

Considerations in Japanese academia in advancing pediatric medical device development: Insight from Japan's Agency for Medical Research and Development

Takanari Fujii

Pediatric Heart Disease and Adult Congenital Heart Disease Center
SHOWA Medical University Hospital

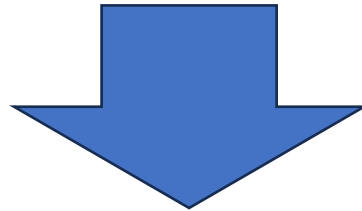
Environment of pediatric medical device development

Barriers for pediatric medical device development

1. Universal problems specific to children

- Small market size
- Rare disease
- Wide variety in body and lesion size (Somatic growth of children)

2. High cost for device development



Device-lag Off-label use

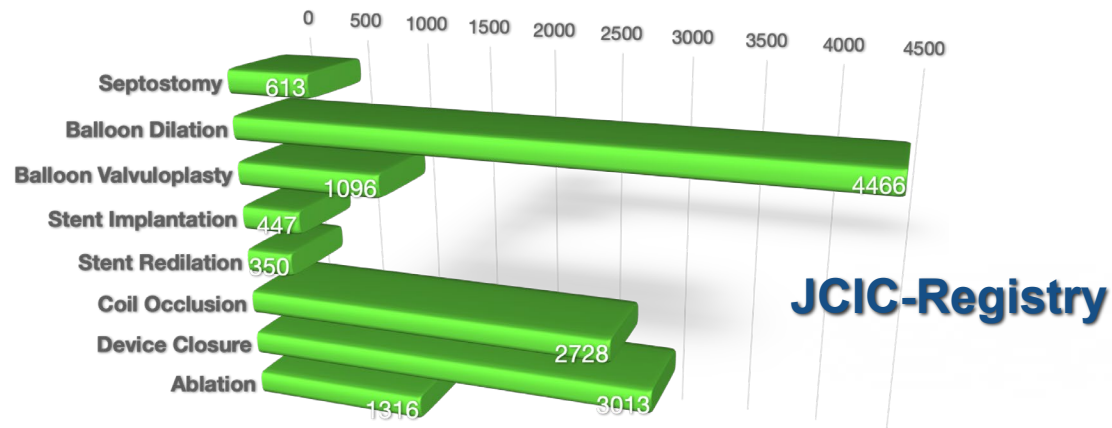
HBD for children



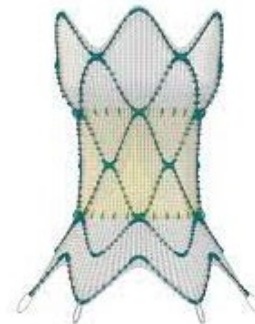
JCIC Registry



- ✓ Conducted by National Clinical Database (NCD) and JCIC
- ✓ High completeness (>90% of procedures in Japan)



- ✓ Previously used for post-marketing database surveys in some devices



Update - AMED research

Japan Agency for Medical Research and Development

Research on the Improvement of the Environment to Promote Pediatric Medical Device Development

HBD for children



PAS-ARC



July 2023 – March 2026

Budget approved for 2023-2024
9100,000 USD

Objectives

- ✓ To reconstruct the JCIC-R database to be able to applicate effective PMS of the different types of devices and reduce the time/cost of PMS while securing the quality of surveillance.
- ✓ To improve the environment of pediatric medical devices development by strengthen the global collaboration of the stakeholders.

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Projects

- #1 Reconstitution of the JCIC-R database to facilitate device development
- #2 Standardization of definitions and endpoints (PAS-ARC project)
- #3 Quality Improvement of the JCIC-R dataset
- #4 Research of the clinical needs based on the RWD on the JCIC-R

Reconstitution of the JCIC–R database to facilitate device development

“Minimum data set” project

The new concept to minimize the number of data-set while ensuring effectiveness and safety evaluation in PMS using JCIC-R.

