

Safety & Performance
Appraisal

Level of	Study	Question Applied	Oxford LOE

Evidence	Method/Design		2011				
	Retrospective review	To retrospectively analyze the indications and short-term outcomes of BAV, not directly associated with TAVI, since that procedure was launched in our institution.	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	Numed Z-Med II-X	**D1**	D2	D3
Application	BAV	**A1**	A2	A3
Patient	Patients with advanced hemodynamically unstable heart failure (HF) including cardiogenic shock Sampling: n=25 Mean age: 72 ± 11.4 years Sex: 6 M; 19 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 maximal transaortic gradient	**Yes 1**	No 2
Follow-up	Median = 20.5 ± 11.4 months	**Yes 1**	No 2
Statistical analysis	Continuous variables were reported as mean and standard deviation. For nonparametric data, the nonparametric Mann-Whitney test was used for continuous variables. Discrete variables were reported as counts or percentages. P values less than 0.05 were considered statistically significant.	**Yes 1**	No 2
Clinical significance	50% reduction in maximal transaortic gradient	**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

Objective: To retrospectively analyze the indications and short-term outcome of BAV, not directly associated with TAVI.
Method: Retrospective review of patients who underwent BAV
Relevant Results:.

Criteria	Results	P value
In-hospital mortality	N=5 (20%)	N/A
50% reduction in peak transaortic gradient	Obtained in all patients who survived procedure	N/A

Safety concern:

Criteria	Results	P value
Adverse Events	In-hospital mortality was 20%. Other major complications included permanent pacemaker implantation (n=2), major vascular complications (n=4) (one patient required bailout vascular surgery), and cardiac tamponade in one patient. There were no	NA

	patients who required conversion to cardiac surgery.	

Conclusion: Short-term results are good with relatively low mortality and morbidity related to the procedure.
Device used: Z-Med II-X

Witzke et al. 2010

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

Safety & Performance
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective review	To evaluate the clinical and hemodynamic impact of RP in high-risk patients undergoing elective BAV for severe calcific AS.	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	Z-Med (NuMed Inc)	**D1**	D2	D3
Application	BAV	**A1**	A2	A3
Patient	Patients with severe AS undergoing BAV Sampling: n=111 Mean age: 82 ± 8.1 years Sex: 49 M; 62 F	**P1**	P2	P3
Report	High quality	**R1**	R2	R3
Suitability Grade (Range 4-12)		**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Composite of hospital death, peri-procedural myocardial infarction, cerebrovascular accident (CVA), and need for cardiopulmonary resuscitation (CPR)	**Yes 1**	No 2
Follow-up	Not Stated	**Yes 1**	No 2
Statistical analysis	Categorical variables were compared by chi-square analysis, or Fisher's exact test when appropriate. Continuous variables were compared by Student's t-test. Stratified analyses were performed to evaluate RP in four prespecified subsets of patients.	**Yes 1**	No 2
Clinical significance	Comparison between RP and no-RP	**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

Populations: Patients with severe AS undergoing BAV

Sampling: n=111

M/F: 49/62
Mean age: 82 years

			Excluded, 22-25

Objective: Evaluates the immediate results and in-hospital adverse events in patients with severe AS undergoing BAV with and without RP.
Method: Patients who underwent BAV with RP (n=64) were compared to those who did not receive RP during BAV (n=47). Procedural outcomes, complications, and in-hospital adverse events were compared between both groups.
Relevant Results:

Criteria	Results	P value
Aortic valve area	Mean increased from 0.64cm^2 pre-procedure to 0.87 cm^2 in the RP group and 1.02 cm^2 in the no RP group.	P=0.02
Procedural success	There was a strong trend toward fewer successful valvuloplasties in the RP group compared to the no-RP group (67.2% vs. 82.9%)	P=0.06

Safety concern:

Criteria	Results	P value
Adverse Events	Intraprocedural complications - 1 death in RP group. 2 patients in the no-RP group developed tamponade. Cardiopulmonary resuscitation n=10 in both groups. In-Hospital complications included: n=8 acute renal injury n=6 myocardial infarction and n=9 deaths (including the Intraprocedural death). In the RP group, there were 4 deaths; 2 due to progressive heart failure, 1 due to pulmonary infection and 1 from a pulseless electrical activity arrest just prior to discharge. In the no-RP group, there were 4 deaths; 2 due to septic shock not related to BAV and 2 due to progressive heart failure. The in-hospital mortality rate was similar in both groups. Access site complications included: n=5 pseudo aneurysm, n=9 severe bleeding, n=1 arterio-venous fistula and n=12 composite vascular complications.	NA

Conclusion: BAV using RP is feasible and safe. It offers greater balloon positioning and stability during inflation without affecting the incidence of in-hospital adverse events. However, the clinical benefit may be outweighed by a less increase in aortic valve area.
Device used: Z-Med balloon

