

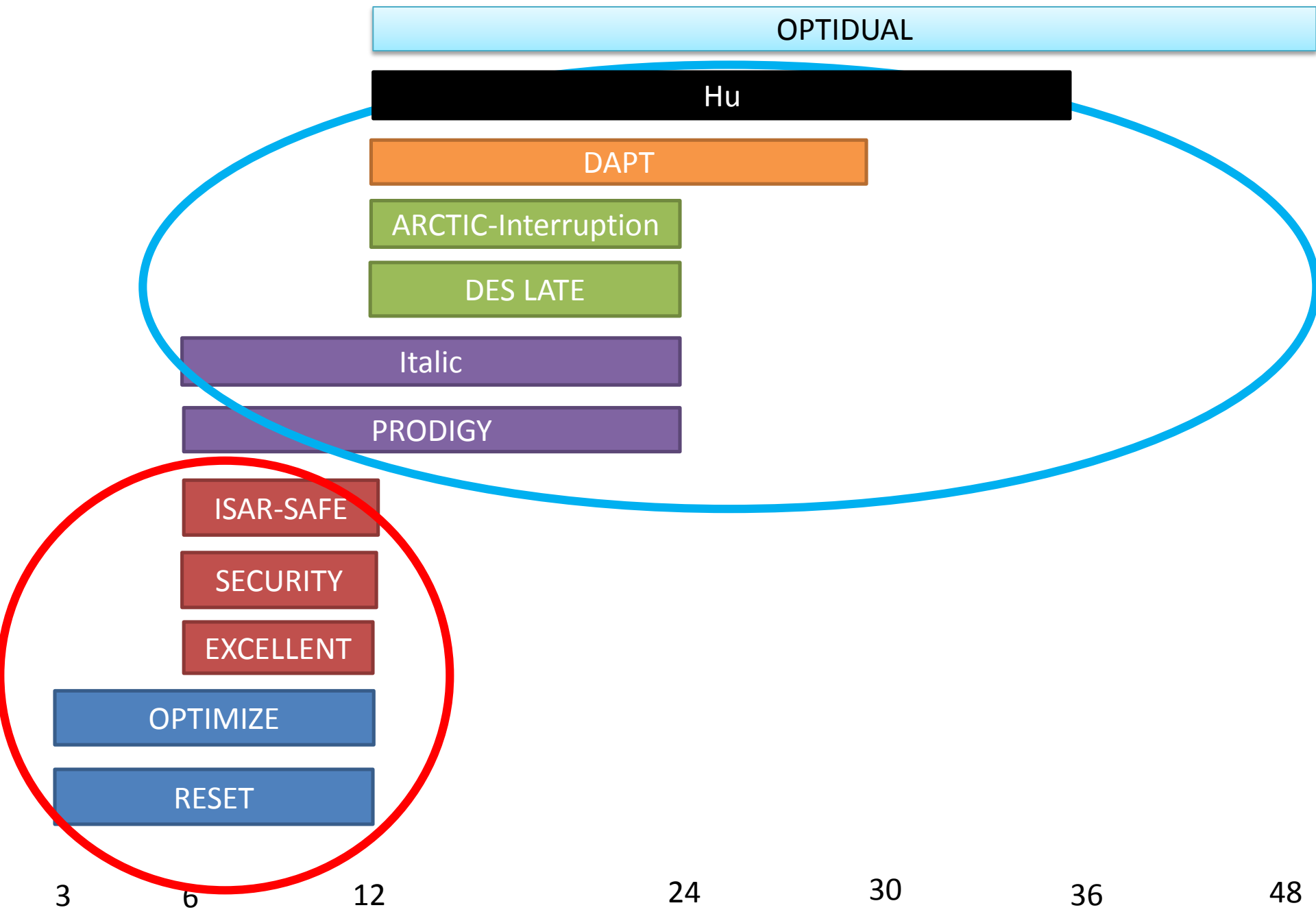
The Bottom Line – Duration of DAPT Following PCI with Drug Eluting Stents

Margaret L. Ackman, BSc(Pharm), PharmD
Clinical Practice Leader, Pharmacy Services
Alberta Health Services

What are we comparing?

