10 min

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

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COI Disclosure

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⑩Grant : none

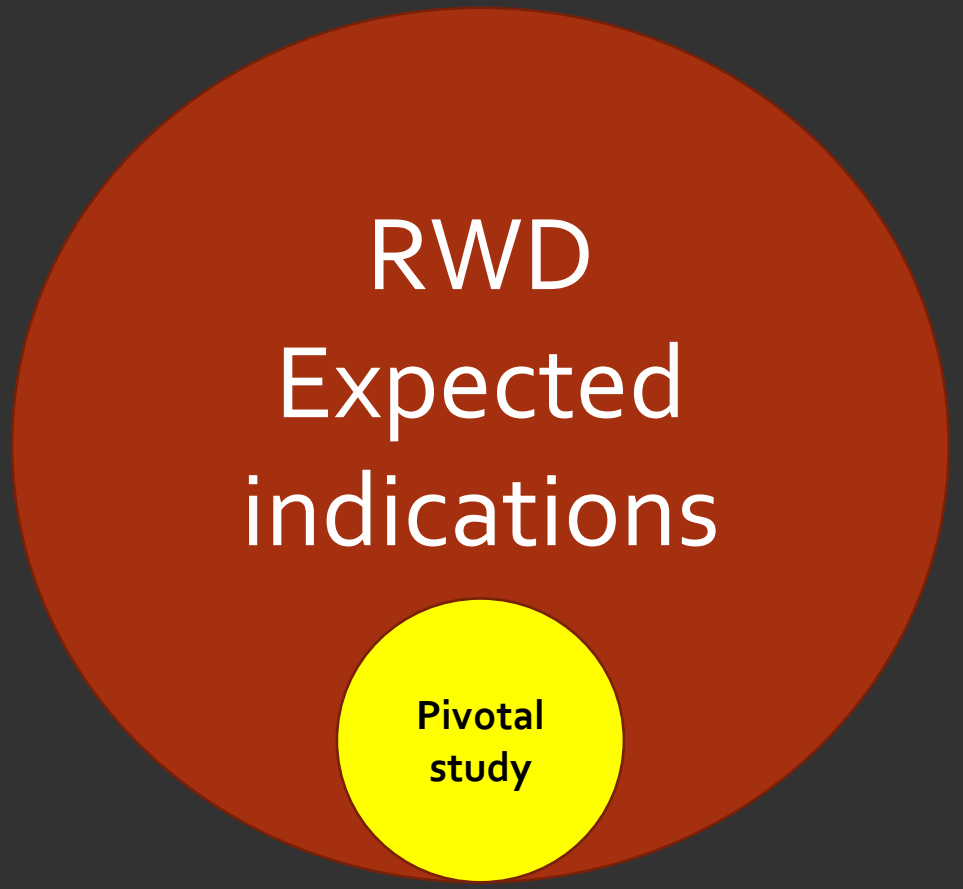
AGENDA

- Background
  - Current situation in Japan
- RWD for the pre and post marketing evaluation
  - The use of Paclitaxel related medical device in Japan
  - RWD for establishing adequate use criteria(AUC)
  - Sustainability

CARDIOVASCULAR MEDICAL DEVICES ARE IN PARTICULARLY GREAT DEMAND, AND ACTUAL INDICATIONS VARY GREATLY?

Current status

- The device lag issue has been resolved.
  - The information gap between Japan and other countries regarding new devices is getting smaller.
- Studies to obtain approval for new devices are small and limited to simple cases.
  - Narrow indication of initial approval .
  - Practice has been controlled by guidance for appropriate use
  - Facility and operator criteria
- Large gap between real indication and on-level use.