Boland et al. 2014

Safety & Performance Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective study	To compare differences in procedure time, fluoroscopy time and dose-area product (DAP) between single-vessel percutaneous coronary intervention (standard PCI) and various SHIs	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	NuCLEUS (NuMED, Inc.)	**D1**	D2	D3
Application	BAV	**A1**	A2	A3
Patient	Patients undergoing standard percutaneous coronary intervention and structural heart	**P1**	P2	P3

Population: Patients undergoing standard percutaneous coronary intervention and structural heart interventions including BMV and BAV procedures

Sampling: N=385; n=49 for

	interventions including BMV and BAV procedures Sampling: n=385; n=57 for BAV Mean age: 84.3 ± 6.6 years for BAV Sex: 30 M; 27 F for BAV				BMV and n=57 for BAV
Report	High quality	**R1**	R2	R3	
Suitability Grade (Range 4-12)		**4**			

Data Contribution	**Relevant Data**	**Grading**	
Outcomes/Endpoints	Fluoroscopy time Procedure time DAP	**Yes 1**	No 2
Follow-up	Not stated	**Yes 1**	No 2
Statistical analysis	We compared proportions using the $\chi 2$ test, and means using a two sample t-test for normally distributed data. Normality of the variables was tested using a normal probability plot and by comparing a histogram of the sample data with a normal probability curve. For data that did not conform to a normal distribution, medians were compared using the Wilcoxon Rank Sum test for non-normally distributed data.	**Yes 1**	No 2
Clinical significance	Median case times, fluoroscopy times and DAP increased with increasing PCI complexity. There was significant variability and spread in case time, fluoroscopy time and DAP for both SHI and PCI.	**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

Objective: Compared differences in procedure time, fluoroscopy time and dose-area product (DAP) between single-vessel percutaneous coronary intervention (standard PCI) and various structural heart interventions.
Method: The authors compared data from 91 consecutive single-vessel percutaneous coronary interventions, 69 patent foramen ovale closures, 25 atrial septal defect closures, 49 percutaneous transluminal mitral valvuloplasties, 57 balloon aortic valvuloplasties, 53 trans-catheter aortic valve implantations (TAVI), 21 left atrial appendage occlusions and 7 MitraClip procedures.
Relevant Results:

Criteria	**Results**	**P value**
Fluoroscopy and dose-area product	BMV - 14.3, 11.4-24.2 minutes; 37.4, 19.8-87.0 $Gycm^2$ BAV - 8.4, 5.2-13.2 minutes; 19.8, 10.2-30.0 $Gycm^2$ Median dose –area product (DAP) was less than standard PCI for BMV and BAV.	NA

Conclusion: For structural heart interventions, dose-area product was not significantly greater than for coronary angiography with single-vessel percutaneous coronary artery intervention. This should be reassuring to patients and staff attending prolonged structural heart interventions.
Device used: BMV – Inoue balloon and BAV – NuCLEUS balloon

Ussia et al. 2011

Safety & Performance Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	3 Case studies	N/A - Presentation of findings to allow operator to prevent and diagnose cusp perforation at each step	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	Tyshak and NuCLEUS	**D1**	D2	D3
Application	BAV	**A1**	A2	A3
Patient	Patients undergoing BAV prior to transcatheter aortic valve implantation Sampling: n=3 Mean age: 83 years Sex: 2 M; 1 F	**P1**	P2	P3
Report	High quality	**R1**	R2	R3
Suitability Grade (Range 4-12)		**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Cusp perforation	**Yes 1**	No 2
Follow-up	Not Stated	**Yes 1**	No 2
Statistical analysis	N/A	Yes 1	**No 2**
Clinical significance	Not stated	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 (4) + Data Contribution (6) = 14	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Objective: Presents clinical scenarios and important findings that allow the operator to prevent and diagnose cusp perforation at each step of the BAV/TAVI and take appropriate steps to correct the problem before initiating the next step in the procedure.
Method: NA
Relevant Results: Article provides information on a procedural complication during BAV. Cusp perforation was suspected during BAV 1) due to high resistance encountered when a catheter was advanced over a SSA wire into the left ventricle and subsequent difficulty of manipulation of the wire, 2) based on the difficulty in positioning the balloon catheter and unusual behavior on inflation and deflation.
Safety concern:
The most common complication of a cusp perforation is acute severe regurgitation, and the worst is an implant failure.
Conclusion: Perforation of an aortic cusp during attempts to cross a stenotic aortic orifice should be suspected if unusual resistance to crossing and difficulty is encountered at any stage of the procedure. The use of TEE and multi-slice computed tomography helps in identification of valvar anatomy that can predispose to this complication as well as aid in early diagnosis when it is feasible to use TEE intra-procedurally. A high index of clinical suspicion and indirect signs should be kept in mind during the procedure to enable an early

