DAPT STUDY VS. CONTEMPORARY TRIALS: HOW CAN WE REDUCE THE KNOWLEDGE GAP

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Disclosures

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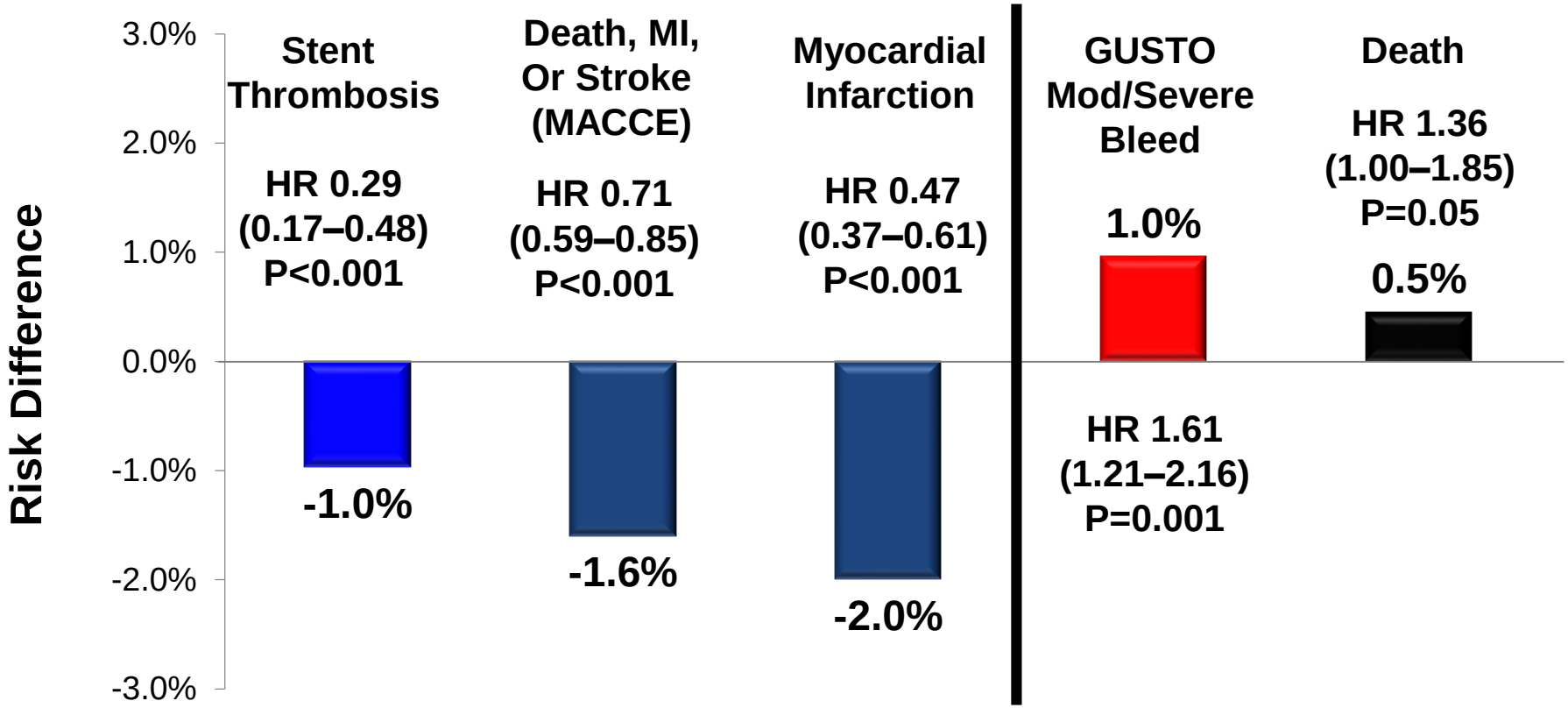
Scylla and Charybdis
Navigating between Bleeding and Thrombosis

Bleeding

Thrombosis

The DAPT Study – Longer is better?
Longer vs. Shorter Duration of Dual Antiplatelet After Coronary Intervention

30 vs. 12 Months of Dual Antiplatelet Therapy in the DAPT Study



Mauri, et al. NEJM. 2014.