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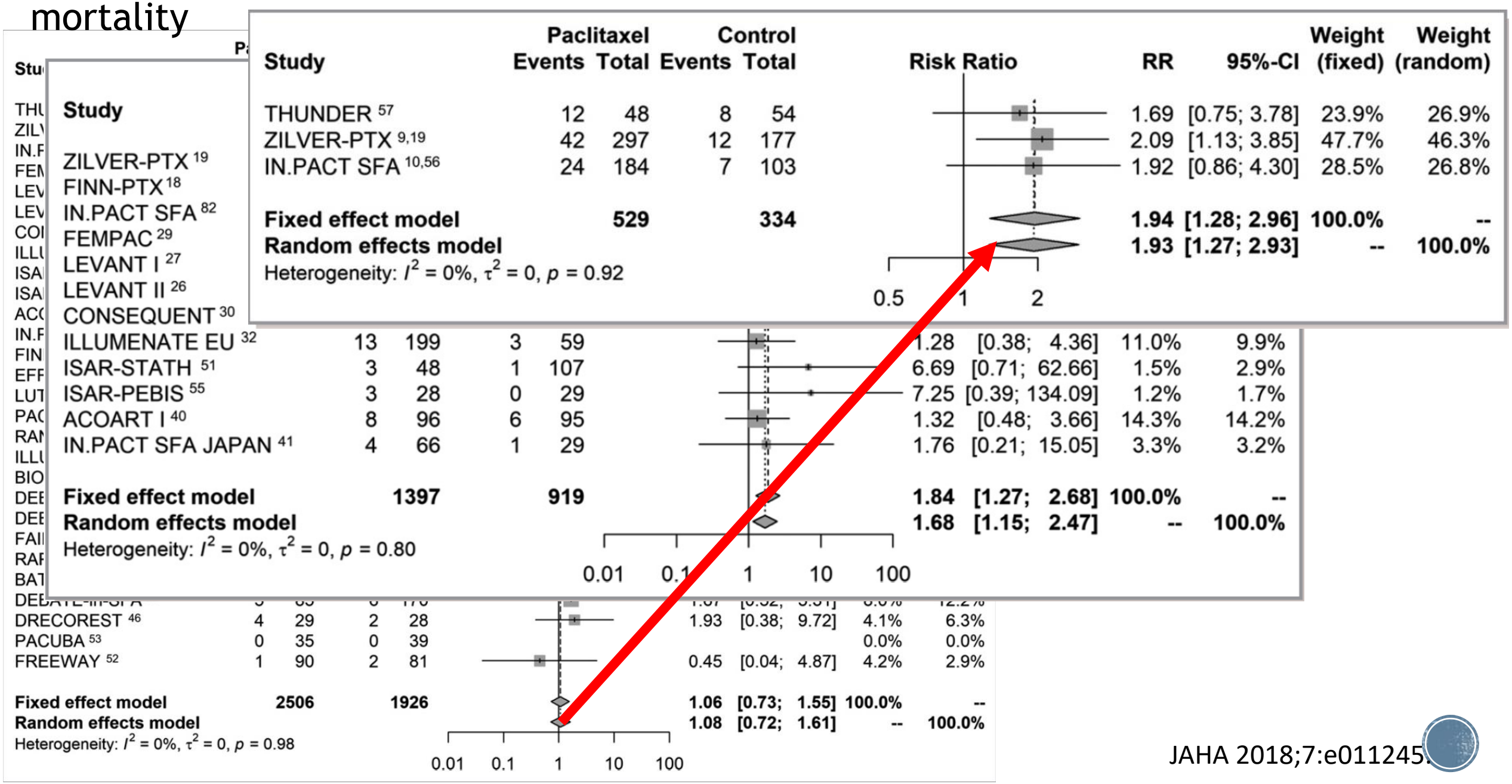
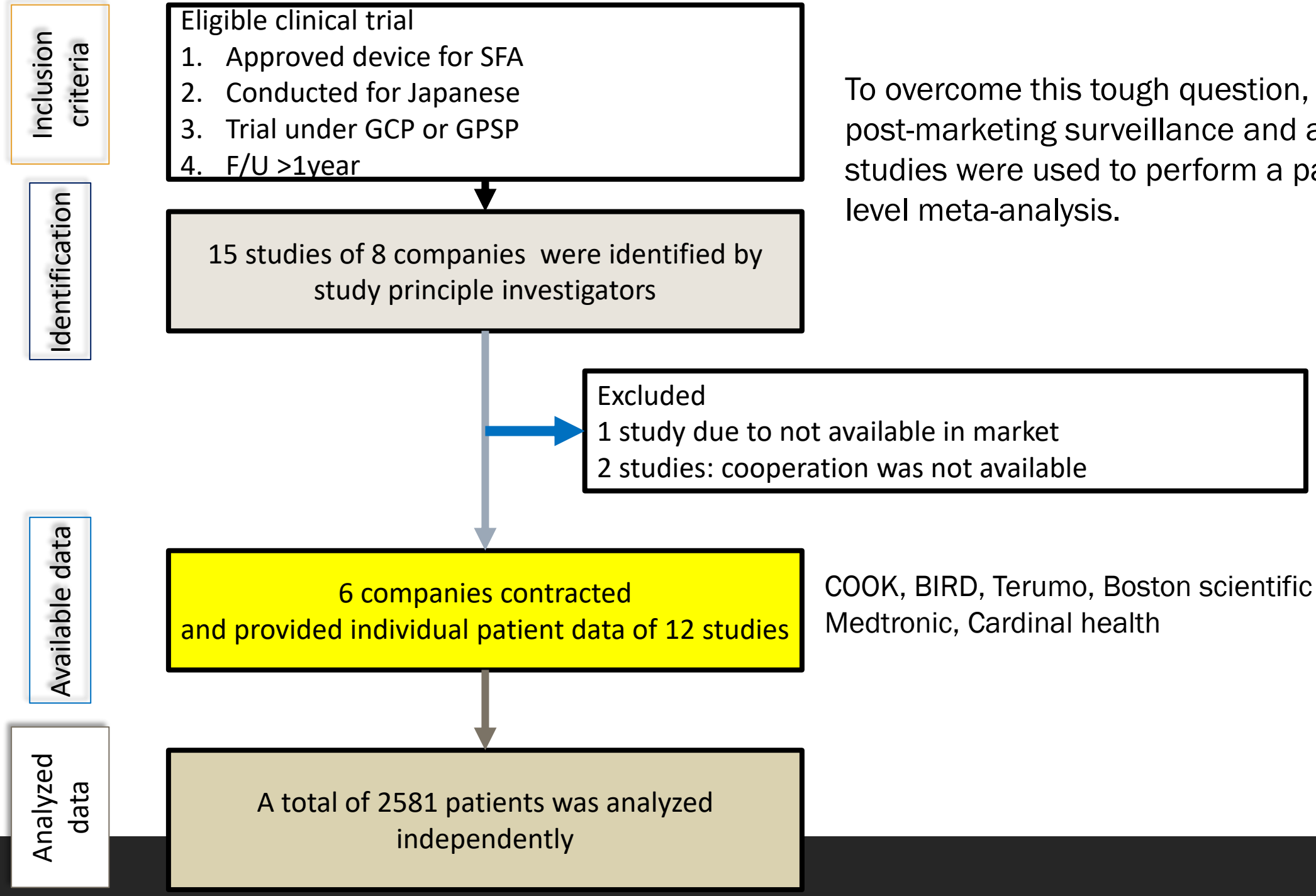
A meta-analysis of Katsanos et al suggested the harmful effect of PTXD on long-term mortality



