How to Proceed to Generate More Evidence on Patient Safety With Drug-eluting Devices

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Disclosure

Peter A. Schneider, MD

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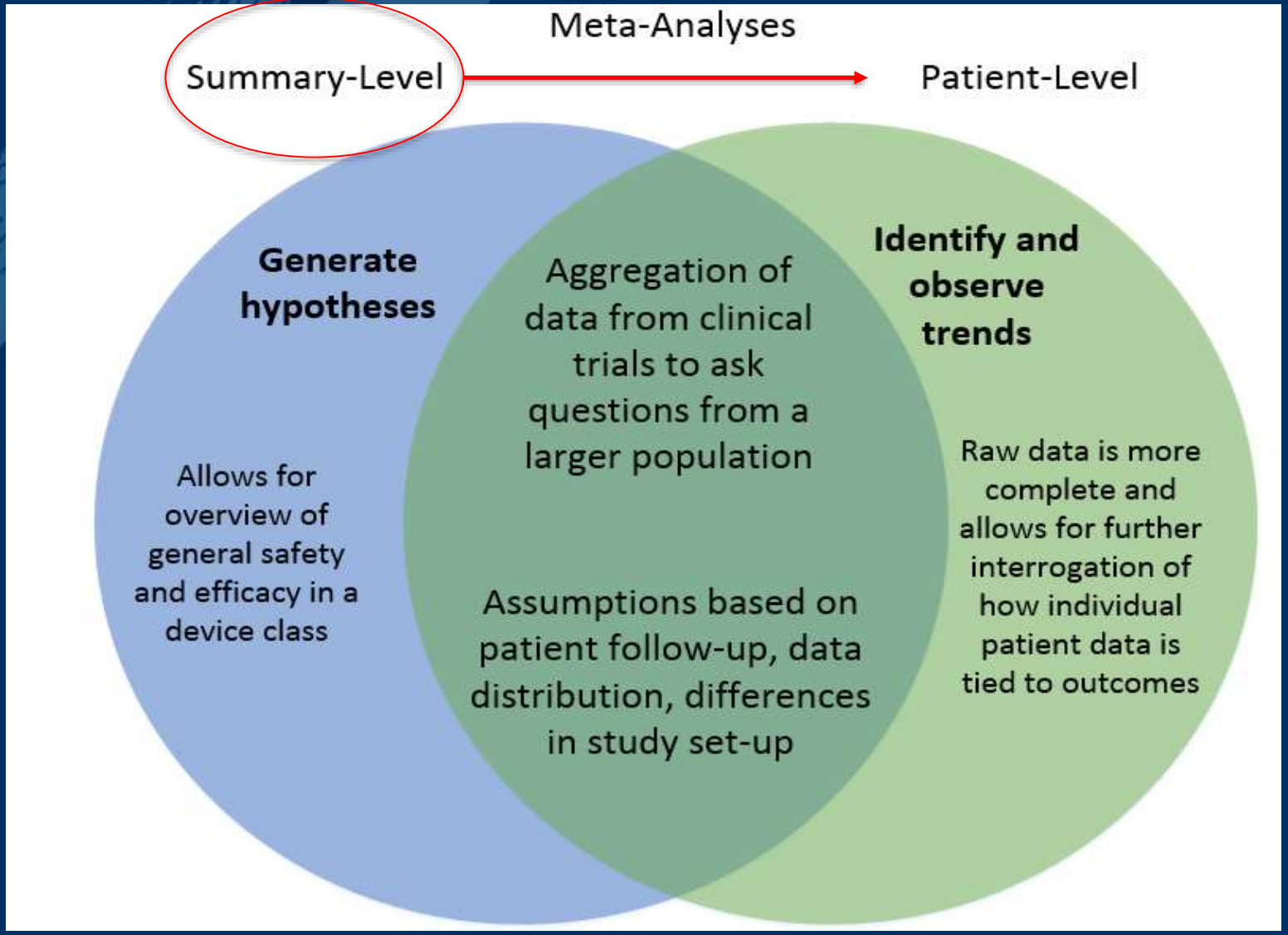
Potential conflicts of interest to report:

Consulting: Silk Road, Surmodics, Profusa, CSI, Cardinal, Terumo

Chief Medical Officer: Intact Vascular, Cagent, Vesper

Scientific Advisory Board: Abbott, Medtronic, Boston Scientific

Summary-level versus Patient-level Meta-Analysis



Drug-eluting Devices
Some unique characteristics of these trials.

- Powered for shorter-term patency, not long-term mortality.
- Control groups are small (some RCTs 2:1).
- Not clear if valid to include DCB and DES in same analysis.
- Expected attrition due to age and co-morbid factors.
- Missing data, censored patients.
- Assumptions about drug kinetics.
- Chance results (lowest mortality ever reported in PTA group in an RCT).