Shorter is Better

ITALIC, PRODIGY, RESET, OPTIMIZE, EXCELLENT, NIPPON, SECURITY

– Contemporaneous comparators to the DAPT Study with different top line results

MASTER DAPT

– Contemporary HBR population

TWILIGHT, STOP DAPT-2, GLOBAL LEADERS, SMART CHOICE, TICO

– More contemporary studies evaluating shorter DAPT.

Why the differences?
Reason 1: Different Study Designs

Apart from the DAPT study:

- None of the contemporaneously conducted DAPT duration trials were individually powered for ischemic endpoint including stent thrombosis.
- Most included randomization at index procedure, such that the treatment arms were not different for the first 3-6 months of the study (bias to the null).
- None were placebo controlled and blinded.
- Several were terminated early

The DAPT Study provided the highest quality evidence at the time of its publication

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Reason 2: Different Patient Populations

- **Lots of HBR studies, but few RCTs of DAPT duration**
  - LEADERS FREE - compared stents, not DAPT duration
  - ONYX ONE - compared stents, not DAPT duration
  - Xience 28/90, EVOLVE Short DAPT – single arm.

MASTER DAPT –

- High bleeding risk
- No events in the first month after PCI.

DAPT Study-

- Excluded patients on oral anticoagulation and those with a history of bleeding.
- Excluded patients with any events in the first year after PCI.

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Reason 3: Different Treatments

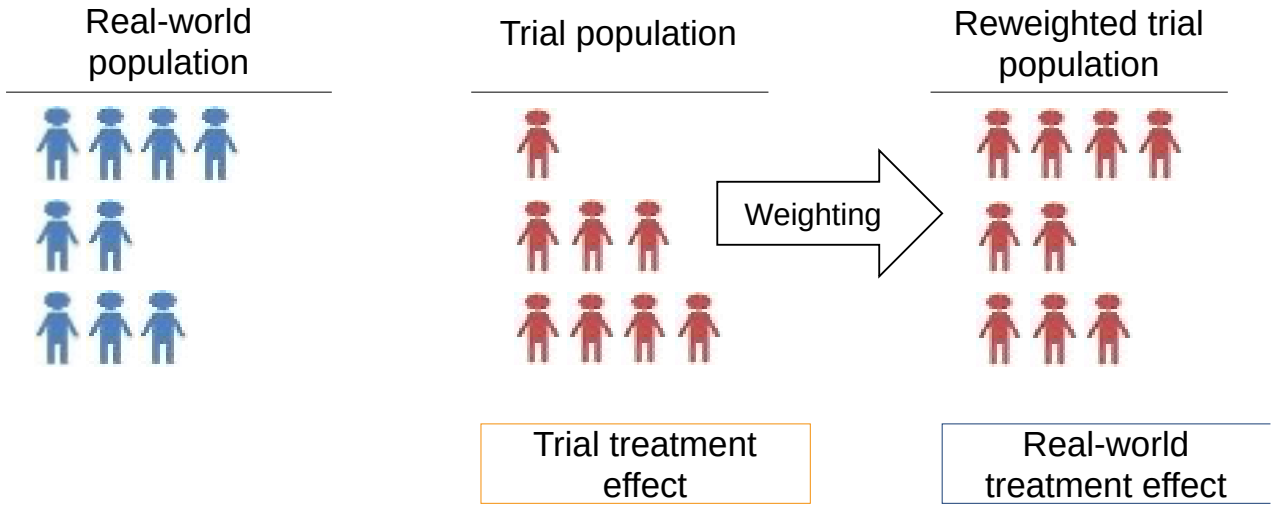
What does 3 months of DAPT mean in 2011 vs. 2021?

