CHALLENGES IN ESTABLISHING RWE FOR PRE- AND POST-MARKET CLINICAL EVALUATION

Toho University, Ohashi Medical Center

Masato Nakamura

COI Disclosure

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⑩Grant : none

AGENDA

- Utilization of RWDs
  - Current situation in Japan
- Issues in RWD utilization

PURPOSE OF RWD UTILIZATION THERE ARE THREE CATEGORIES OF USE

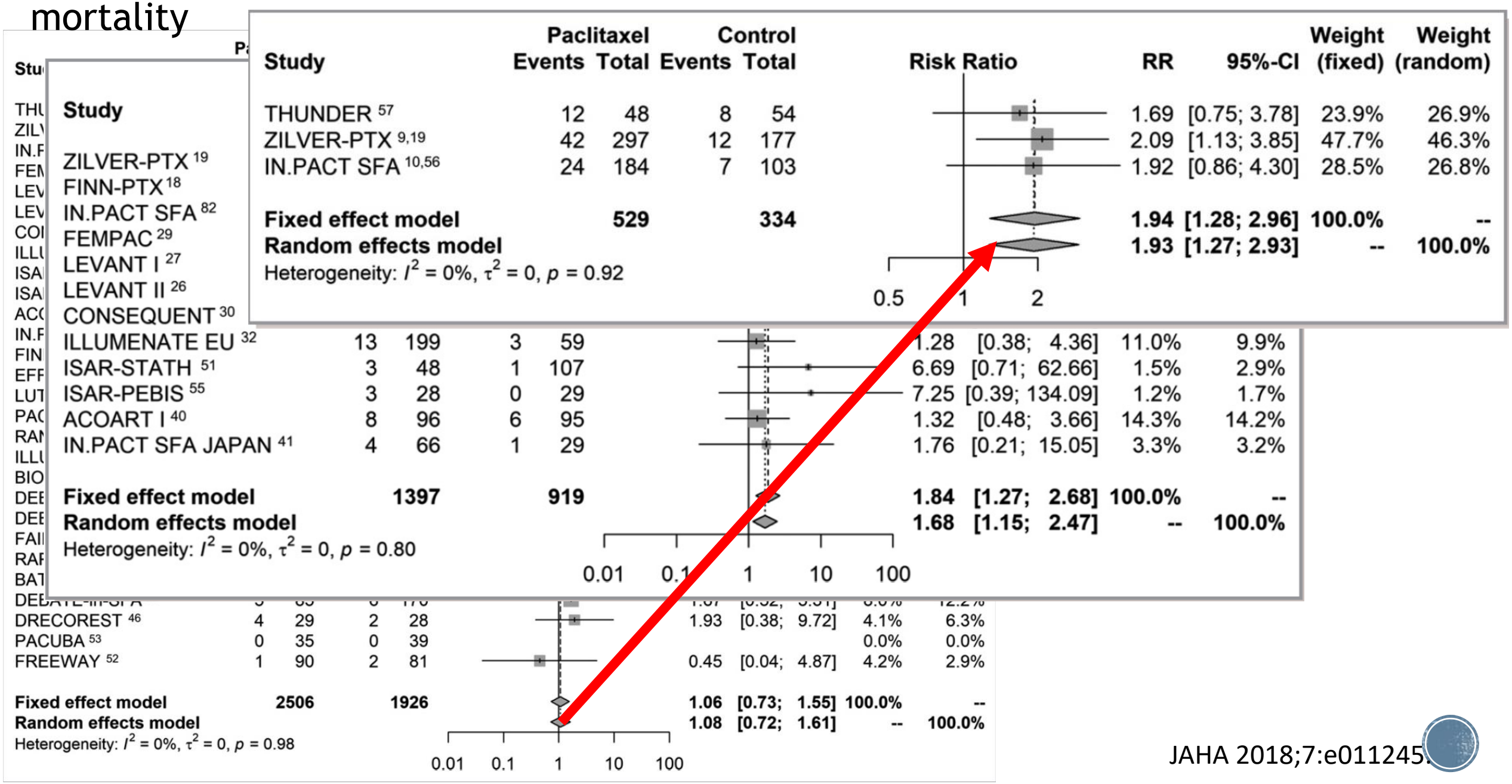
1. Post-marketing surveillance
- Confirmation of long-term safety and efficacy