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

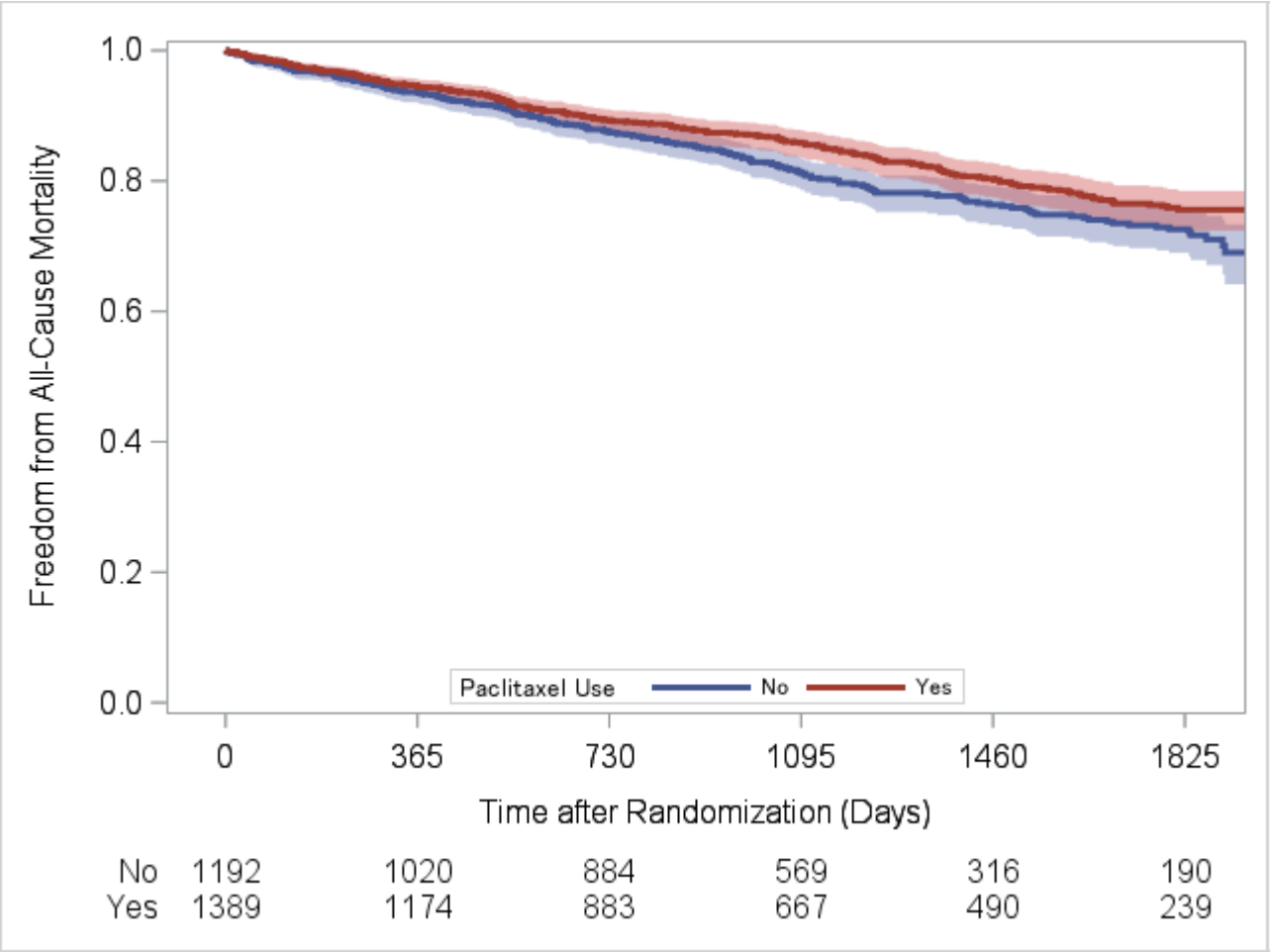
6 companies, 12 trials

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

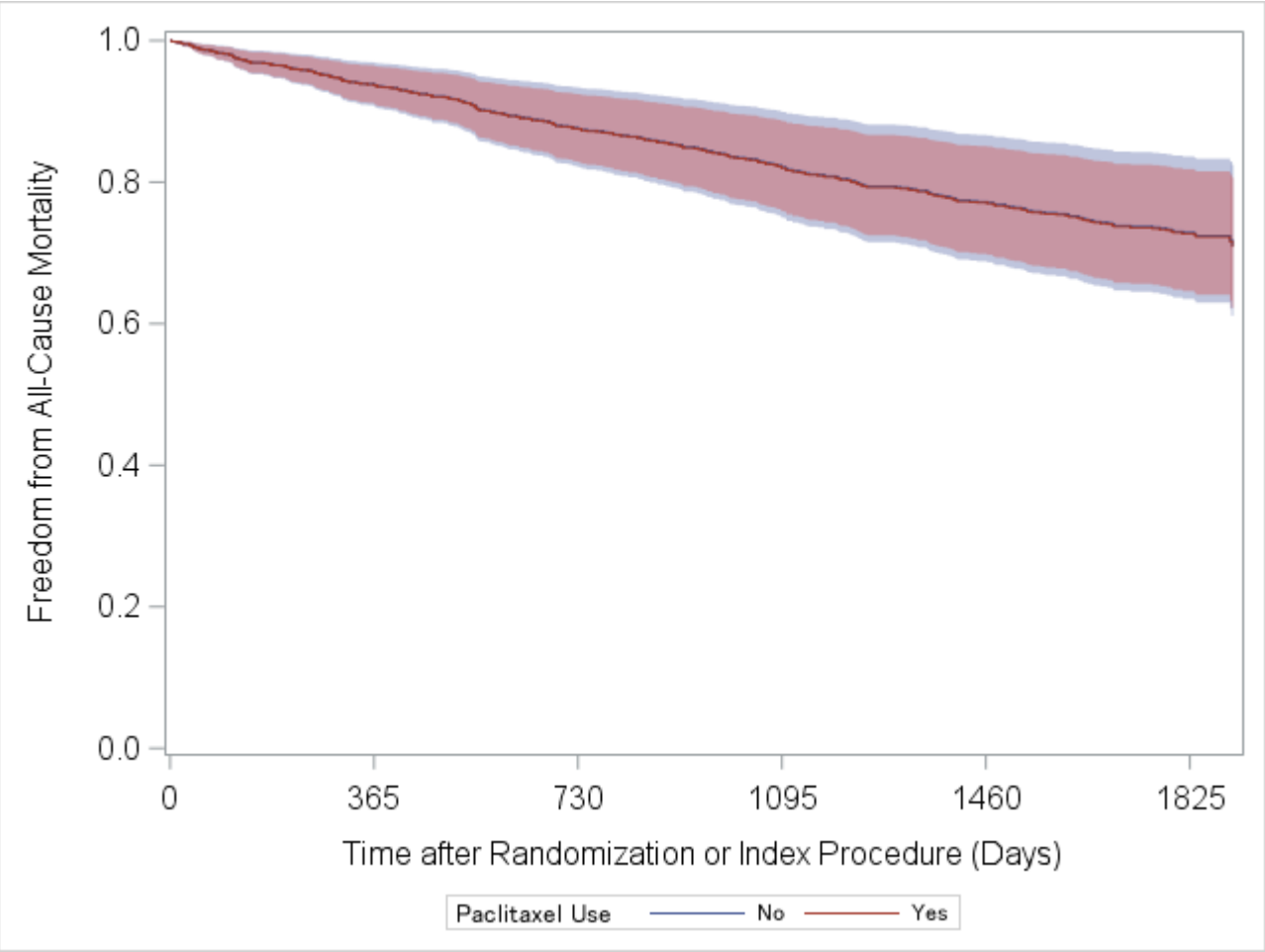