Heart and Vessels
<https://doi.org/10.1007/s00380-020-01691-0>

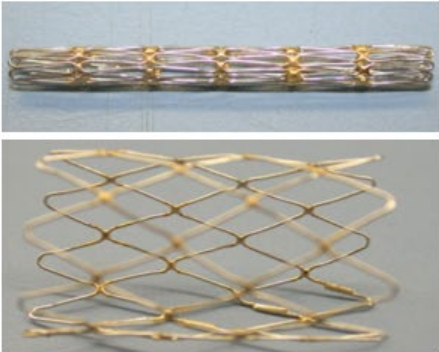
ORIGINAL ARTICLE



Clinical trial of the CP stent for pulmonary artery stenosis: the first investigator-initiated clinical trial for pediatric interventional cardiology in Japan

Takanari Fujii¹ · Hideshi Tomita¹ · Toshiki Kobayashi² · Hitoshi Kato³ · Hisashi Sugiyama⁴ · Ayumi Mizukami⁵ · Hideaki Ueda⁶

PMS of CP stent



CP Stent™ Specifications				
Stent Length (CM)	Configuration (Number of Zigs)	Platinum Wire (Inches)	Bare Stent Catalog No.	Covered Stent Catalog No.
1.6	8	0.013	CP8Z16	Cvrd. CP8Z16
2.2	8	0.013	CP8Z22	Cvrd. CP8Z22
2.8	8	0.013	CP8Z28	Cvrd. CP8Z28
3.4	8	0.013	CP8Z34	Cvrd. CP8Z34
3.9	8	0.013	CP8Z39	Cvrd. CP8Z39
4.5	8	0.013	CP8Z45	Cvrd. CP8Z45

“Minimum data set” project

Minimizing collection frequency

Minimizing the No. of items

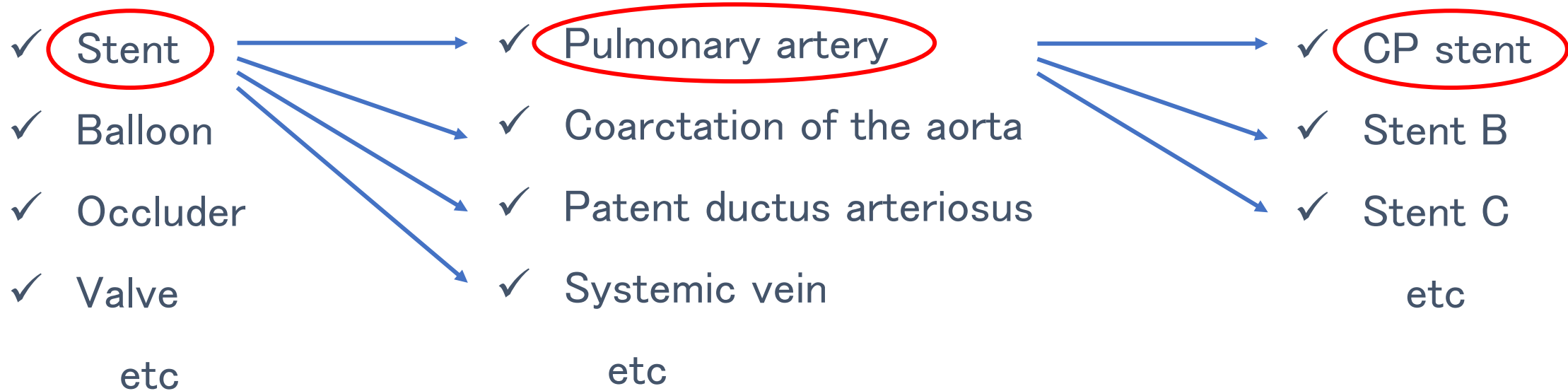
	Hopital	1 M	3 M	6 M	1 Y	2 Y	3 Y
Effectiveness							
Clinical outcome							
Device performance							
Procedure-related endpoints		88% Reduction !!					
Safety Issues							
Device related AEs							
Procedure related AEs							
Unknown AEs							

Patient background is collected from existing JCIC-R data

Reconstitution of the JCIC-R database to facilitate device development

“Minimum data set” project

The new concept to minimize the number of data-set while ensuring effectiveness and safety evaluation in PMS using JCIC-R.