- Short duration – 3 to 6 months
- Standard duration – 12 months
- Extended duration – 18 to 36 months

3 to 6 Months Discontinuation	24 to 36 Month Discontinuation
EXCELLENT (6 vs 12)	ARCTIC-Interruption (12 vs 24)
ISAR-SAFE (6 vs 12)	DAPT (12 vs 30)
OPTIMIZE (3 vs 12)	DES LATE (REAL & ZEST LATE) (12 vs 24)
RESET (3 vs 12)	PRODIGY (6 vs 24)
SECURITY (6 vs 12)	ITALIC (6 vs 24)
	Hu (12 vs 36)
	OPTIDUAL (12 vs 48)



The Patients

- Mid sixties
- Mostly male
- One-third diabetic
- Proportion with ACS varies from 25% to 75%

Outcomes

- Composite:
 - Cardiac death, all-cause mortality, MI, stroke, stent thrombosis and TVR
 - +/- Major bleeding
- TIMI major bleeding, GUSTO major bleeding, BARC bleeding

Overall

- **Results**

- Thrombosis – either not significant or met criteria for non-inferiority
- Bleeding – rates higher with longer duration
 - Dependent upon bleeding definitions and length of therapy

- **Limitations**

- Underpowered
 - Low risk population – landmark analysis
 - Stopped early
- Clinical relevance of wide non-inferiority margins
- Generation of DES

Meta Analyses

- Angiology 2016;67(3):224-238.
- JACC 2015;65(13):1298-310.
- BMJ 2015;350:h1618.

Meta Analysis

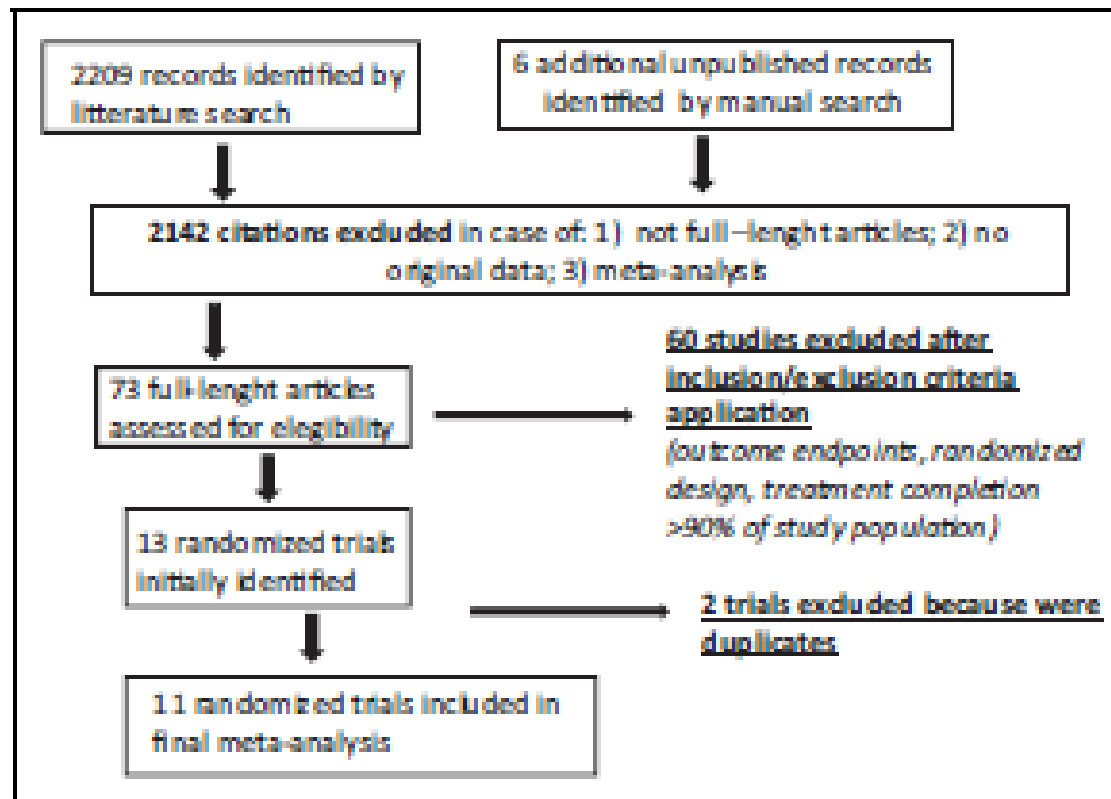


Figure 1. Flow diagram of the systematic overview process.