Population: Patients undergoing BAV prior to transcatheter aortic valve implantation

Sampling: n=3

diagnosis and remediation.
Device used: Z-Med, Tyshak

Babaliaros et al. 2010

Safety & Performance
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective study	To describe the use of BAV to select proper THV size	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	Z-MED (NuMED, Inc.)	**D1**	D2	D3
Application	BAV	**A1**	A2	A3
Patient	Patients undergoing implantation of THV for aortic stenosis Sampling: n=27 Mean age: 83 years (range: 66-95) Sex: 13 M; 14 F	**P1**	P2	P3
Report	High quality	**R1**	R2	R3
Suitability Grade (Range 4-12)		**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Annulus size Aortic insufficiency	**Yes 1**	No 2
Follow-up	N/A	**Yes 1**	No 2
Statistical analysis	Comparison of aortic insufficiency and annulus size were performed using a paired t test. Differences were considered statistically significant at a value of $p < 0.05$. All values were expressed as mean ± SD.	**Yes 1**	No 2
Clinical significance	Not Stated	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

Objective: Aims to describe the use of BAV to select proper transcatheter heart valve (THV) size.
Method: Patients underwent dilatation of the aortic valve and sizing of aortic annulus by BAV and transeosophageal echocardiogram (TEE). The minimal THV size that was greater than the annulus measured by BAV was implanted.
Relevant Results:

Criteria	Results	P value
Annulus measurement	Measured by TEE was 21.3±1.6 mm and by BAV was 22.6±1.8 mm. Annulus measurement by BAV was most helpful in selecting THV's in 7 patients (26%) with TEE annulus considered borderline.	P<0.001

Safety concern:

Criteria	Results	P value
Adverse Events	No patient experienced coronary occlusion, annular damage, or THV embolization.	NA

Population: Patients undergoing implantation of THV for aortic stenosis

Sampling: n=27

M/F: 13/14
Mean age: 83 years

Conclusion: BAV sizing of the aortic annulus is safe and is an important adjunct to TEE when selecting THV size. Implanting the minimal THV greater than the BAV annulus size resulted in no adverse events. These data suggest that the use of BAV for THV selection may improve the safety and efficacy of THV implantation. No adverse consequences of THV oversizing (annular disruption, vagally mediated hypotension secondary to annular stretch, coronary occlusion) or under sizing (THV embolization or PVL greater than grade 1) occurred using this method.
Device used: Z-Med balloon

Kozor et al. 2014

Safety & Performance
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Case report	N/A – Describes rare complication of percutaneous aortic valvuloplasty balloon rupture	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	NuCLEUS-X (NuMED Canada)	**D1**	D2	D3
Application	BAV	**A1**	A2	A3
Patient	Patient undergoing palliative BAV for symptomatic heavily calcified severe aortic valve stenosis Sampling: n=1 Mean age: 86 years Sex: 1 F	**P1**	P2	P3
Report	High quality	**R1**	R2	R3
Suitability Grade (Range 4-12)		**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Balloon Rupture	**Yes 1**	No 2
Follow-up	Not Stated	**Yes 1**	No 2
Statistical analysis	N/A	Yes 1	**No 2**
Clinical significance	Teh patient made a full recovery will no sequele.	**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

Objective: Describes the rare complication of percutaneous aortic valvuloplasty balloon rupture with subsequent mass micro-bubble embolism and hemodynamic collapse.
Method: NA
Relevant Results:

Criteria	Results	P value
Peak aortic pressure gradient	After use of second balloon dilatation, improved to 49 mmHg	NA
Mean pressure gradient	After use of second balloon dilatation, improved to 29 mmHg	NA

Safety concern:

Population: Patient undergoing palliative BAV for symptomatic heavily calcified severe aortic valve stenosis

Sampling: 86 year old female

Criteria	Results	P value
Adverse Events	Upon first balloon inflation, there was sudden balloon rupture. This was associated with the release of mass micro-bubbles into the left heart, new onset left bundle branch block on surface electrocardiogram, and subsequent hemodynamic collapse. There was severe LV dysfunction with marked hypokinesis of the LV inferior wall, septum and posterior walls, with micro-bubbles seen throughout these regions of myocardium. Once the patient was stabilised a second dilatation with a new balloon was performed without complication. Cause of balloon rupture has been thought to be caused by heavy valve calcification tearing the balloon, and the hemodynamic collapse was as a result of micro-bubbles causing coronary air embolization and acute myocardial ischemia with subsequent severe LV dysfunction.	NA

Conclusion: This case serves as a cautionary reminder that despite routine standard preparation and technique balloon rupture during BAV can still occur.
Device used: Nucleus-X

Mozumdar *et al.* (2018)