Research of the clinical needs based on the RWD on the JCIC-R

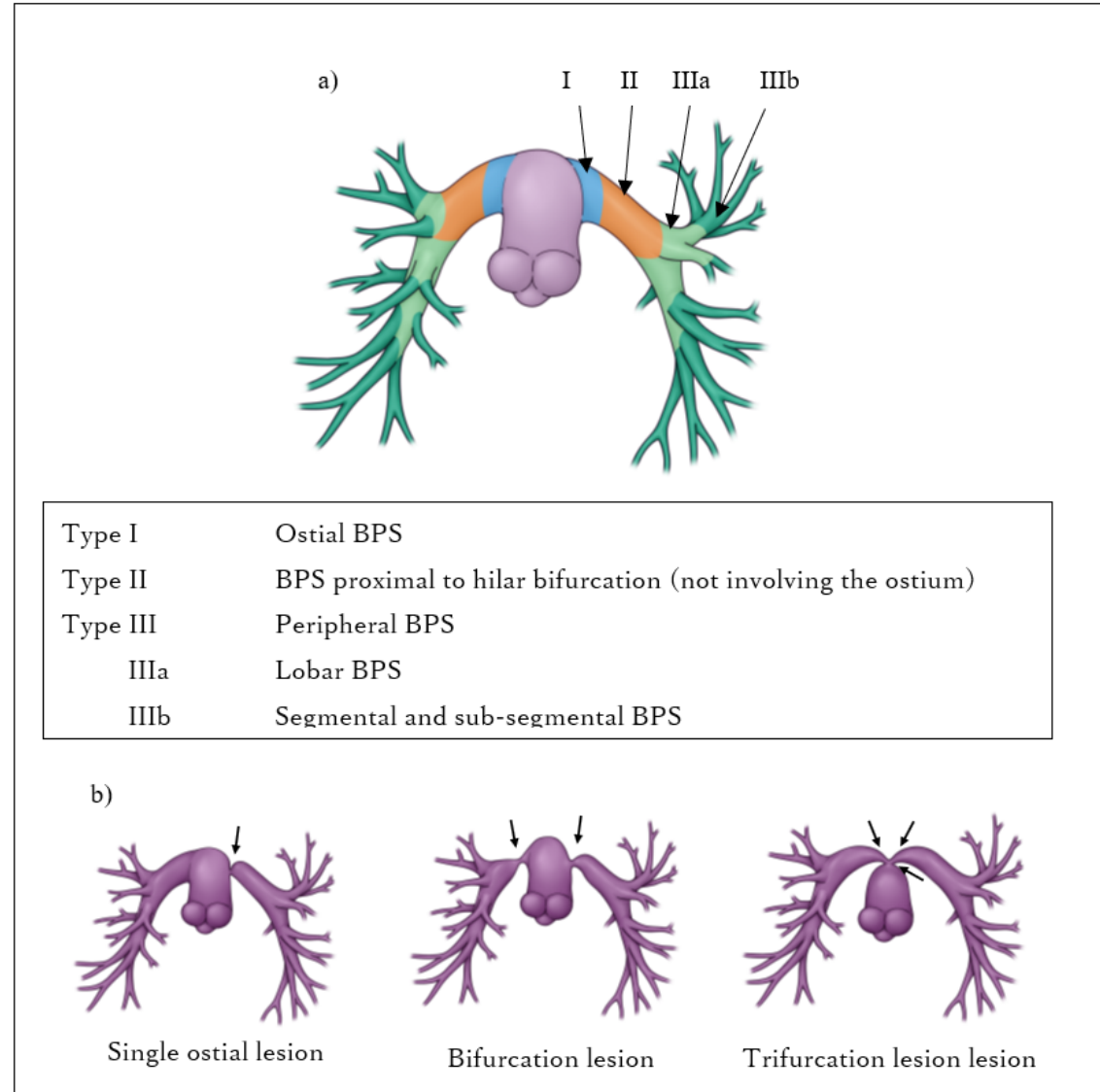
		Procedural Approval		
		On-label	On-label (inadequate)	Off-label
Device Approval	On-label	O.	B.	D.
	Off-label	A.	C.	E.

Procedure registered in the JCIC-R (2016-2023) are being analyzed, categorized into the above six categories.

Standardization of definitions and endpoints (PAS-ARC project)