  Ex: Implantable devices, artificial devices

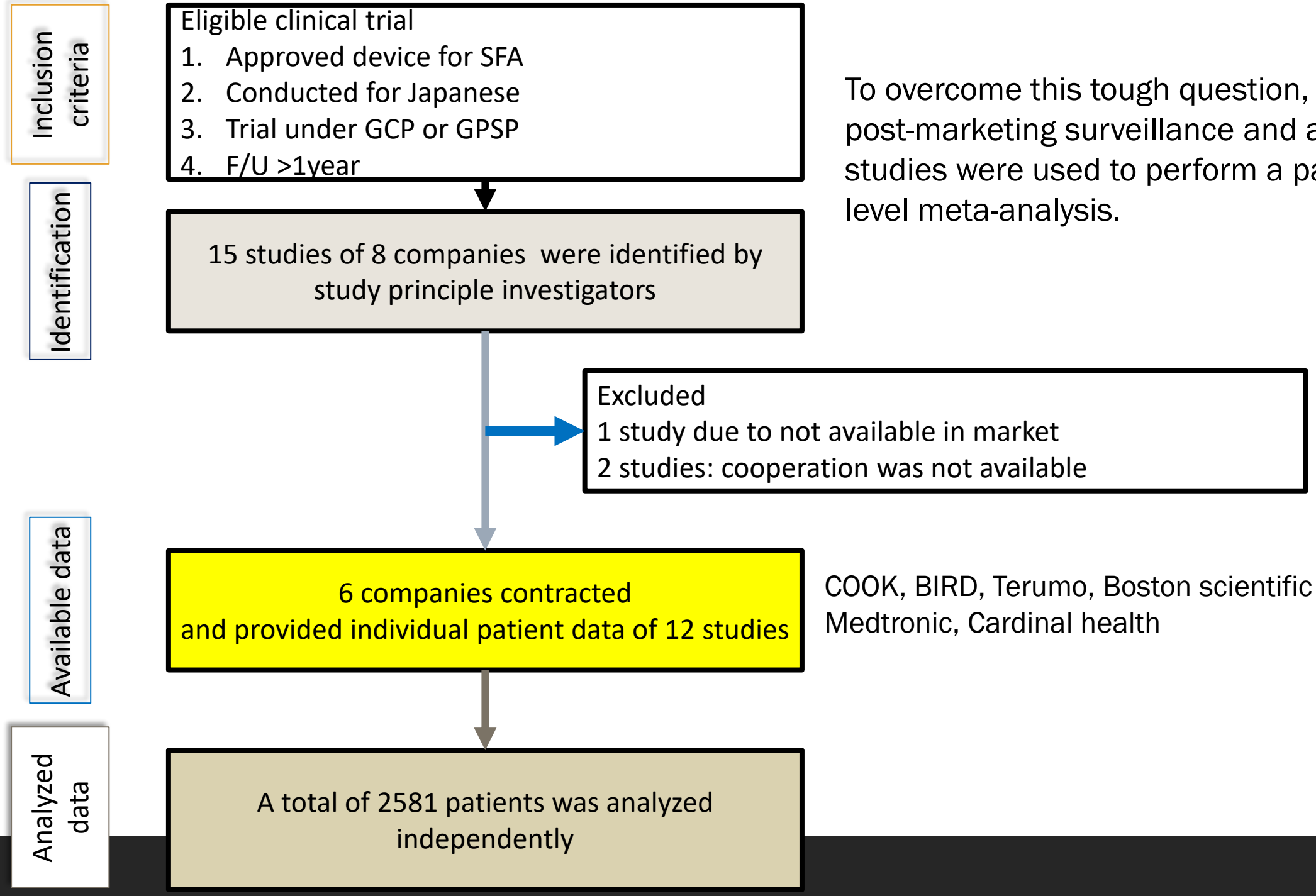
2. Single arm study to get approval
- Historical control
- Evaluate the appropriateness of the intended use range

3. Promotion of appropriate use
- Expansion of indications
- Revision of guidelines for appropriate use etc.

A meta-analysis of Katsanos et al suggested the harmful effect of PTXD on long-term mortality



JAHA 2018;7:e011245.