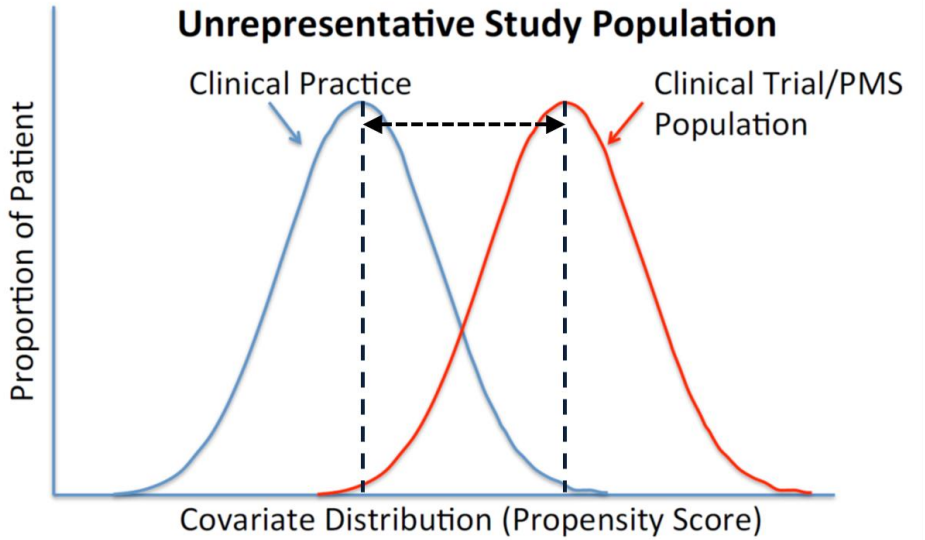
- ASA, clopidogrel followed by ASA monotherapy
- ASA, ticagrelor or prasugrel followed by ASA monotherapy
- ASA, clopidgrel followed by clopidogrel monotherapy
- ASA, ticagrelor followed by ticagrelor monotherapy
- Etc etc.

The DAPT vs. SAPT nomenclature is no longer meaningful

What would the DAPT Study show if conducted today?
Reason 4: Different Eras

- Patient characteristics have changed.
- Stents have changed





New methods to “transport” randomized trial results to new population

Study Designs for Extending Causal Inferences From a Randomized Trial to a Target Population

Issa J. Dahabreh*, Sebastien J.-P. A. Haneuse, James M. Robins, Sarah E. Robertson, Ashley L. Buchanan, Elizabeth A. Stuart, and Miguel A. Hernán

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Dahabreh et al, Biometrics 2019. Am J Epi 2021.

Reweighting of Trial Results Can Inform Treatment Effect In Undersampled Subgroups