“PAS” Pulmonary Artery Stenosis

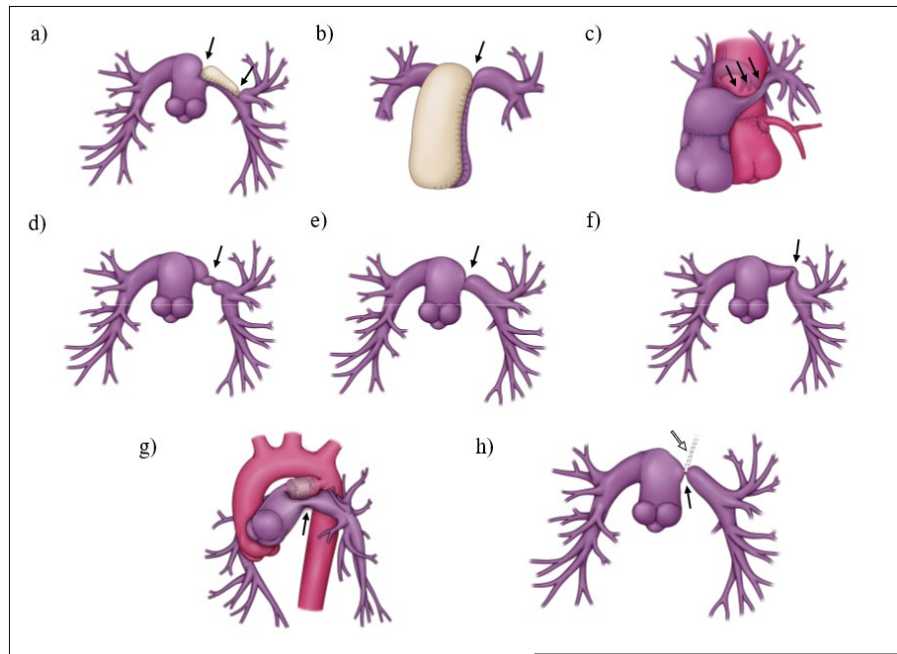
“Location”



Standardization of definitions and endpoints (PAS-ARC project)

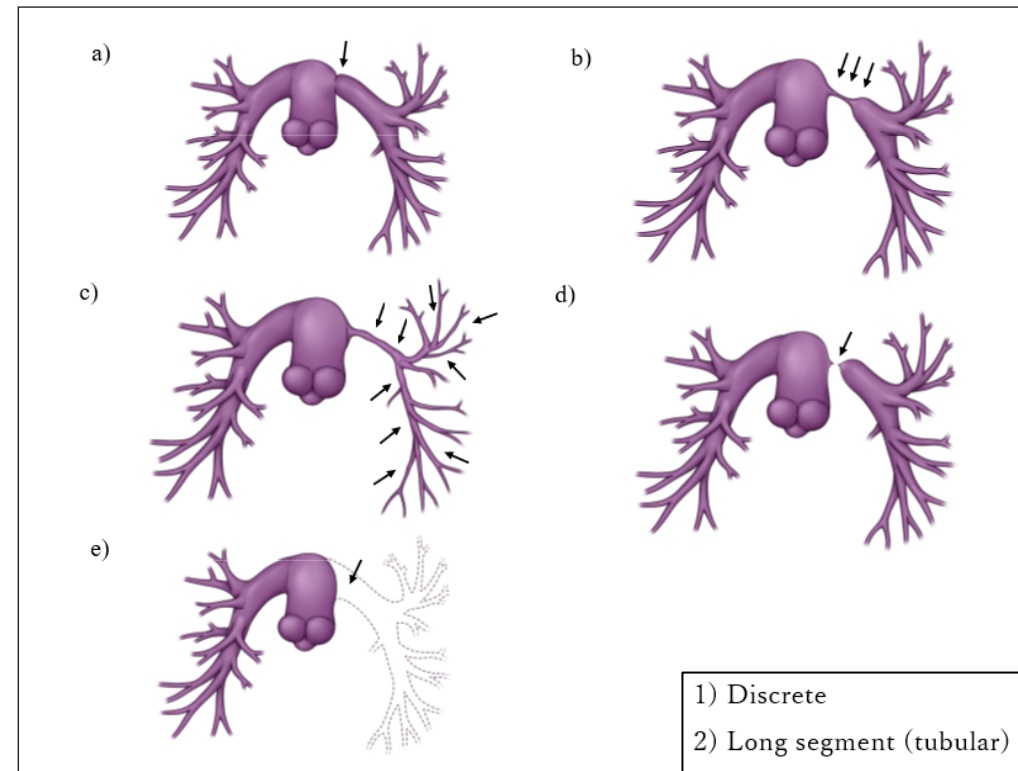
“PAS” Pulmonary Artery Stenosis

“Mechanism”



- 1) Scar
- 2) Inadequate PA-plasty
- 3) Stretching
- 4) Torsion/ twist
- 5) Fold/kink
- 6) External compression
- 7) Constriction (due to ductal tissue)
- 8) Somatic growth
- 9) Low blood flow
- 10) Inflammation/thromboembolic disease
- 11) Other iatrogenic obstruction (due to endovascular devices)