Meta Analysis

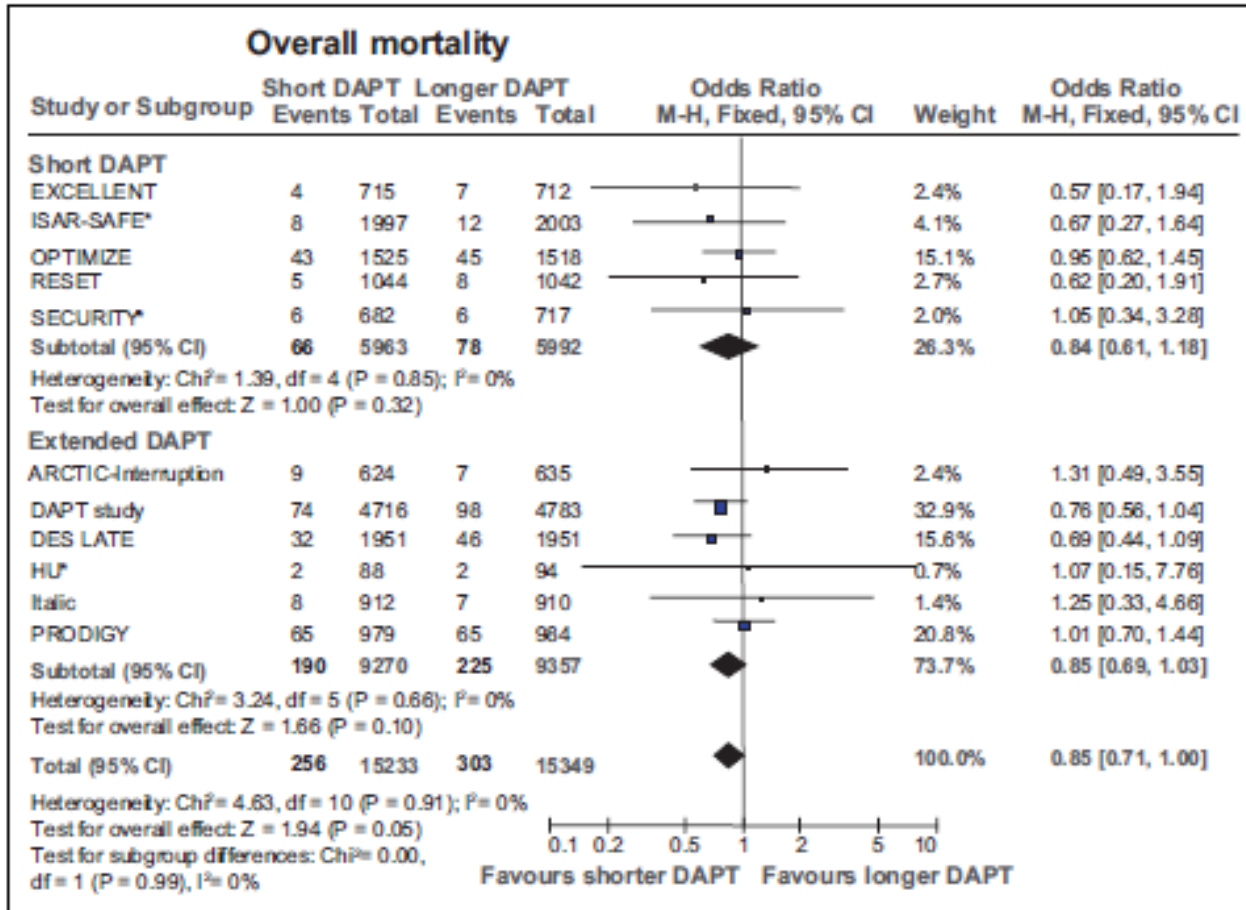


Figure 2. Shorter versus longer dual antiplatelet therapy (DAPT) duration on mortality with odds ratios and 95% confidence intervals (CI). The size of the data markers (squares) is approximately proportional to the statistical weight of each trial. * Defined as cardiovascular mortality.

