



# Industry Perspective on Paclitaxel DCB and DES Evaluations

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# Background

SYSTEMATIC REVIEW AND META-ANALYSIS



## Risk of Death Following Application of Paclitaxel-Coated Balloons and Stents in the Femoropopliteal Artery of the Leg: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Konstantinos Katsanos, MD, PhD, MSc, EBIR; Stavros Spiliopoulos, MD, PhD; Panagiotis Kitrou, MD, PhD; Miltiadis Krokidis, MD, PhD; Dimitrios Kamabatidis, MD, PhD

**Conclusions**—There is increased risk of death following application of paclitaxel-coated balloons and stents in the femoropopliteal artery of the lower limbs. Further investigations are urgently warranted.



# Result

- All Peripheral Products containing PACLITAXEL are on **mandatory suspension** for the next 90 days. These includes the following:

BSCI Eluvia- DES PV

Cook PTX Zilver- DEZS PV

- MDT- IN Pact Admiral- DCB

Bard/Becton- Lutonix DCB

Spectranetics- Stellarex- DCB



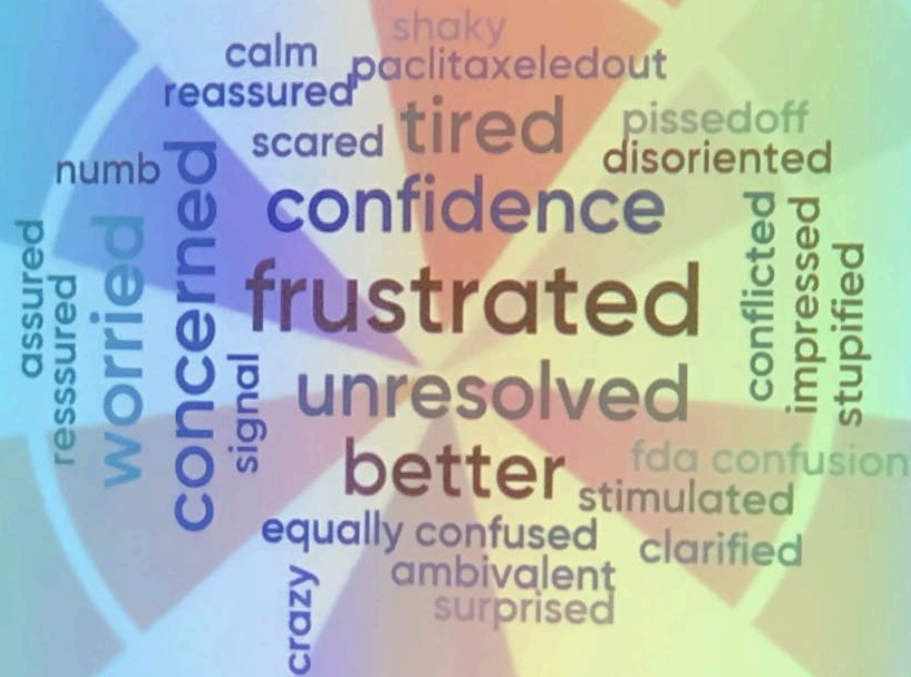
# Result

- Industry is committed to patient safety
  - Individual companies have performed additional analyses of patient-level data, and are presenting and publishing results
  - Close cooperation with regulators and physician groups to determine if signal is real and identify cause
- Requests from multiple regulators for additional information
  - FDA, PMDA request for patient-level data; perform own analyses
- FDA Letters to Healthcare Providers
  - January 17: “Currently, the FDA believes that the benefits continue to outweigh the risks...”
  - March 15: “Identified a potentially concerning signal... alternative treatment options... should generally be used until additional analysis... has been performed”
- Numerous townhalls and a standalone forum
  - LINC, ISET, JET, CRT, CX, VIVA-VLF, etc.
  - Lots of discussion...lots of continued uncertainty



# Result

Give us one word about how you're feeling coming out of this meeting.