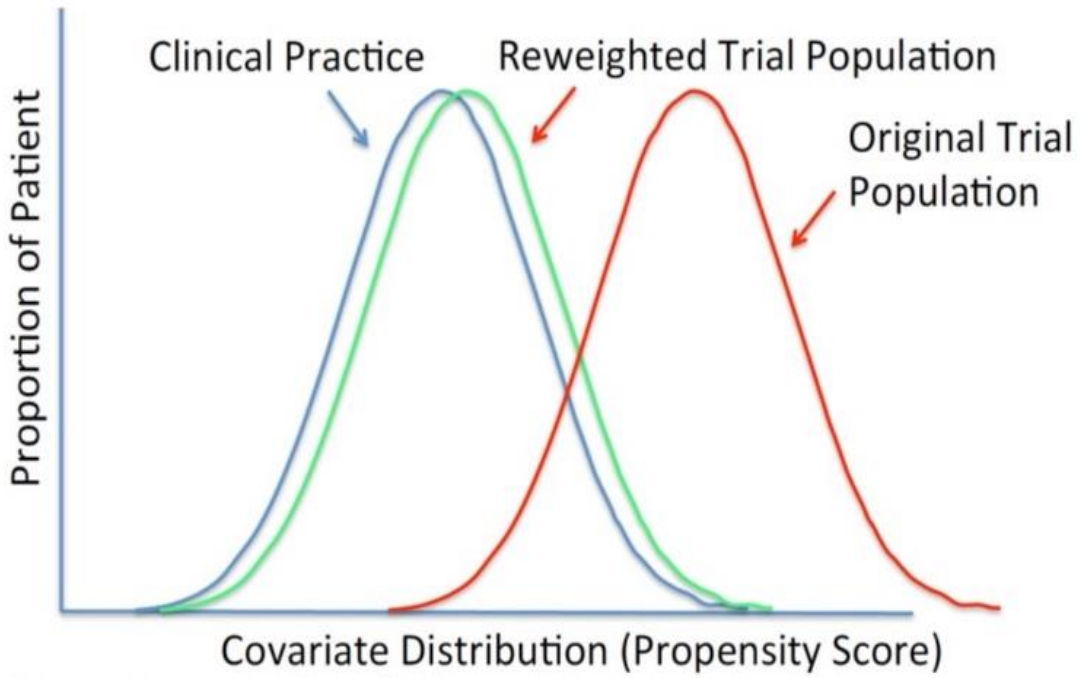


Figure 2. Reweighting of trial populations based on inverse probability of enrollment

