regurgitation and an RV-PA conduit that supports placement of the TPV device in the pulmonary position.

No.	Rationale
1	TPVI is a well accepted and FDA-approved therapy for RV-PA conduit and bioprosthetic valve (BPV) regurgitation, regardless of the surgical risk, because of 5-7 year follow-up data from multiple prospective studies showing excellent results and durability. • Cabalka AK, Hellenbrand WE, Eicken A, et al. Relationships Among Conduit Type, Pre-Stenting, and Outcomes in Patients Undergoing Transcatheter Pulmonary Valve Replacement in the Prospective North American and European Melody Valve Trials. JACC Cardiovasc Interv. Sep 11 2017;10(17):1746-1759. PMID 28823778 • Cheatham JP, Hellenbrand WE, Zahn EM, et al. Clinical and hemodynamic outcomes up to 7 years after transcatheter pulmonary valve replacement in the US melody valve investigational device exemption trial. Circulation. Jun 2 2015;131(22):1960-70. PMID 25944758 Freedom from TPVI valve dysfunction is comparable to that for surgical conduits and BPVs, particularly when comparing age-matched studies, as valve dysfunction is age-related (). • Batlivala SP, Emani S, Mayer JE, et al. Pulmonary valve replacement function in adolescents: a comparison of bioprosthetic valves and homograft conduits. The Annals of Thoracic Surgery. May 04 2012; 93(6):2007-2016. PMID 22560964 • Buber J, Assenza GE, Huang A, et al. Durability of large diameter right ventricular outflow tract conduits in adults with congenital heart disease. Int J Cardiol. Aug 20 2014; 175(3):455-63. PMID 25002319 Comparing valve dysfunction is more useful than comparing reintervention rates, as many surgical patients were left with dysfunction without undergoing reoperation, prior to the availability of TPVI therapy. One of the great benefits of TPVI therapy is treatment of conduit and BPV dysfunction without open heart surgery and redo sternotomy operations. STS-CHSD data show that unadjusted mortality and other complications increase with the increasing number of prior cardiopulmonary bypass (CPB) operations. • Khanna AD, Hill KD, Pasquali SK, et al. Benchmark Outcomes for Pulmonary Valve Replacement Using The Society of Thoracic Surgeons Databases. Ann Thorac Surg. Jul 2015;100(1):138-45. PMID 26007205 Therefore, it is beneficial to decrease the number of CPB operations over a patient's lifetime. In addition, TPVI has fewer complications of death/stroke/early reoperation than surgical valve replacement (0.8% vs. 4.3%). • Bishnoi RN, Jones TK, Kreutzer J, et al. NuMED Covered Cheatham-Platinum Stent™ for the treatment or prevention of right ventricular outflow tract conduit disruption during transcatheter pulmonary valve replacement. Catheter Cardiovasc Interv. Feb 15 2015; 85(3):421-7. PMID 25459038 • Batlivala SP, Emani S, Mayer JE, et al. Pulmonary valve replacement function in adolescents: a comparison of bioprosthetic valves and homograft conduits. The Annals of Thoracic Surgery. May 04 2012; 93(6):2007-2016. PMID 22560964 Furthermore, hospital length of stay averages 1 day with TPVI compared to 4-7 days with surgical conduit or valve replacement. Cost effectiveness studies have shown TPVI cost to be comparable to or less than surgical pulmonary valve replacement. • Vergales JE, Wanchek T, Novicoff W, et al. Cost-analysis of percutaneous pulmonary valve implantation compared to surgical pulmonary valve replacement. Catheter Cardiovasc Interv. Dec 1 2013; 82(7):1147-53. PMID 23857801 • O'Byrne ML, Gillespie MJ, Shinohara RT, et al. Cost comparison of Transcatheter and Operative Pulmonary Valve Replacement (from the Pediatric Health Information Systems Database). Am J Cardiol. Jan 1 2016; 117(1):121-6. PMID 26552510 • Steinberg ZL, Jones TK, Verrier E, et al. Early outcomes in patients undergoing transcatheter versus surgical pulmonary valve replacement. Heart (British Cardiac Society). Mar 28 2017; 103(18):1455-1460. PMID 28351873

b. Native or patched RVOT with at least moderate pulmonic regurgitation: This includes individuals with at least moderate pulmonary regurgitation and native or patched RVOT that supports placement of the TPV device in the pulmonary position.