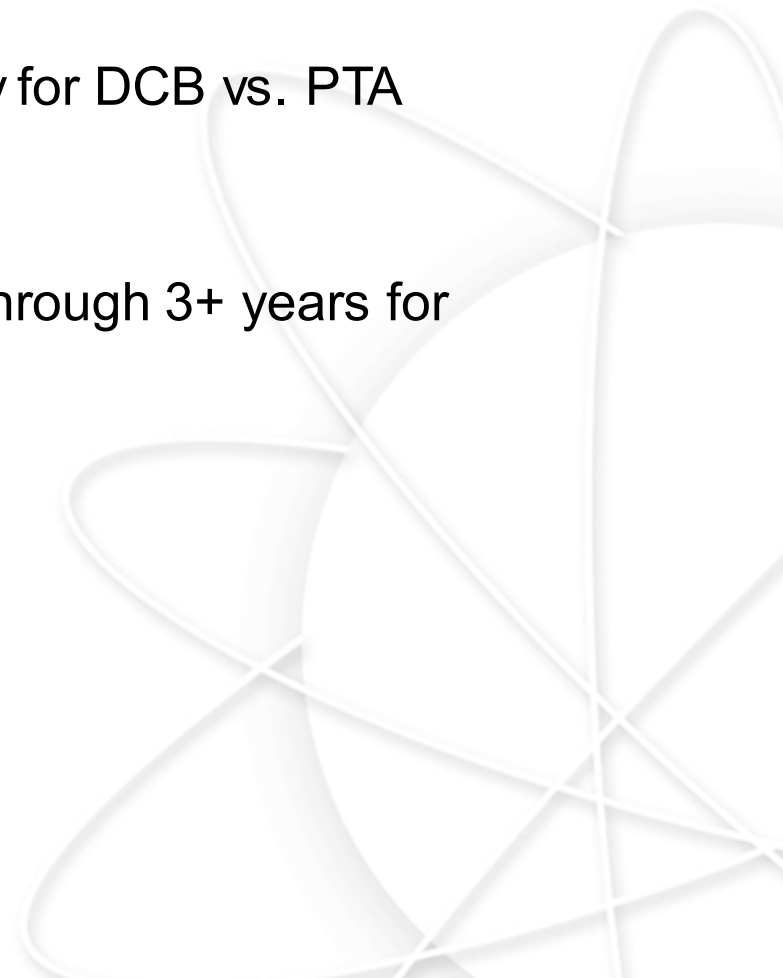
# What is the Path Forward?

- Patient-level analyses
  - All industry RCT data
    - Ongoing (FDA, VIVA, others?)
  - ALL data (RCT + Registries)
    - Individual company efforts
    - Combined efforts?
    - Major challenge – how to compare non-randomized data?
      - e.g., claudicants vs. CLI



# What is the Path Forward?

- “Big Data” Sources?
  - Jones, CRT 2019
    - Significantly **lower** 1-year mortality for DCB vs. PTA
  - Secemsky, et al.
    - No mortality difference, including through 3+ years for Zilver PTX DES
    - Limited to in-patient only



# What is the Path Forward?

JAMA Cardiology | Original Investigation

## Association of Survival With Femoropopliteal Artery Revascularization With Drug-Coated Devices

Eric A. Secemsky, MD, MSc; Harun Kundi, MD; Ido Weinberg, MD; Michael R. Jaff, DO; Anna Krawisz, MD; Sahil A. Parikh, MD; Joshua A. Beckman, MD; Jihad Mustapha, MD; Kenneth Rosenfield, MD; Robert W. Yeh, MD

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March 1, 2019

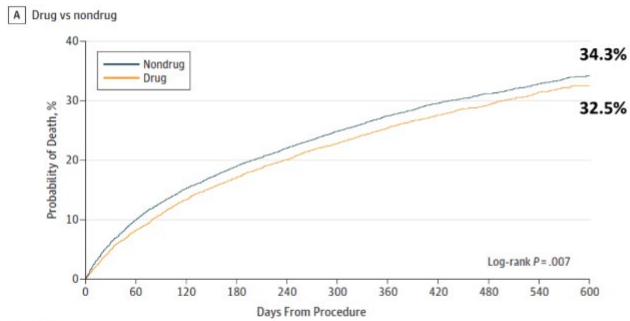
### Drug-Eluting Stent Implantation and Long-Term Survival Following Peripheral Artery Revascularization