Link the DAPT Study the NCDR Cath PCI Study

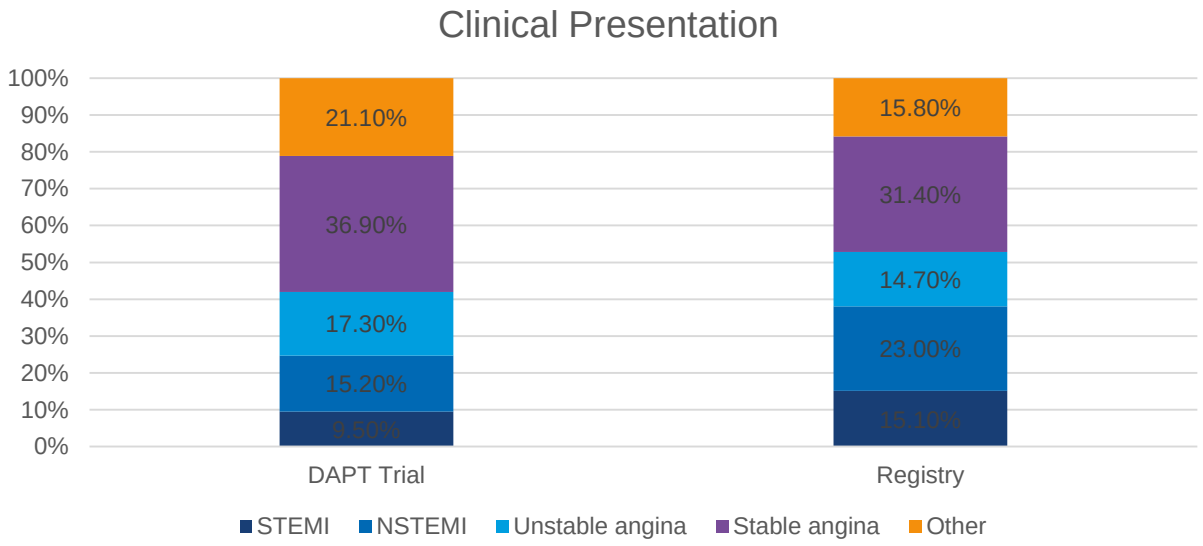
Logistic model for trial partication

$$log\frac{p_i}{1-p_i} = \beta_0 + \beta_1 X_{i1} + \cdots + \beta_p X_{ip}$$

Reweight sample based on inverse odds of trial participation

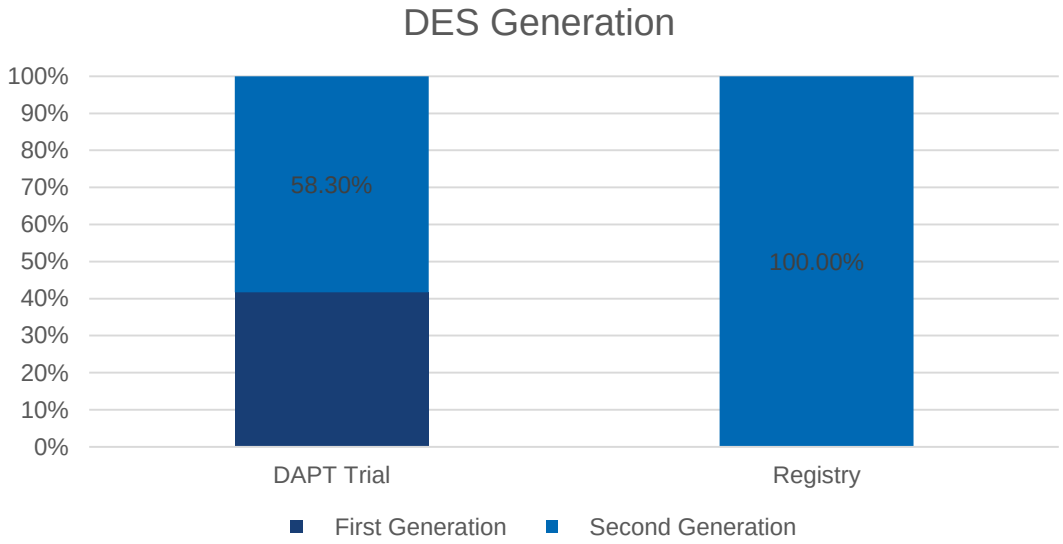
$$w_i = \frac{1-\hat{p}_i}{\hat{p}_i}$$

DAPT Study patients vs. Contermporary All Comer US PCI Patients



Different clinical characteristics

Different technology



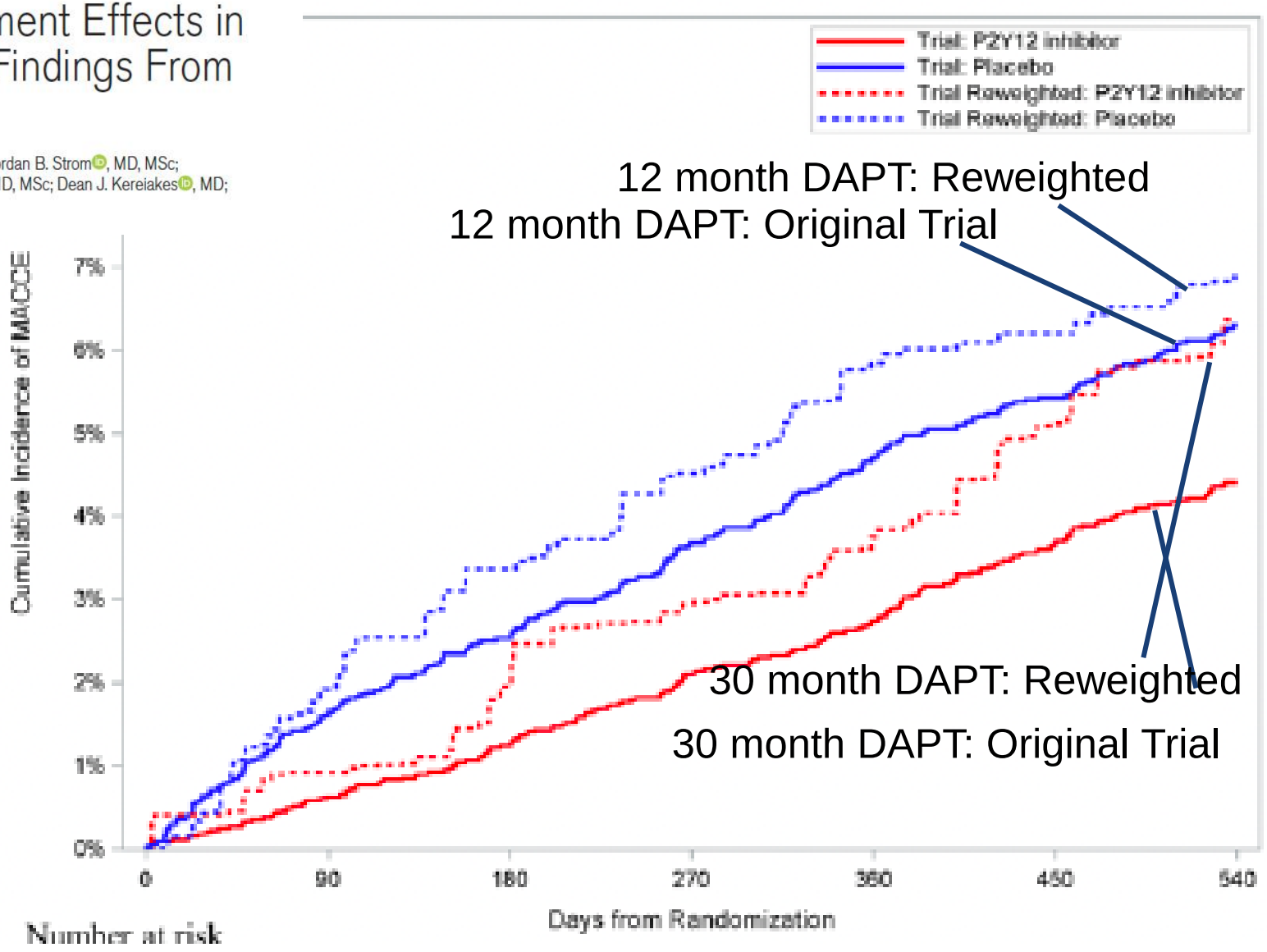
Butala, et al. Circulation 2022

ORIGINAL RESEARCH ARTICLE

Estimation of DAPT Study Treatment Effects in Contemporary Clinical Practice: Findings From the EXTEND-DAPT Study

Neel M. Butala, MD, MBA; Kamil F. Faridi, MD, MSc; Hector Tamez, MD, MPH; Jordan B. Strom, MD, MSc; Yang Song, MSc; Changyu Shen, PhD; Eric A. Secemsky, MD, MSc; Laura Mauri, MD, MSc; Dean J. Kereiakes, MD; Jeptha P. Curtis, MD; C. Michael Gibson, MD, MS; Robert W. Yeh, MD, MSc

MACCE



Butala, et al. Circulation 2022

Persistent Harms, Attenuated Benefits

After transporting DAPT study randomized treatment effect to the NCDR CathPCI target population:

No significant reduction in stent thrombosis or MACCE in reweighted sample.

Persistent increase in bleeding with longer DAPT duration.

DAPT score still distinguishes patients with net benefit vs. harm.

The Evolution of Evidence-Based Medicine: When the Magic of the Randomized Clinical Trial Meets Real-World Data

Seng Chan You and Harlan M. Krumholz

Originally published 10 Jan 2022

Butala, et al. Circulation 2022
You and Krumholz. Circulation 2022.

Reconciling Old and New

The DAPT Study data are reconcilable with contemporary DAPT duration trials

- The DAPT Study demonstrated the strong need for individualization of antiplatelet strategies. This is still true today.
- Improvements in stent design have diminished the benefits of longer DAPT duration. Increased patient complexity has increased the risks.
- DAPT and SAPT may no longer be a useful terms in our lexicon, as the regimens we use become more nuanced.
- Randomized clinical trials testing one strategy vs. another in a broad population may be less useful than those focusing on specific target populations of high interest.

Thank you!

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