No.	Rationale
1	While there are no transcatheter valves FDA-approved for use in a native or patched RVOT, this therapy is considered a reasonable alternative to surgical pulmonary valve replacement (SPVR), regardless of surgical risk. Levi et al presented 10 patients with a patched RVOT who were taken to the catheterization laboratory for TPVI with a Sapien XT valve, and 7 patients underwent successful valve implantation with no residual stenosis or regurgitation. Three were excluded due to an inadequate landing zone or coronary compression risk. • Levi DS, Sinha S, Salem MM, et al. Transcatheter native pulmonary valve and tricuspid valve replacement with the Sapien XT: Initial experience and development of a new delivery platform. Catheter Cardiovasc Interv. Sep 2016; 88(3):434-43. PMID 27142960 At this time, the literature is limited to case reports and case series, but larger retrospective and prospective studies are forthcoming. This practice is currently considered standard-of-care in many centers, when a landing zone is adequate, in order to decrease the number of cardiopulmonary bypass operations, hospital length of stay, and time off of work for patients.

c. Right ventricle-to-pulmonary artery connection (RV-PA conduit) with or without bioprosthetic valve with pulmonic stenosis (mean RVOT gradient at least 35 mm Hg): This includes individuals with pulmonic stenosis with a mean RVOT gradient greater or equal to 35 mm Hg and RV-PA conduit that supports placement of the TPV device.

No.	Rationale
1	Transcatheter pulmonary valve placement in the setting of stenosis has been reported to have excellent procedural success and has been noted to have durable improvements in patient status. Perhaps one argument against transcatheter pulmonary valve placement when compared to surgical intervention is the published rate of reintervention with TPVR. This is an effect of the pre-stent era and in this population of stenotic conduits, reinterventions were often a result of stent fracture. Additionally, previously reported risk in this population of a stenotic conduit includes conduit rupture, now able to be adequately treated with covered stents now available following the COAST and PARCS trials in nearly all cases. Eliminating at least one sternotomy, often more, in patients that will require several reentry stenotomies most arguably can be lifesaving. A recent paper by Calbalka et al describes outcomes in prospective North American and European Melody valve trials. In this study, freedom from reintervention in 358 patients was 85% at 3 years. This improved rate of freedom from reintervention was attributed to the adopted practice of prestenting, thus reducing Melody frame fracture. In this study, 162 patients had stenosis or mixed disease (stenosis and regurgitation) with good results. • Cabalka AK, Hellengrand WE, Eicken A, et al. Relationships Among Conduit Type, Pre-Stenting, and Outcomes in Patients Undergoing Transcatheter Pulmonary Valve Replacement in the Prospective North American and European Melody Valve Trials. JACC Cardiovasc Interv. Sep 11 2017; 10(17):1746-1759. PMID 28823778 A recent metaanalysis by Chatterjee et al. entitled Transcatheter Pulmonary Valve Implantation: A Comprehensive Systematic Review and Meta-Analyses of Observational Studies pooling 19 studies describes the improved reintervention rates post pre-stent era (4.8 per 100 patient year). Taking current practices of prestenting into account, longevity of the valve has been shown to be comparable to surgical conduits. • Chatterjee A, Bajaj NS, McMahon WS, et al. Transcatheter Pulmonary Valve Implantation: A Comprehensive Systematic Review and Meta-Analyses of Observational Studies. J Am Heart Assoc. Aug 4 2017; 6(8). pii: e006432. PMID 28778940

d. Native or patched RVOT with pulmonic stenosis (mean RVOT gradient at least 35 mm Hg): This includes individuals with pulmonic stenosis with a mean RVOT gradient greater

or equal to 35 mm Hg and native or patched RVOT that supports placement of the TPV device in the pulmonary position.

No.	Rationale
1	The stenotic native RVOT carries fewer risks for transcatheter valve placement compared to dilated RVOT and severely stenotic conduit cohort. This group additionally has highly variable and dynamic RVOT anatomy which can make patient selection key in success. This was outlined in a recent article by Meadows et al (2014). This study highlights the importance of selection in this native RVOT population. In this population of patients from 5 centers, 3 of the 31 patients had stenosis as the primary indication and were mixed (stenosis and regurgitation) in an additional 14 patients. All implants were successful without risk of stent migration in the stenotic group. Follow up results were good with median gradient across the RVOT of 23 mmHg and mild TPV insufficiency. Stent fracture was associated with higher gradients. This population can undergo transcatheter pulmonary valve insertion safely, thus offering an alternative to surgical intervention. • Meadows JJ, Moore PM, Berman DP, et al. Use and Performance of the Melody Transcatheter Pulmonary Valve in Native and Postsurgical, Nonconduit Right Ventricular Outflow Tracts. Circ Cardiovasc Interv. Jun 2014; 7(3):374-80. PMID 24867892

2. Based on the evidence and your clinical experience for each of the clinical indications described in Question 1a-1d when performing TPVI using the Melody Transcatheter Pulmonary Valve (TPV):
    a. Clinically Meaningful Improvement in Net Health Outcome
        - Respond YES or NO for each clinical indication whether the use of TPVI would be expected to provide a clinically meaningful improvement in net health outcome; AND
        - Rate your level of confidence in your YES or NO response using the 1 to 5 scale outlined below.