Eric A. Secemsky, Harun Kundi, Ido Weinberg, Marc Schermerhorn, Joshua A. Beckman, Sahil A. Parikh, Michael R. Jaff, Jihad Mustapha, Kenneth Rosenfield and Robert W. Yeh

<http://www.onlinejacc.org/content/early/recent>



### All Patients, All Devices



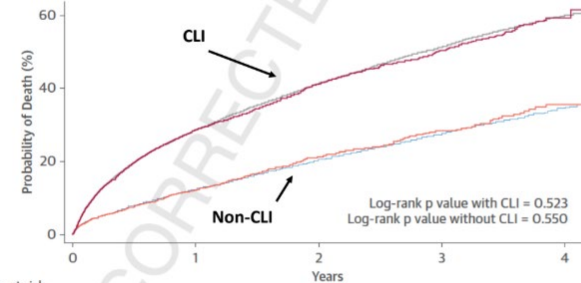
**\*No difference in survival in adjusted analysis**

- **Adjusted HR 0.97; 95% CI, 0.91-1.04; P = .43**

No. at risk	0	60	120	180	240	300	360	420	480	540	600
Drug	5989	5500	5189	4966	4785	4229	3363	2552	1817	1046	298
Nondrug	10571	9517	8955	8560	8237	7321	5935	4610	3337	2016	670



### Long-Term Survival after Peripheral DES



**\*No difference in survival in adjusted analyses**

- **CLI: Adjusted HR 0.97; 95%CI, 0.92-1.03; P = .32**
- **Non-CLI: Adjusted HR 1.01; 95%CI, 0.91-1.13; P = .80**

No. at risk	0	1	2	3	4
BMS without CLI	19,305	16,878	11,923	6,443	666
DES without CLI	1,443	1,267	800	378	35
BMS with CLI	28,046	19,996	12,280	5,570	534
DES with CLI	2,662	1,896	1,020	418	33





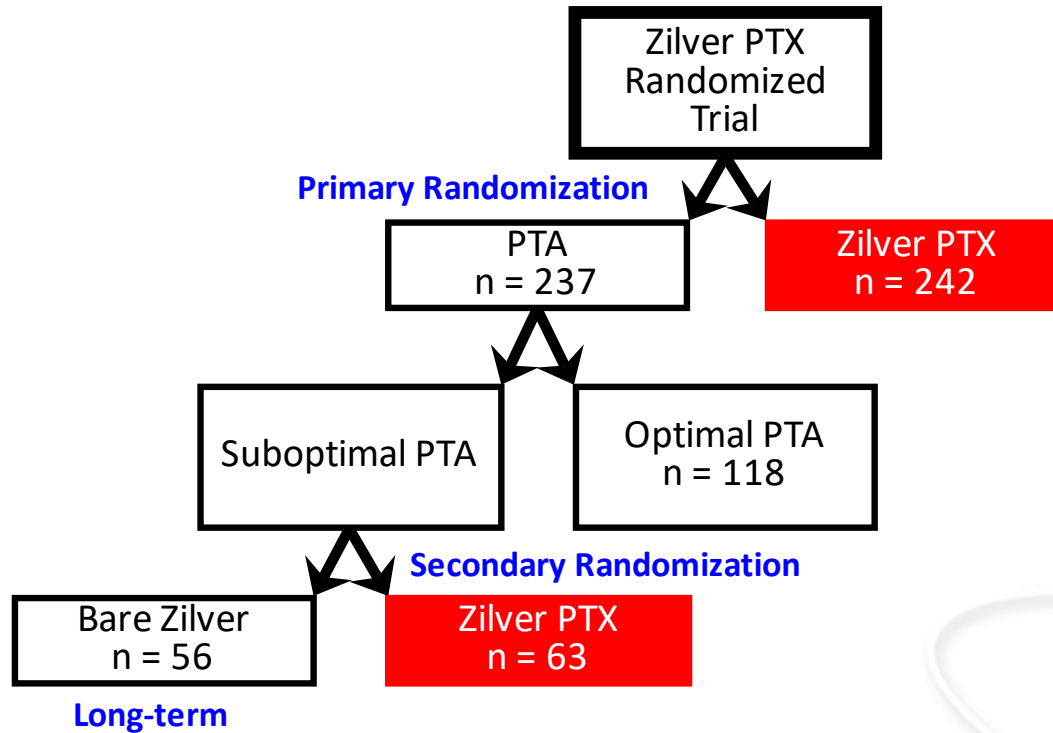
# What is the Path Forward?