To overcome this tough question, post-marketing surveillance and approval studies were used to perform a patient-level meta-analysis.

COOK, BIRD, Terumo, Boston scientific Medtronic, Cardinal health

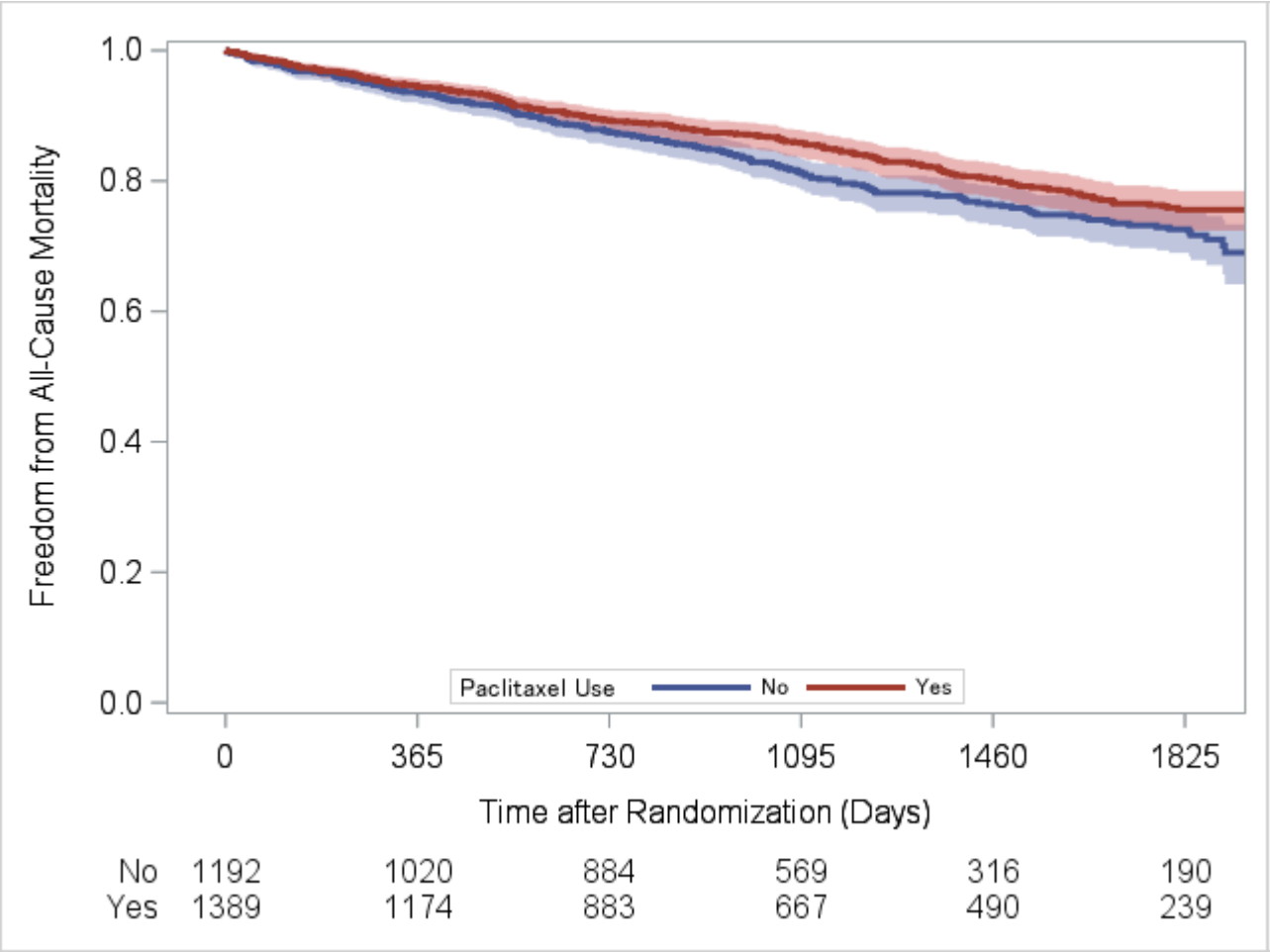
6 companies, 12 trials

Pivotal study
6RCT＋1Single arm study
n=626

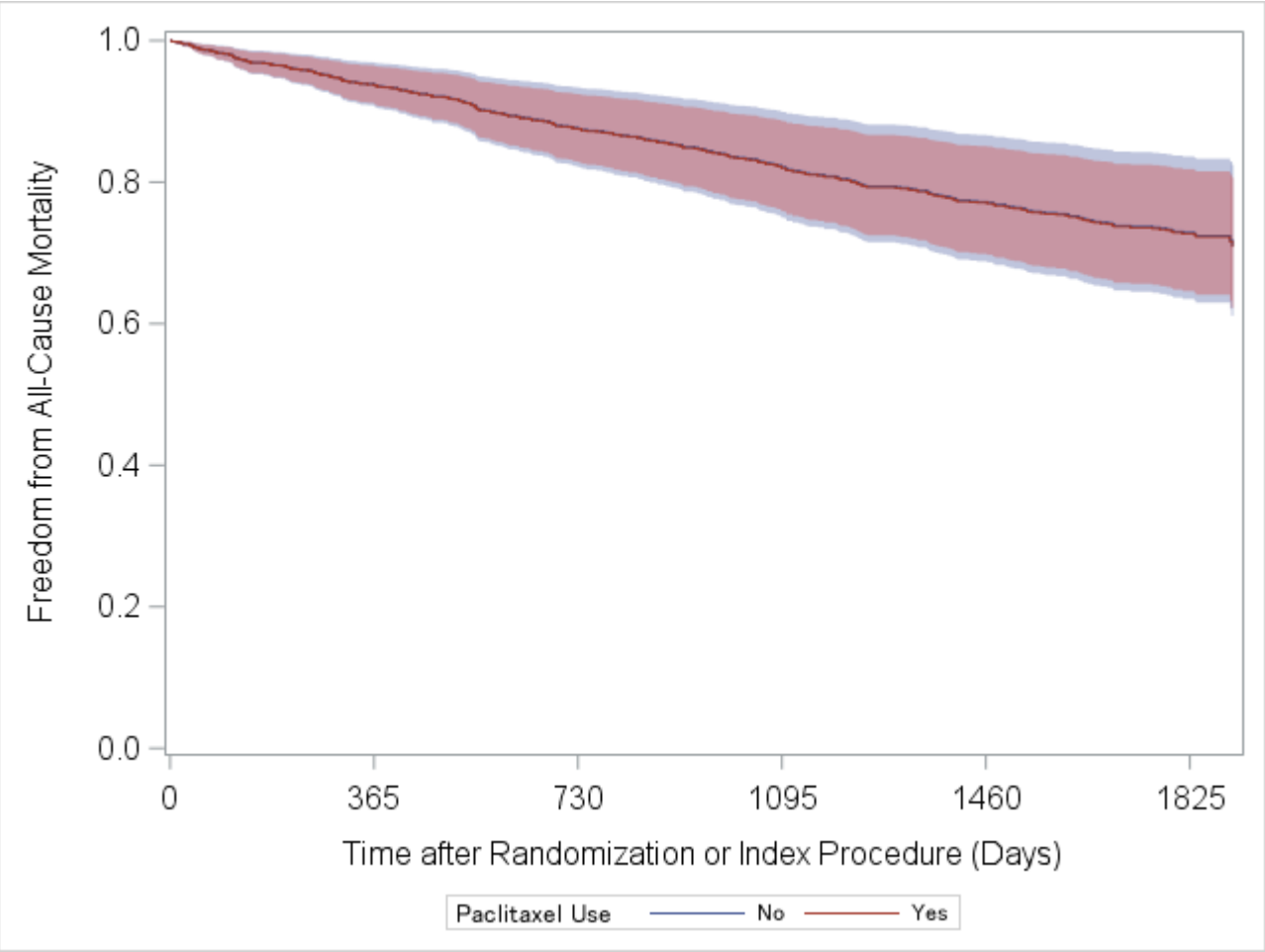
Post marketing surveillance
5 single arm study
n=955