No.	Indications	Yes/No	Low Confidence		Intermediate Confidence		High Confidence
			1	2	3	4	5
1	Q1a: RV-PA conduit with or without bioprosthetic valve with at least moderate pulmonic regurgitation	Yes					X
	Q1b: Native or patched RVOT with at least moderate pulmonic regurgitation	Yes				X	
	Q1c: RV-PA conduit with or without bioprosthetic valve with pulmonic stenosis (mean RVOT gradient at least 35 mm Hg)	Yes					X
	Q1d: Native or patched RVOT with pulmonic stenosis (mean RVOT gradient at least 35 mm Hg)	Yes				X	

    b. Generally Accepted Medical Practice
        - Respond YES or NO for each clinical indication whether the use of TPVI is consistent with generally accepted medical practice; AND

- Rate your level of confidence in your YES or NO response using the 1 to 5 scale outlined below.

No.	Indications	Yes/No	Low Confidence		Intermediate Confidence		High Confidence
			1	2	3	4	5
1	Q1a: RV-PA conduit with or without bioprosthetic valve with at least moderate pulmonic regurgitation	Yes					X
	Q1b: Native or patched RVOT with at least moderate pulmonic regurgitation	Yes				X	
	Q1c: RV-PA conduit with or without bioprosthetic valve with pulmonic stenosis (mean RVOT gradient at least 35 mm Hg)	Yes					X
	Q1d: Native or patched RVOT with pulmonic stenosis (mean RVOT gradient at least 35 mm Hg)	Yes				X	

3. Based on the evidence and your clinical experience for each of the clinical indications described in Question 1a-1d when performing TPVI using the SAPIEN XT Transcatheter Heart Valve (pulmonic) or SAPIEN 3 Transcatheter Heart Valve[1]:
    a. Clinically Meaningful Improvement in Net Health Outcome
        - Respond YES or NO for each clinical indication whether the use of TPVI would be expected to provide a clinically meaningful improvement in net health outcome; AND
        - Rate your level of confidence in your YES or NO response using the 1 to 5 scale outlined below.

No.	Indications	Yes/No	Low Confidence		Intermediate Confidence		High Confidence
			1	2	3	4	5
1	Q1a: RV-PA conduit with or without bioprosthetic valve with at least moderate pulmonic regurgitation	Yes					X
	Q1b: Native or patched RVOT with at least moderate pulmonic regurgitation	Yes				X	
	Q1c: RV-PA conduit with or without bioprosthetic valve with pulmonic stenosis (mean RVOT gradient at least 35 mm Hg)	Yes					X
	Q1d: Native or patched RVOT with pulmonic stenosis (mean RVOT gradient at least 35 mm	Yes				X	

	Hg)

b. Generally Accepted Medical Practice
   - Respond YES or NO for each clinical indication whether the use of TPVI is consistent with generally accepted medical practice; AND
   - Rate your level of confidence in your YES or NO response using the 1 to 5 scale outlined below.

No.	Indications	Yes/No	Low Confidence		Intermediate Confidence		High Confidence
			1	2	3	4	5
1	Q1a: RV-PA conduit with or without bioprosthetic valve with at least moderate pulmonic regurgitation	Yes					X
	Q1b: Native or patched RVOT with at least moderate pulmonic regurgitation	Yes				X	
	Q1c: RV-PA conduit with or without bioprosthetic valve with pulmonic stenosis (mean RVOT gradient at least 35 mm Hg)	Yes					X
	Q1d: Native or patched RVOT with pulmonic stenosis (mean RVOT gradient at least 35 mm Hg)	Yes				X	

4. Additional narrative rationale or comments and/or any relevant scientific citations (including the PMID) supporting your clinical input on this topic.

No.	Additional Comments
1	Not applicable to TPVI

5. Is there any evidence missing from the attached draft review of evidence that demonstrates clinically meaningful improvement in net health outcome?

No.	Yes/No	Citations of Missing Evidence
1	No	