Safety & Performance Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective cohort study	Comparison of the acute efficacy and safety of anterograde versus retrograde catheter approaches in the management of neonates with aortic stenosis	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	Tyshak (NuMED, Inc.), Symmetry (Boston Scientific), Sterling & Talon	**D1**	D2	D3
Application	BAV	**A1**	A2	A3
Patient	Neonates (age ≤ 30 days) with valvar aortic stenosis Sampling: n=42 [n=13 (42%) Tyshak] Mean age: 4 days (range 1-29 days) Sex: 32 M; 10 F	**P1**	P2	P3
Report	High quality	**R1**	R2	R3
	Suitability Grade (Range 4-12)	**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Procedural time and change in gradient	**Yes 1**	No 2
Follow-up	Long-term (not stated)	**Yes 1**	No 2
Statistical analysis	Standard descriptive statistics were used to summarize the data using mean ± standard deviation for normally distributed continuous variables, median with range for skewed continuous variables, and count with percentage of total for categorical variables. Assessment of differences between the two approaches was evaluated using either t test, Wilcoxon rank-sum, Chi-square, or Fisher's exact test, as appropriate. Statistical significance was set at a two-tailed alpha less than 0.05. All statistical analyses were performed using STATA v10 (Stata Corp., College Station, TX).	**Yes 1**	No 2
Clinical significance	Not stated	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	Complications during the procedure were rare and included one patient in the retrograde group with supraventricular tachycardia, and one in the anterograde group with two episodes of ventricular fibrillation. The patient in the anterograde group experienced an episode of ventricular fibrillation during initial attempt to cross the atrial septum, and the second episode occurred as the catheters were being pulled from the left ventricle. The patient was appropriately defibrillated with resolution. There were no procedural mortalities. Femoral artery thromboses developed in 19 patients (61%) in the retrograde group and 2 patients (18%) in the anterograde group, p = 0.014. 62% of all cases resolved prior to hospital discharge.
Performance data	The anterograde and retrograde approaches were equally efficacious in gradient reduction, and there was no difference in procedural times.
Benefits/claims data	Both anterograde and retrograde approaches to neonatal BAV have equal acute efficacy with no observed difference in post-intervention AI and MR. The anterograde approach, when possible, avoids the use of a larger catheter in the femoral artery, which may reduce the risk of arterial thrombosis.
Strengths	None Stated
Weaknesses/ Potential bias	This study was limited by its retrospective design and small sample size. The sample size precluded the ability to adjust for cofounding factors. However, this potential limitation is mitigated by the lack of significant differences between the two treatment groups on baseline factors. Some data were not available, notably complete assessment of post-intervention mitral regurgitation.

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	In many centers, BAV is the intervention of choice in neonates requiring treatment for aortic stenosis. Since its introduction in 1984, BAV has become an effective alternative to surgical valvotomy in reducing the severity of valvar aortic stenosis. Recent studies show that BAV may confer a higher risk of re-intervention, but benefits of the procedure may include a shorter hospital stay and decreased morbidity.
Comments	None

Yamen *et al.* (2010)

Safety & Performance
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective review of medical records	To determine the safety and immediate efficacy after BAV with a new, low-profile balloon	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	Tyshak	**D1**	D2	D3

Application	BAV	**A1**	A2	A3
Patient	Patients with severe aortic stenosis Sampling: n=20 Mean age: 79 ± 12 years Sex: 11 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	Transaortic gradients and AVAs	**Yes 1**	No 2
Follow-up	7.3 ± 6.7 months	**Yes 1**	No 2
Statistical analysis	Values are expressed as mean ± standard deviation. Categorical variables were compared using Fisher's exact test. Continuous variables were compared using paired or unpaired Student's t-test, as appropriate. SPSS version 15 software was used for statistical analyses	**Yes 1**	No 2
Clinical significance	Procedural success was defined as a decrease in invasively measured transaortic gradient to <40 mm Hg	**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	There was one in-hospital death that occurred in an 88-year-old patient on post-procedure day 28; the patient had been fed via a percutaneous gastrostomy and the cause of death was respiratory failure after aspiration. There were no major vascular complications. The mean hemoglobin concentration fell from 11.4 ± 1.6 pre-procedure to 10.5 ± 1.3 g/dL after (P = 0.022). One patient, with a baseline hemoglobin concentration of 9.9 g/dL, was semi-electively transfused two units of red blood cells after BAV; no access site bleeding was evident and subsequently the hemoglobin remained stable at 11.4 g/dL. One patient developed complete heart block during the BAV necessitating placement of a permanent pacemaker at day 3. In one patient the balloon ruptured and upon removal of the catheter, the balloon portion was sheared off. This was successfully removed with a snare device and no clinical sequelae. The mean severity of AR was not significantly different before and after BAV (P = 0.72). One patient had increase in AR severity from 2+ to 2-3+, but had no clinical sequelae from this. None of the patients developed severe AR after BAV.
Performance data	The mean gradient, measured by catheterization and echocardiography, decreased significantly (15 ± 9 and 21 ± 14 mm Hg, respectively; P < 0.001), with a corresponding significant increase in the calculated AVA (0.26 ± 0.17 and 0.23 ± 0.14 cm^2, respectively; P < 0.001). After BAV, mean NYHA class fell from 3.5 ± 0.7 to 2.7 ± 0.8 (P < 0.001).
Benefits/claims data	The use of a compliant valvuloplasty balloon for retrograde BAV is technically feasible and achieves acceptable hemodynamic and symptomatic results with a low rate of access site complications. This technique should be considered for patients with severe AS who are not candidates for traditional surgical AVR, do not yet have access to TAVR or as a bridging procedure to reduce the risk of noncardiac surgery.
Strengths	None Stated
Weaknesses/ Potential bias	The retrospective nature as well as the lack of a control group mean that we could make no direct comparison with traditional BAV using compliant balloons. However, our cohort had similar comorbidities and risk profiles to other recent series. Lack of routine late echocardiographic follow-up means that the durability of the hemodynamic response following BAV could not be examined in detail.