Integration of masked data
Individual level meta-analysis
PTXD n=1389, non-PTXD n=1192

Unadjusted



Adjusted



An Individual-Level Meta-Analysis Using Real-World and Pivotal Studies on Mortality From the Use of Paclitaxel-Containing Devices in Japanese Femoropopliteal Disease Patients

Masato Nakamura, MD, PhD; Munenori Takata, MD, PhD; Hiroyoshi Yokoi, MD; Takafumi Ueno, MD, PhD; Yuka Suzuki, PhD; Koji Ikeda, PhD; Takuhiro Yamaguchi, PhD

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Therefore, there were no specific restrictions from the administration on the use of PTX devices.

RWD is useful to confirm the safety and efficacy

PURPOSE OF RWD UTILIZATION

1. Post-marketing surveillance
- Verification of long-term safety and efficacy

2. Single arm study to get approval
- Historical control
- Evaluate the appropriateness of the intended use range

3. Promotion of appropriate use
- Expansion of indications
- Revision of guidelines for appropriate use etc.

APPLICATION EXAMPLES IN MEDICAL DEVICE APPROVAL REVIEW

Device	Product Overview	Application	Utilized Registry
EXCOR Pediatric	Extracorporeal Assistive Artificial Heart	External Comparison	ELSO-DB/ECMO
Najuta stent grafy	Stent graft	External Comparison	JACVSD
HVAD	Extracorporeal Assistive Artificial Heart	External Comparison	INTERMACS
daVinci	Robotic surgery	External Comparison	STS-DB
MitraClip NT		External Comparison	Duke University-DB
SATAKE・HotBalloon catheter	Catheter ablation	External Comparison	J-CARAF
HeartMate3	Extracorporeal Assistive Artificial Heart	External Comparison	INTERMACS
Paxman Scalp Cooling	Head cooling device	Reference information	Netherlands Comprehensive Cancer Organisation（IKNL）
Edwards Sapien 3	TAVA valve	Reference information	TVT Registry
Evolut R	TAVA valve	Reference information	TVT Registry

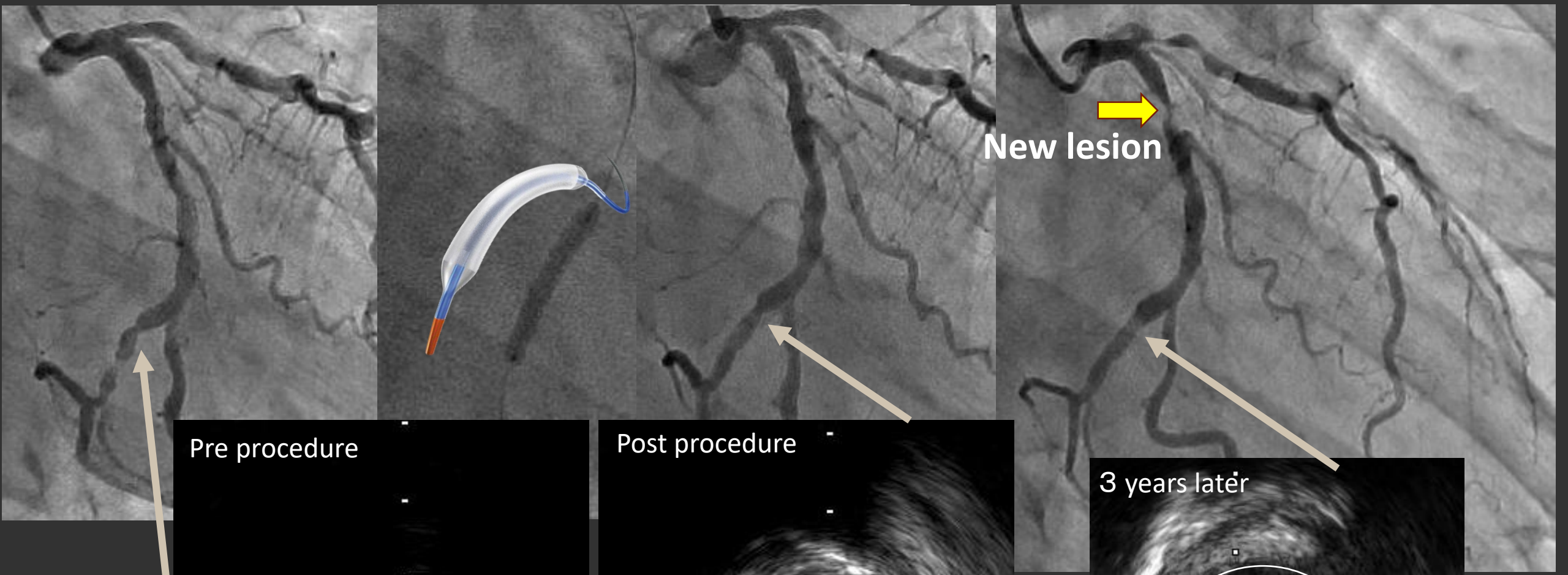
石井健介,医療機器分野におけるRWDの活用、医薬う品医療機器レギュラトリーサイエンス　Vol.52　Ｎｏ．５（2021）Table3改編