“Morphology”

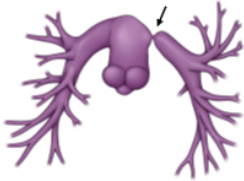
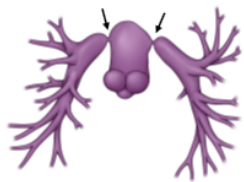
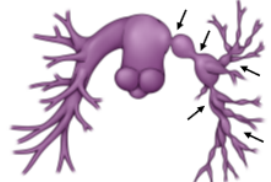
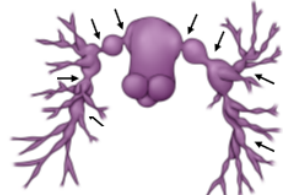


- 1) Discrete
- 2) Long segment (tubular)
- 3) Hypoplasia
- 4) Discontinuous / nonconfluent
- 5) Absent / Atretic

Standardization of definitions and endpoints (PAS-ARC project)

“PAS” Pulmonary Artery Stenosis

“Category of lesions and Applicable Metrics”

Category	Applicable metrics (Diameter / PG/ RV pressure)
1) Unilateral/single stenosis 	If contralateral PA dilates to accommodate more flow, both PG and RV pressure may underestimate degree of stenosis. Lesion diameter may be the most accurate way to evaluate degree of stenosis. Flow scan will be valuable.
2) Bilateral/single stenosis 	PG typically exists across the stenosis and reflects severity. RV pressure typically elevated and systolic RV pressure and/or RV/systemic pressure ratio may accurately reflect severity of stenoses.
3) Unilateral/multi-level stenosis 	Both PG and RV pressure may underestimate degree of stenosis. Lesion diameter and flow scan may be the most accurate way to evaluate degree of stenosis.
4) Bilateral/multi-level stenosis 	The most important metric is RV systolic pressure and/or RV/systemic pressure ratio.

Summary of Our Current Effort

Current Activities

HBD for children

- Deregulation
- Global Clinical Trials
- Utilization of RWD

Challenges remaining :

- Birthrate deceleration
- Growing unprofitability
- Difficulty of introducing devices with foreign regulatory approvals

New device development

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Off-label use

On Label

Number of devices available
in Japan

Off Label

**An emerging critical situation caused by
the lack of alternative medical devices.**

Off-label use is becoming more difficult due to...

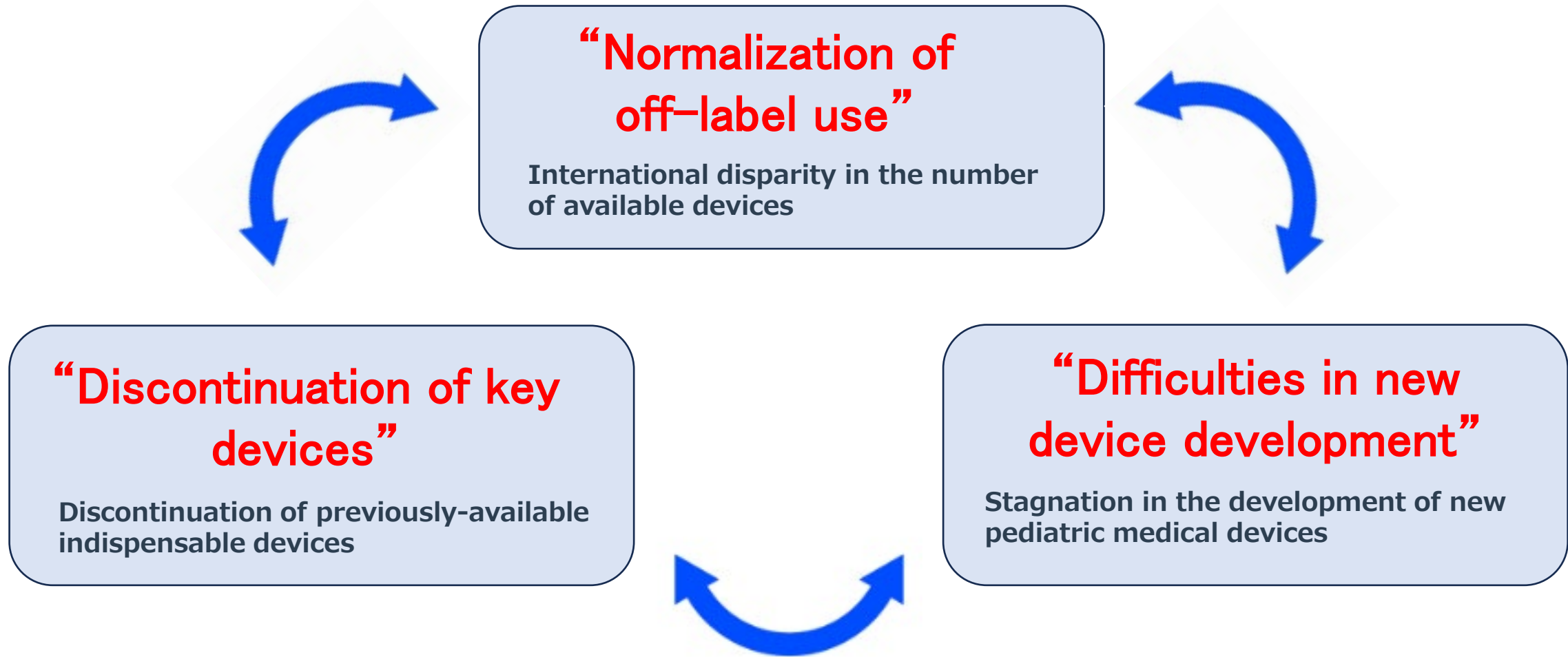
- Tighter regulations under the Clinical Research Act.
- Discontinuation of device due to the transition to the MDR.