Ford *et al.* (2017)

Safety & Performance
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective review of clinical and procedural notes	To report experience with BAV focusing on indications, procedural success and 30-day outcomes	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	NuCLEUS-X (NuMED, Inc.) or Cristal (Balt)	**D1**	D2	D3
Application	BAV	**A1**	A2	A3
Patient	Adult patients with severe symptomatic aortic stenosis Sampling: n=51 patients underwent n=55 procedures [n=20 (36.4%) NuCLEUS-X; n=35 (63.6%) Cristal] Mean age: 88 ± 5.7 years Sex: 11 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	Procedural success	**Yes 1**	No 2
Follow-up	30 days	**Yes 1**	No 2
Statistical analysis	Analyses were performed using SPSS (V.22 SPSS, Chicago, IL, USA). Results were reported as mean (Standard deviation) for continuous variables; and counts (percentages) were reported for categorical variables. After confirming non-Gaussian distribution, paired sample Wilcoxon rank tests were applied to echocardiographic and haemodynamic variables before and after BAV.	**Yes 1**	No 2
Clinical significance	Procedural success was defined by at least one balloon inflation with a measured reduction in the invasively measured gradient across the aortic valve without occurrence of a major intraprocedural complication.	**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	Three patients (5.5%) required permanent pacemaker for conduction disease (bradycardic arrest and complete AV dissociation). Periprocedural ventricular arrhythmias occurred in two cases (3.9%) with successful resuscitation to discharge in one of these patients. No major vascular access site or access-related complications occurred, however, six patients (10.9%) had minor vascular complications of groin haematoma with blood transfusion (≤2 units) during the hospital admission. No patients had a stroke, myocardial infarction, tamponade or developed new severe AR during 30-day follow-up. Two patients (3.6%) had worsening of pre-existing AR to the moderate-severe range.
Performance data	BAV resulted in a significant reduction in the mean aortic gradient (as measured by cardiac catheterization) by 16.5 mmHg (45%) from 36.5 ± 17.5 mmHg to 20.0 ± 14.8 mmHg. Mean gradient (by echocardiography) was also significantly reduced by 11.7 mmHg (25%) from

	46.9 ± 19.25 mmHg to 35.2 ± 11.7 mmHg. The mean AVA estimated by echocardiography significantly improved by 0.16cm^2 (26%) from 0.62 ± 0.19 cm^2 to 0.78 ± 0.33cm^2.
Benefits/claims data	BAV can be performed safely and effectively in a high-risk and very elderly cohort of patients with symptomatic severe AS with high procedural success. BAV plays an important role in palliation of symptoms for frail high-risk patients in whom the role of TAVI is uncertain or inappropriate. It may offer a bridge to definitive valve replacement or can be used as a trial to determine who may derive most benefit from limited TAVI resources.
Strengths	None Stated
Weaknesses/ Potential bias	Limitations of this report arise from the small patient numbers treated in a single centre. The data is observational without randomization and all analyses collected retrospectively.

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	Untreated severe symptomatic AS in the elderly is associated with significant mortality and a 3-year survival of 25%, compared to 77% in a matched population. Initial enthusiasm for BAV as an alternative to SAVR was affected by early high procedural morbidity with a lack of mortality benefit. The introduction of TAVI has driven refinements in BAV technique including smaller arteriotomy, use of rapid pacing and vascular closure devices leading to improved safety and a renewed vigor for BAV. TAVI is currently the preferred treatment option for many patients with severe AS who are inoperable or are at high surgical risk. However, patients with AS and significantly reduced life expectancy due to comorbidities including malignancy, dementia, primary liver disease, chronic obstructive pulmonary disease (COPD) are not appropriate for either TAVI or SAVR. These patients, together with the frail and very elderly, make up a large cohort of patients, often with disabling symptomatic AS, in whom BAV may be used for palliation of symptoms or to evaluate a clinical response to relieving their AS. In addition, BAV may be used as a bridge to definitive AVR (TAVI or SAVR) or occasionally to facilitate non-cardiac surgery, particularly in patients with a combination of severe AS and congestive heart failure, depressed left ventricular ejection fraction (LVEF), or cardiogenic shock.
Comments	None