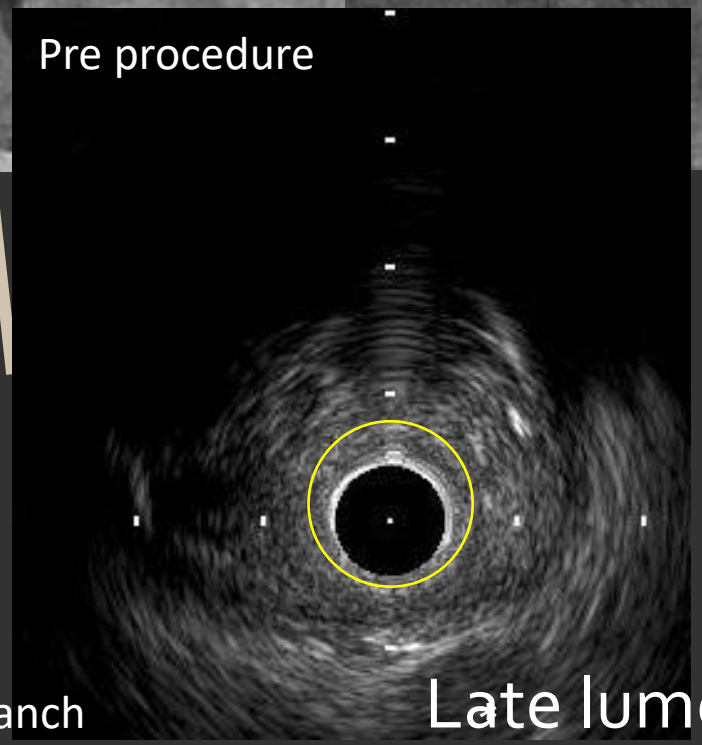
PURPOSE OF RWD UTILIZATION

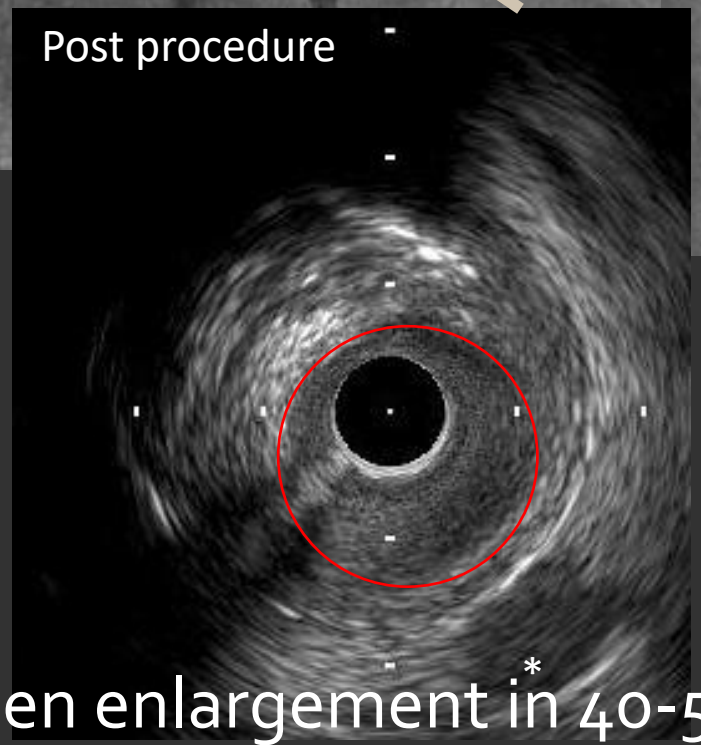
1. Post-marketing surveillance
   - Verification of long-term safety and efficacy
2. Single arm study to get approval
   - Historical control
   - Evaluate the appropriateness of the intended use range
3. Promotion of appropriate use
   - Expansion of indications
   - Revision of guidelines for appropriate use etc.