Post marketing surveillance
5 single arm study
n=955

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

Circulation Journal
doi:10.1253/circj.CJ-21-0171

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

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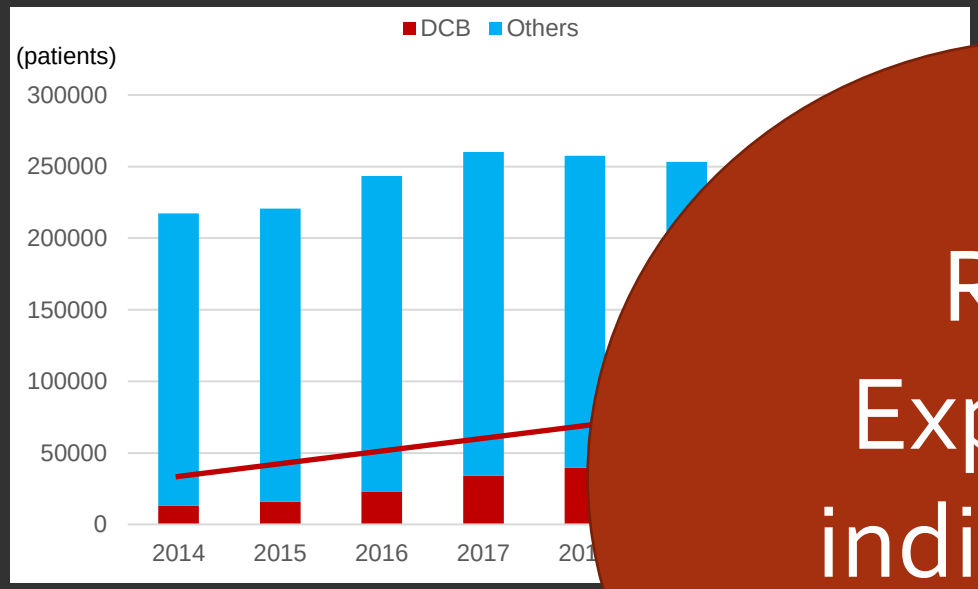
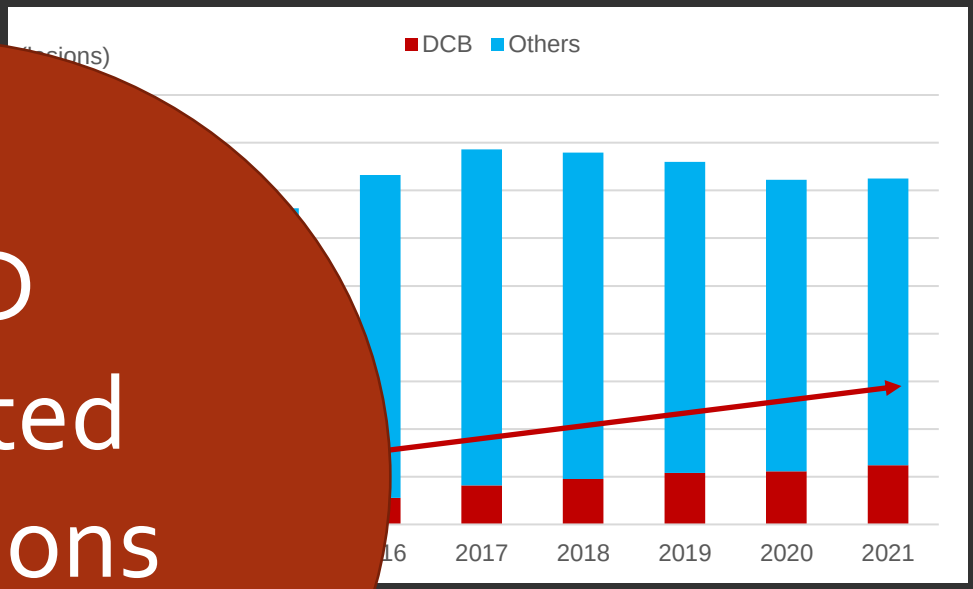
CHANGES OF THE DCB USAGE IN THE J-PCI REGISTRY (2014-2021) ON LEVEL USE IS ISR AND SMALL VESSEL DISEASE