Eugene *et al.* (2018)

Safety & Performance
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Observational, retrospective study	To assess the early and late outcomes of rescue PBAV in patients with CS or refractory pulmonary edema because of sever AS	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	NuCLEUS (NuMED, Inc.) or Cristal (Balt)	**D1**	D2	D3
Application	BAV	**A1**	A2	A3

Patient	Patients with CS or refractory pulmonary edema because of severe aortic stenosis Sampling: n=40 Mean age: 79 ± 9 years Sex: 22 M; 18 F	**P1**	P2	P3
Report	High quality	**R1**	R2	R3
	Suitability Grade (Range 4-12)	**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Transaortic gradient, systolic pulmonary artery pressure, AVA and LVEF	**Yes 1**	No 2
Follow-up	11 months (range 5 to 39 months)	**Yes 1**	No 2
Statistical analysis	Continuous variables are presented as mean ± standard deviation except for the interval between PBAV and TAVI or SAVR, and for the length of follow-up, which are presented as median with 25th to 75th percentiles. They were compared using the t test when normally distributed or Mann-Whitney U test when non-normally distributed. Categorical variables are reported as n (5) and were compared between groups with the χ^2 or Fisher exact test. Changes in echocardiographic data were analyzed only in patients with known values at baseline and after PBAV with the Wilcoxon signed rank test. Survival rates after PBAV were estimated with the Kaplan-Meier method and cumulative survival rates were compared with the log-rank test. A p-value <0.05 was considered to indicate a statistically significant difference. All statistical calculations were performed with the JMP version 9.0 software (SAS Institute Inc., Cary, NC).	**Yes 1**	No 2
Clinical significance	Not stated	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	Several major complications were observed during PBAV: 3 resuscitated cardiac arrests (2 asystoles and 1 ventricular fibrillation), 1 severe aortic regurgitation, and 3 complete atrioventricular blocks. However, there was no procedural death. Early deaths occurred in 12 patients (30%): 8 patients had CS (48%) and 4 patients had refractory pulmonary edema (24%). Median time to death was 5 days (3 to 9). The causes of deaths were related to pre-existing co-morbidities in 5 cases, to baseline multiorgan failure in 4 cases and to serious adverse events in 3 cases: septic shock in a 77-year-old patient with COPD and home-oxygen; massive hemoptysis in an 87-year-old patient, requiring orotracheal intubation and bronchial artery embolization; and aspiration pneumonia 6 days after PBAV, requiring orotracheal intubation in a 76-year-old patient on chronic dialysis.
Performance data	PBAV was associated with a reduction in mean transaortic gradient (from 47 ± 16 to 32 ± 10 mm Hg, p<0.0001), a systolic pulmonary artery pressure (from 61 ± 15 to 48 ± 12 mm Hg, p=0.002) and an increase in AVA (from 0.60 ± 0.18 to 0.88 ± 0.22 cm2, p<0.0001) and LVEF (from 35 ± 15 to 37 ± 14%, p=0.02).
Benefits/claims data	Rescue PBAV is feasible and safe in critically ill patients with severe aortic stenosis who cannot undergo immediate SAVR or TAVI, because of the severity of their hemodynamic condition.
Strengths	This is the largest series of patients with CS treated with PBAV with a mid-term follow-up so far reported in the literature.
Weaknesses/ Potential bias	This is an observational study from a single center with a retrospective design and patients were included over 8 years. However, they were consecutively and homogenously treated by

	the same heart team and data was homogenously collected.

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	PBAV to treat patients with severe aortic stenosis was first described by Alain Cribier in 1986. Unfavourable mid-term outcomes related to early restenosis have rapidly limited its indications. However, in patients with aortic stenosis and cardiogenic shock (CS), PBAV was shown to be lifesaving in some circumstances. Since the development of TAVI, PBAV is considered with a renewed interest as part of the procedure, and may be indicated as a bridge to further interventions in very high-risk patients.
Comments	None

Masaki et al. 2020

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 Data for SoA	**Results**
Device concept	BAV was first proposed in 1986, offering an alternative to conventional SAVR in elderly and frail patients with severe AS for whom there were no other effective options.
	The current American College of Cardiology/American Heart Association guidelines state that BAV may be considered as a bridge-to-SAVR or -TAVR in patients with severe symptomatic AS (Class IIb, Level of Evidence C)
	With the aging of the general population, there is an increasing prevalence of elderly and frail patients presenting with severe AS for whom BAV can provide a beneficial therapeutic intervention, expanding the indications for BAV, despite the TAVR era
Benefits	Mitral regurgitation (MR) is commonly observed in patients with severe AS. The resolution of AS, by means of SAVR or TAVR, leads to an immediate drop in left ventricular systolic pressure, which reduces the pressure gradient across the mitral valve and, thus, improves MR severity.
	In this study, we demonstrate that good clinical outcomes can be achieved at 1 and 3 months after BAV, including an improvement in cardiac status among patients with severe AS and significant MR.