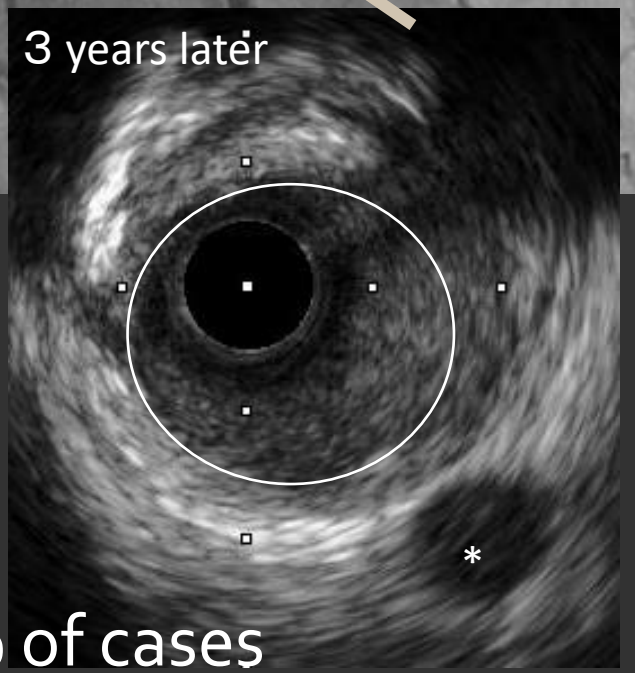
NEXT WAVE OF DEVICE LAG RESOLVED
LIMITATIONS ON GROWTH OF SOCIAL HEALTH CARE SPENDING

- What are the indications for new therapeutic devices (after elimination of device lag)?
- Limited use
  - Approved indication is narrow.
  - Clinical use is restricted by Appropriate use criteria
- There is a large gap between approved and expected indication
  - These are disadvantages of elimination of device lag exposed.