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)

Japanese current situation 2

- In Japan, reimbursement is based on approved indication.
- Off level use is basically not recommended and reimbursement is not sure.
- Therefore, package insert is crucial.

WHEN CONSIDERING THE EXPANSION OF ADAPTATION USING RWD

Challenges

1. Need to revise the attached text.

2. Need to submit plans in advance and address concerns such as selection bias, misclassification, and confounding factors

3. Reliability and validity must be assured for the use of RWDs

CHALLENGE : ESTABLISHMENT OF RWD

- Meaningful Real world data
  - Available for assessment

- Protocol
  - How large is the registry
    - To approve the hypothesis
  - Avoidance of selection bias
  - Assurance of reliability

- All comer
  - All cases to the extent deemed appropriate

  ⇒Collaboration with CVIT
  - How to evaluate being an all-comer

  ⇒Check it in the log
- Assurance of reliability (EDC is the principle)
  - Select the facilities with extensive experience in clinical trials
  - Monitoring and Auditing (How rigorous)
  - Managed by many procedure manuals

ALLIANCE Registry

- DCB all comer trial planned
- Consultation with PMDA completed
- Trial started in August at 60 sites with a target enrollment of (1,500, up to 2,000) patients.
- More than half of the patients have already been enrolled

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EXPECTED EFFECTS ON PRACTICE

- This trial will open up new avenues and promote the rebalancing of new medical devices before and after approval.
- It will be possible to review and revise the guidelines for appropriate use crioteria, which will promote proper use in actual clinical practice.
- The established EDC can continue to be used for similar devices.
- Know how of highly reliable RWD accumulation will be accumulated, and various procedure manuals will serve as milestones for future registries.
- If an optimal performance goal (OPG) can be established based on the accumulated data, it will be possible to conduct an approval trial using a short-group study.

FINAL CHALLENGE

- The Spirit of HBD
- Success story is mandatory

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.
- Reliability and means to avoid bias are needed.
- Challenging, but we believe that a new world will unfold.

THANK YOU FOR YOUR ATTENTION

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 indications based on pivotal trial.
  - Often not enough experience in daily practice
- Limited use
  - Clinical use is restricted by Good Clinical Practice Standards
  - Use is permitted only in limited facilities.
  - These are disadvantages of elimination of device lag exposed.