Large/Extra Large Size Stents Available in Each Country

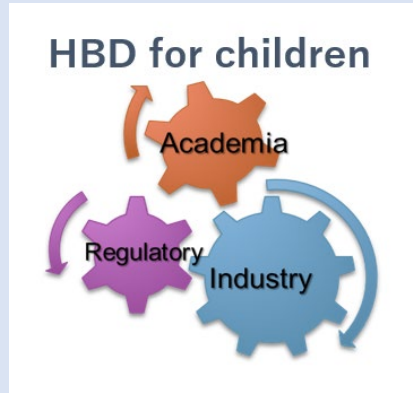
Stent specificities					Status in each country							
Type (Size)	Stent Name	Manufact ure	Diameter (mm)	Length (mm)	USA (FDA)		EU (CE mark)		Japan (PMDA)		Canada (Health Canada)	
					Availability	Approval for CHD	Availability	Approval for CHD	Availability	Approval for CHD	Availability	Approval for CHD
Extra large size	Palmaz XL stent	Cordis	25	39-59	○	—	○	—	△ Unstable supply	—	○	—
	Andra XL/XXL Stent	Andramed	XL:25 / XXL:32	18.6-57	×	—	○	CoA	×	—	○	
	Optimus XL/XXL Stent*	AndraTec	XL:24 / XXL:28	13.8-57	×	—	○	—	×	—	×	
	Max LD	Medtronic	25	22-43	○	—	○	—	×	—	○	—
	CP Stent/Covered CP stent*	NuMED	24	13-39	○	CoA RVOT	○	CoA	×	—	○	CoA RVOT
Large size	Palmaz stent	Cordis	20	8-20	○	—	○	—	×	—	○	—
	BeGraft stent**	Bentley InnoMed	24	19-59	×	—	○	CoA	×	—	×	
	Formula 535	Cook	20	16-59	×	—	○	—	×	—	○	
	IntraStent Mega LD/Maxi LD (EV3)	Medtronic	Mega:18 / Maxi:25	22-43	○	—	○	—	×	—	○	—
	Palmaz Mullins stent (Genesis XD)	Cordis	18	19-59	○	PAS	○	—	×	—	○	
	Valeo stent (Large)	BD	20	22-57	×	—	○	—	×	—	×	
	Renata Minima stent	Renata Medical	22	12-24	○	CoA PAS	×	—	×	—	×	

There are no large-size stents available in Japan

Currently identified challenges



To overcome this dilemma, further deregulation, improved reimbursement, and the establishment of a new legal framework specifically for pediatric medical devices may be required.



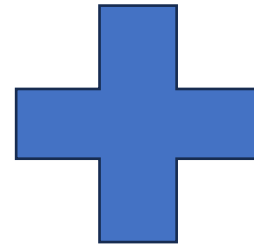
JSPCCS
HBD for children



JCIC-R WG



JSPCCS
JCIC



**Research on the Improvement of the Environment
to Promote Pediatric Medical Device Development**