Objective: Investigate the mid-term effect of BAV on mitral regurgitation in patients with severe AS.
Method: Based on the data from 83 patients with severe AS treated using BAV. Echocardiography was performed before the procedure and at 1 and 3 months after. MR was quantified by measuring the MR jet area, with more-than-moderate MR being clinically significant.
Type of study: Retrospective
Follow-up: 3 months
Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective review	To assess midterm outcomes of BAV on mitral regurgitation in patients with severe AS.	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	Tyshak	**D1**	D2	D3
Application	BAV	**A1**	A2	A3
Patient	Patients with severe AS Sampling: n=83 (unclear how many cases used the Tyshak device) Mean age: 86.2 yrs Sex: M:27, F:56	**P1**	P2	P3
Report	Low quality. Tyshak device was one of many devices used. The study does not describe how many patients were treated with the Tyshak device.	**R1**	R2	**R3**
Suitability Grade (Range 4-12)		**6**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Presence of mitral regurgitation following procedure	**Yes 1**	No 2
Follow-up	3 months	**Yes 1**	No 2
Statistical analysis	As the article does not specify how many patients were treated using the Tyshak device, statistical analysis of outcomes specific to this device cannot be determined	Yes 1	**No 2**
Clinical significance	As the article does not specify how many patients were treated using the Tyshak device, clinical outcomes specific to this device cannot be determined	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 Results:
Safety concern:

Criteria	Results	P value
Adverse Events	The mortality rate even within 3 months after BAV was as high as 22.8% in this study, but most of them were non-cardiac death (78%).	NA

Conclusion: BAV provides a useful therapeutic strategy for elderly patients with severe AS who are not candidates for surgical or transcatheter aortic valve replacement, especially in those with significant MR.
Device used: Tyshak

Toggweiler et al. 2020

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)	11	Disposition (select)	**Accepted, < 12** Excluded, 12

Relevant Data for SoA	Results
Alternatives	Transcatheter aortic valve replacement (TAVR) has been successfully performed in inoperable, high-risk, intermediate-risk, and low-risk patients with low mortality and complication rates,

Objective: Investigate the safety and efficacy of ACURATE neotranscatheter aortic valve replacement (TAVR) facilitated by predilatation with the nonocclusive TrueFlow balloon catheter
Method: Based on the data from 142 patients in a prospective registry. Patients at low risk for intraprocedural third-degree atrioventricular
block (AVB) underwent TAVR with the TrueFlow balloon without rapid pacing and without insertion of a provisional pacemaker (n = 121). The remaining 21 patients were predilated with rapid pacing using a provisional pacemaker and a standard balloon (including the NuMED Z-MED).

Safety & Performance
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective registry	To assess midterm outcomes of BAV on mitral regurgitation in patients with severe AS.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	Z-MED	**D1**	D2	D3
Application	Predilation before TAVR	**A1**	A2	A3
Patient	Patients undergoing TAVR Sampling: n=121 (21 patients used either a TrueDilatation balloonr NuMED Z-MED, unclear how many cases used the Z-MED device) Mean age: 82 yrs Sex: M:55, F:87	**P1**	P2	P3
Report	Low quality. Z-MED device was one of two devices used in "standard balloon" cohort (n=21). The study does not describe how many patients were treated with the Z-MED device.	**R1**	R2	**R3**
Suitability Grade (Range 4-12)		**6**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Successful TAVR	**Yes 1**	No 2
Follow-up	30 days	**Yes 1**	No 2
Statistical analysis	As the article does not specify how many patients were treated using the Z-MED device, statistical analysis of outcomes specific to this device cannot be determined	Yes 1	**No 2**
Clinical significance	As the article does not specify how many patients were treated using the Z-MED device, clinical outcomes specific to this device cannot be determined	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 (3) + Suitability (6) + Data Contribution (6) = 15	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant Results:
Safety concern:

Criteria	Results	P value
Outcomes	Device success – 20/21 (95%)	Not significantly

	Adverse Events	No reports of Major vascular complication at 30 days, Major or life-threatening bleeding at 30 days, Any stroke at 30 days or Mortality at 30 days in "standard balloon" cohort (n=21).	different to TrueFlow balloon cohort (n=121)

Conclusion: Among patients with a low risk for intraprocedural third-degree AVB, the TrueFlow nonocclusive balloon catheter facilitates implantation of the ACURATE neo without the necessity of rapid pacing and a provisional pacemaker.
Device used: Z-MED

Zhang et al. 2021

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 Data for SoA	Results
Alternatives	Transcatheter aortic valve implantation (TAVI) is increasingly applied for treating patients with severe symptomatic aortic stenosis.
Risks	One of the most common complications after TAVI is the need for new permanent pacemaker implantation (PPMI), especially in patients with self-expanding prostheses. New PPMI is related to a longer hospitalization duration, reduced survival, and higher rates of repeated hospitalization
	Multiple reports state that BAV is associated with the development of conduction disorders. However, few studies have investigated the relationship between balloon size in BAV and the rates of PPMI.