- **Challenges**

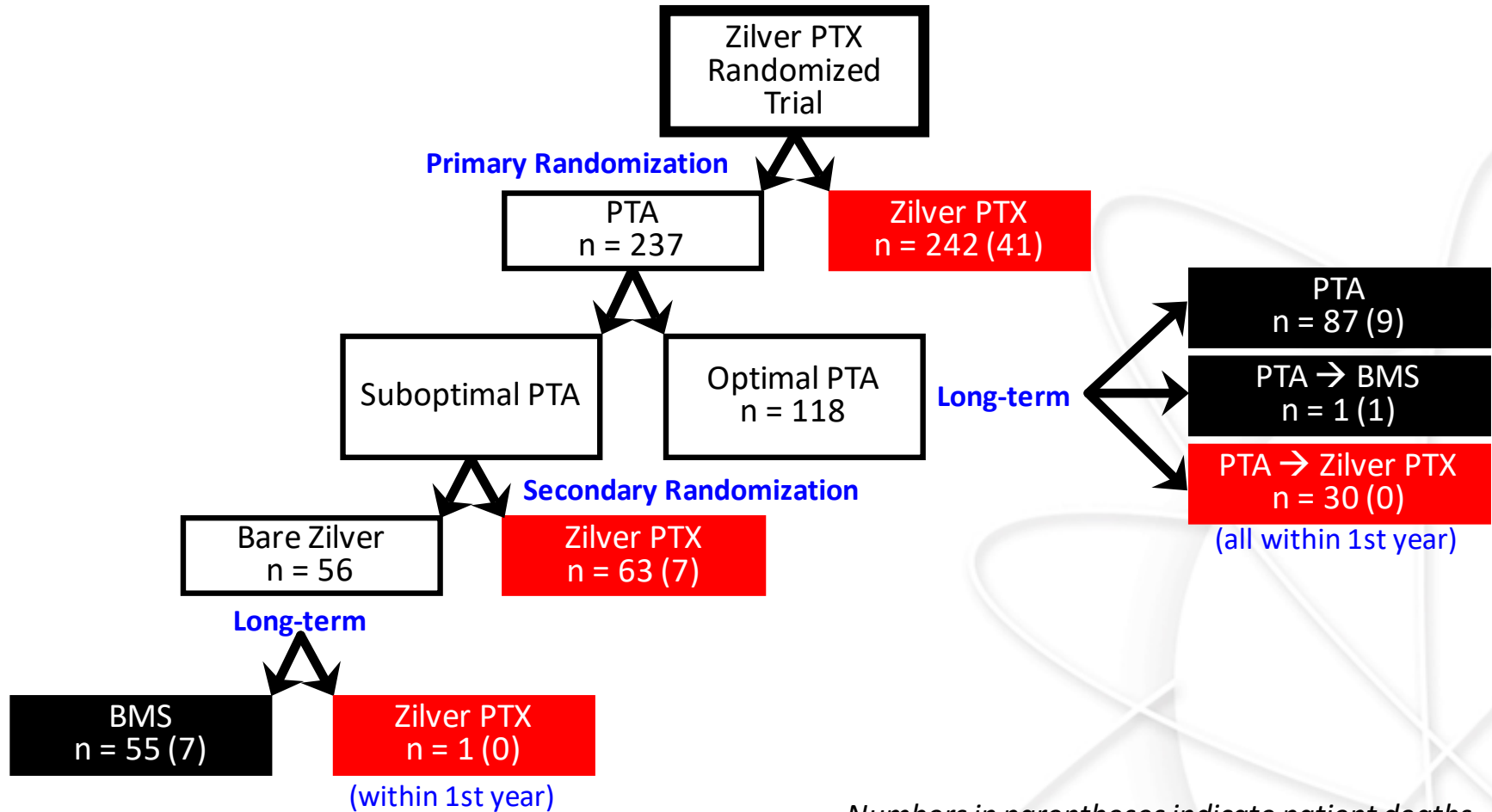
- Long-term follow-up data
  - Can we link datasets to assess long-term mortality?
- Multiple, non-randomized data sources
  - Different devices
  - Different study designs
  - Substantial number of patients lost to follow-up over time
  - Analysis plan needs to accommodate
- Lack of patient-level details
  - Core data elements will help in future
  - Cause of death; detail often limited
  - How to identify ANY use of paclitaxel device