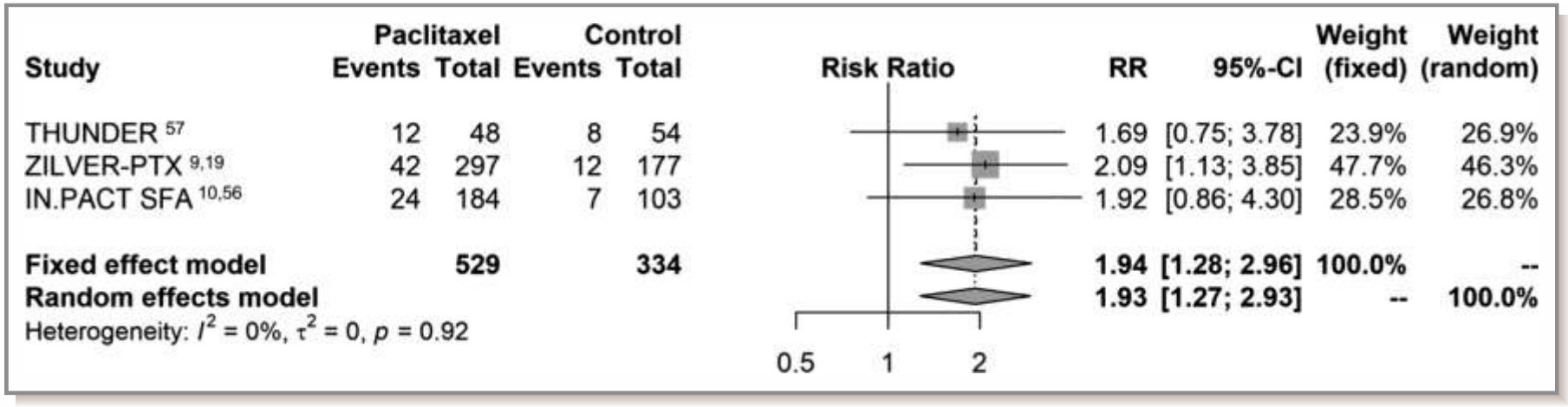


Figure 3. Random effects forest plot of all-cause death at 4 to 5 years. Pooled point estimate was expressed as risk ratio (RR).

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.

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Coincidental, statistical aberration, real danger sign?

What is the mechanism?

Drug-eluting Devices

VIVA: Vascular Leaders Forum

Washington, DC March 1-2

Multidisciplinary, multispecialty vascular specialists

Trial Principal Investigators

Regulatory agencies

Paclitaxel device manufacturers

Oncology, pharmacology, basic science, statistics

Drug-eluting Devices

VIVA: Vascular Leaders Forum

Washington, DC March 1-2

Conflict-of-interest management plan

Answer specific questions that will help inform clinicians until more data is developed

Written report

Steering Committee:

Peter Schneider, Gary Ansel, Josh Beckman, Chris White, Michael Jaff, John Laird, Sean Lyden

Drug-eluting Devices

Patient Level Data

No assumptions about trial conduct or pharmacokinetics or data quality.

Case-by-case analysis.

Calculated doses.

Analyze individual cases of mortality.

Propensity matching.

Test hypotheses: Analyze other potential variables.

Drug-eluting Devices

VIVA: Patient Level Data

VIVA will collaborate will all 5 US companies with commercially available DCB/DES products to share de-identified patient-level data. Vivaphysicians.org

The data sharing agreement will be between each company and an external third party statistical consultant to be selected by a five member Steering Committee via an RFP process with the consent of the VIVA Executive Committee (the RFPs have been distributed).

Krishna Rocha-Singh: Coordinator and Technical Advisor

The SC members are: Chris White, Philip Goodney, Michael Jaff, Juan Granada and Sanjay Misra. This committee will also manage the data presentation/publication process.

Drug-eluting Devices

VIVA: Patient Level Data

A tentative statistical plan to be discussed with a representative from the statistics group at the VLF meeting in March.

The FDA has agreed to comment on the statistic methodologies proposed by the Steering Committee in consultation with the statistical advisor.

All 5 companies (Medtronic, Cook, Boston Scientific, Bard and Philips) are named in a press release about this process.

Drug-eluting Devices

VIVA: Patient Level Data

Unknowns:

- Comparative state of the different databases for these devices and trials.
- Timeline.
- Whether all our concerns will be addressed.
- Whether other trends/issues will be identified.

Drug-Eluting Devices
An Opportunity for the Vascular Community

- Come together and problem-solve.
- Demonstrate best care of our patients.
- To do no harm.
- Dig deeper and understand better the advantages and disadvantages of pharmacologic therapy as part of our lower extremity treatments.

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