Objective: Investigate whether small balloon aortic valvuloplasty (BAV) reduces the need for permanent pacemaker implantation (PPMI) after transcatheter aortic valve implantation (TAVI).
Method: This was a retrospective analysis using data from our local TAVI database. Small BAV was defined as a small balloon size (=18 mm) pre-dilatation. Normal BAV was defined as a balloon size >18 mm. The primary endpoint was the incidence of new PPMI.

Safety & Performance
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective review	To assess need for PPMI after TAVI with BAV	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	Z-MED. Balloon sizes 18-23mm for first 65 patients and 18mm in last 34 patients.	**D1**	D2	D3
Application	Predilation before TAVI	**A1**	A2	A3
Patient	Patients undergoing TAVI Sampling: n=94 Mean age: 78.0 yrs Sex: M:63, F:31	**P1**	P2	P3
Report	High quality. Z-MED devices used in all patients. Outcomes measured include aortic valve regurgitation, aortic gradients, and device success rates.	**R1**	R2	R3
Suitability Grade (Range 4-12)		**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Aortic valve regurgitation, aortic gradients, device success rate,	**Yes**	No

	incidence of new PPMI	**1**	2
Follow-up	30 days	**Yes 1**	No 2
Statistical analysis	The study compares small BAV (18mm) with standard BAV (<18mm);	**Yes 1**	No 2
Clinical significance	All devices are Z-MED devices used for predilation such that the clinical outcomes reported are relevant for the subject devices.	**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 (4) + Data Contribution (4) = 12	**Disposition and Weighting (select)**	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant Results:
Safety concern:

Criteria	**Results**	**P value**
Outcomes	Device success – 91/94 (96.8%) Mean gradient post procedure: 18mm – 11.5mmHg, >18mm – 12.2mmHg PPMI: 18mm – 3.5%, >18mm – 18.9%	Significant difference between "small" and "standard" BAV for PPMI
Adverse Events	Severe or moderate AVR – 18mm – 5.3% , >18mm – 8.1% Conversion to surgery – 1/94 (1%) No reports of stroke or transient cerebral ischemic attack; 30-day mortality – 1/94 (1%)	

Conclusion: The small BAV strategy is associated with a low rate of permanent pacemaker implantation after transcatheter self-expanding valve implantation in this single-center observational study.
Device used: Z-MED

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 PTV Catheters has been carried out and documented in the CER. 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, 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 PTV Catheters, including the IFU, 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 the CER and with the current knowledge/state of the art.

Overall, it is concluded that the risks associated with the use of the PTV Catheters 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 PTV Catheters have been commercialized since 1998 in the EU. Since then, the device is likely to have been used in a variety of patients and populations. A PMCF study is not warranted at this time due to the fact that long-term safety and clinical performance has been established via device use and ample clinical experience. This experience would likely have identified any rare complications or problems that would become apparent only after widespread device use. Continued post-market surveillance activities will provide sufficient data to adequately address clinical risks, and detect emerging risks on the basis of evidence.

A PMCF study was conducted in the past on the Z-MED and Z-MED II, with the introduction of the mitral & aortic valvuloplasty indication, and did not identify any new risks.

Post-market surveillance data as part of the quality system is continually compiled as per an established quality system. Device-related adverse events and complaints are recorded with explicit purpose to identify and investigate any residual risks associated with the use of the device.

6. Possible diagnostic or therapeutic alternatives

The introduction of TAVR has revolutionized the management of patients with AS and is considered a viable option in high-risk and inoperable patients (2).

Surgical aortic valvotomy (SAV) is an alternative initial intervention to BAV for AS, where the choice of primary intervention is typically based on institutional preference.

7. Suggested profile and training for users

The intended users of PTV catheters are Cardiac Surgeons and/or Interventionalists.

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 11135:2014 – 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 15223-1:2021 – Medical devices – Symbols to be used with medical device labels, labelling and information to be supplied – Part 1: General requirements

9. References

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10. Revision History

SSCP revision number	Date Issued	Change Description	Revision validated by Notified Body
00	21 June 2022	Initial implementation	☐ Yes Validation Language: English ☒ No