# Cook Example



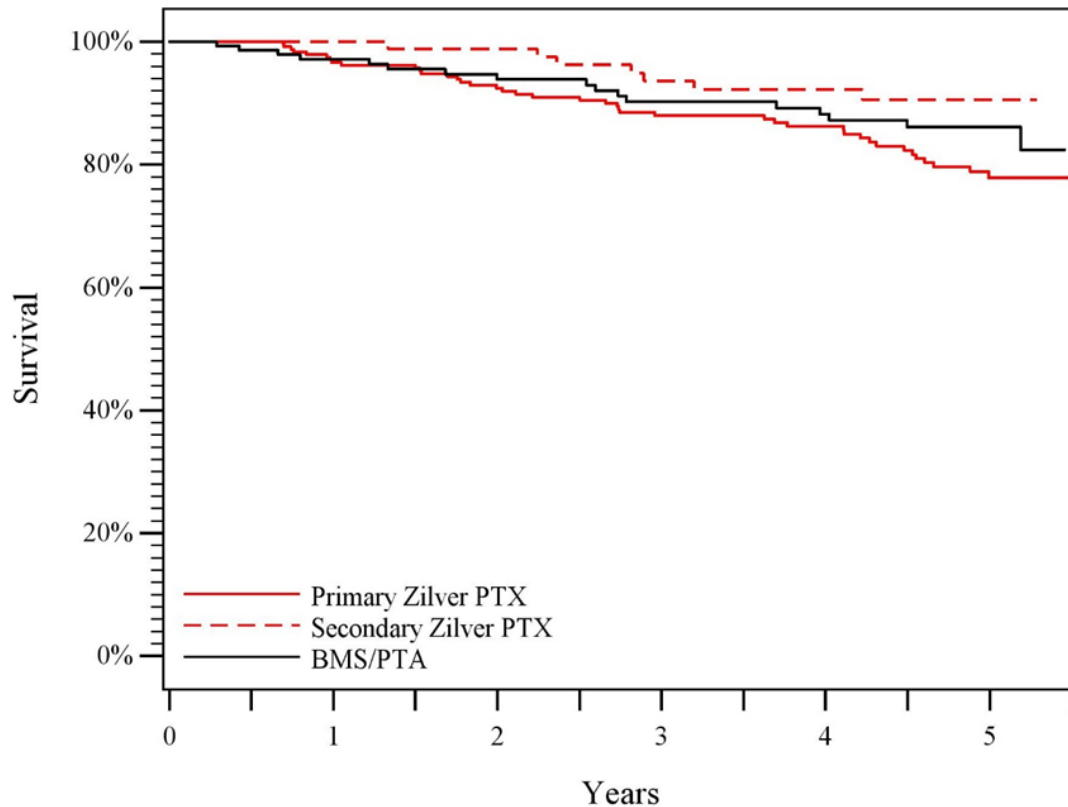
# Cook Example



Numbers in parentheses indicate patient deaths



# Cook Example



PTA / BMS  
 n = 143  
 Died = 17  
 KM = 17.6%

Zilver PTX  
 n = 242  
 Died = 41  
 KM = 22.1%

?

Zilver PTX  
 n = 94  
 Died = 7  
 KM = 9.4%



# What is the Path Forward?

- What can we do **now**, and how can we use this as an example for a potential future role for RAPID, NESTcc, etc.?
  - Signal identified--leverage data to understand signal (is it real?) and its cause
  - Efficient collection of additional data (faster, cheaper)
- FDA Advisory Panel meeting being planned