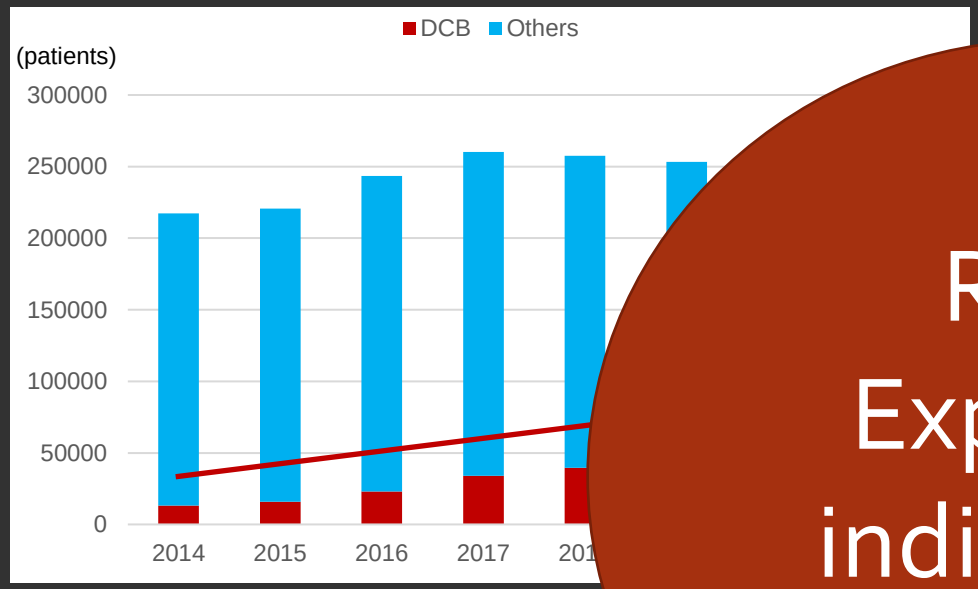


*: side branch

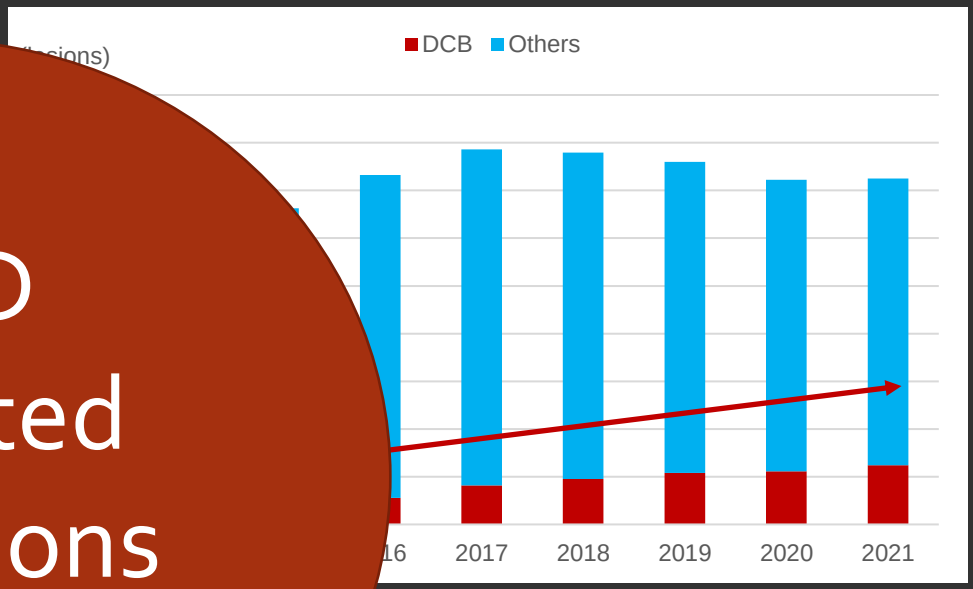
Late lumen enlargement* in 40-50% of cases

CHANGES OF THE DCB USAGE IN THE J-PCI REGISTRY (2014-2021) ON LEVEL USE IS ISR AND SMALL VESSEL DISEASE

Per patient analysis



Per lesion analysis



RWD
Expected
indications

Current indication

Number and the proportion … increasing trend in Japan.
This suggests … and off-level.

Muramatsu T, et.al. Catheter Cardiovasc Interv (Epub ahead of print)

Current indication is limited to ISR and small vessel disease

ALLIANCE Registry

ALLIANCE registry has been launched.

- DCB all comer trial
  - 60 sites in Japan
- Consultation with PMDA completed
- Started in August with a target enrollment of (2,000) patients.
  - 350 cases >3.0mm DCB

- Expected outcomes
  - Expansion of DCB indication
  - Revision of DCB appropriate use criteria

ALLIANCE Registry

2023/December/ 8

AGENDA

- Utilization of RWDs
  - Current situation in Japan
- Issue
  - Data acquisition
  - Reliability
  - Sustainability

ISSUES

- Data must be collected, accumulated, and managed under certain rules to ensure reliability as data used for regulatory applications.
- The purpose of each device is different, and the observation items and time period are not uniform. Many registries will be needed.
- In order to create a registry for sustainable RWD utilization, framework and system need to be established.
- It is necessary to reduce the cost of data collection and increase the volume of accumulated data by enabling secondary use of data in clinical trials for different devices.

SUMMARY

- Due to changes in the historical background, the indications for new medical devices are subject to many restrictions.
- Retrospective Use of RWD shows Paclitaxel related devices does not raise life-effect concerns in Japan.
- A new attempt to utilize RWD in a prospective manner has been initiated.
- PMDA approval applications need credibility and a means to avoid bias.
- Continuous challenge and corporation by industry, government and academia is essential.

THANK YOU FOR YOUR ATTENTION