Meta Analysis

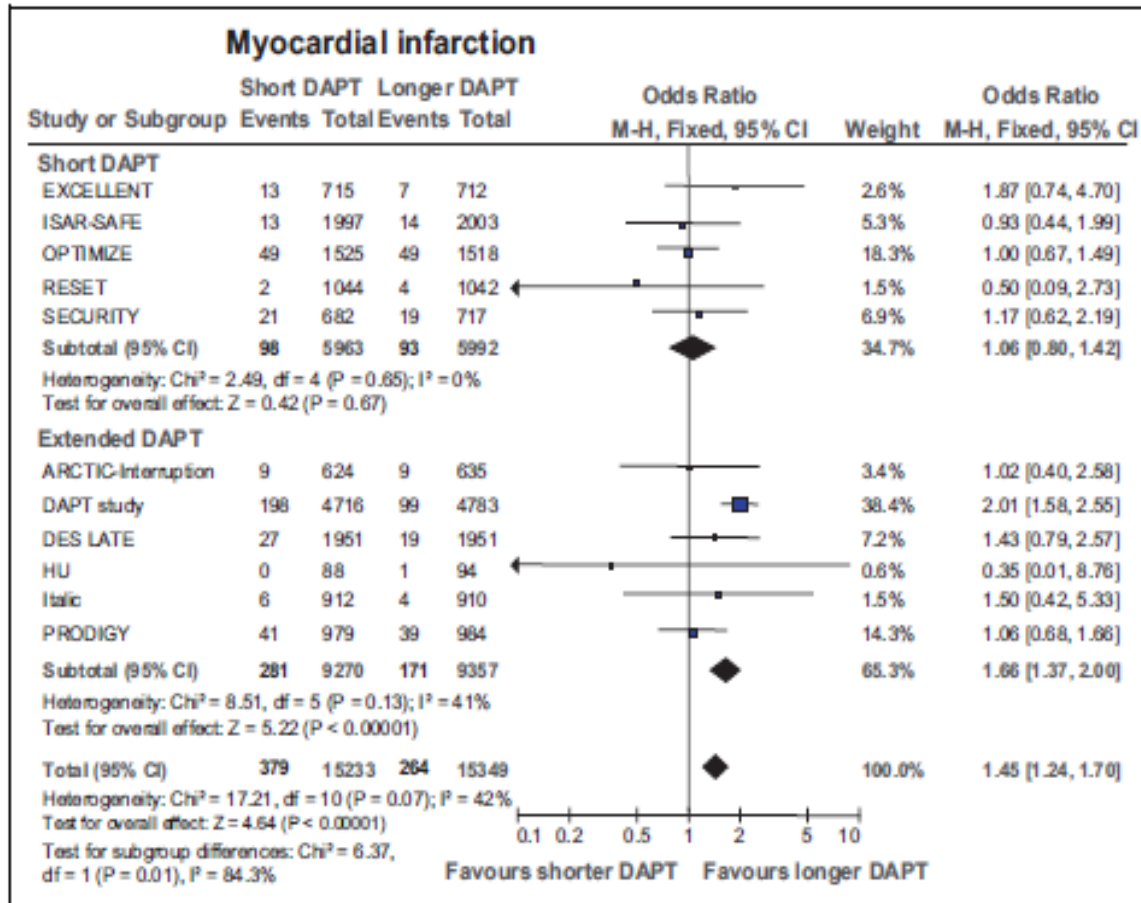


Figure 5. Shorter versus longer dual antiplatelet therapy (DAPT) duration on myocardial infarction with odds ratios and 95% confidence intervals (CIs). The size of the data markers (squares) is approximately proportional to the statistical weight of each trial.

Meta Analysis

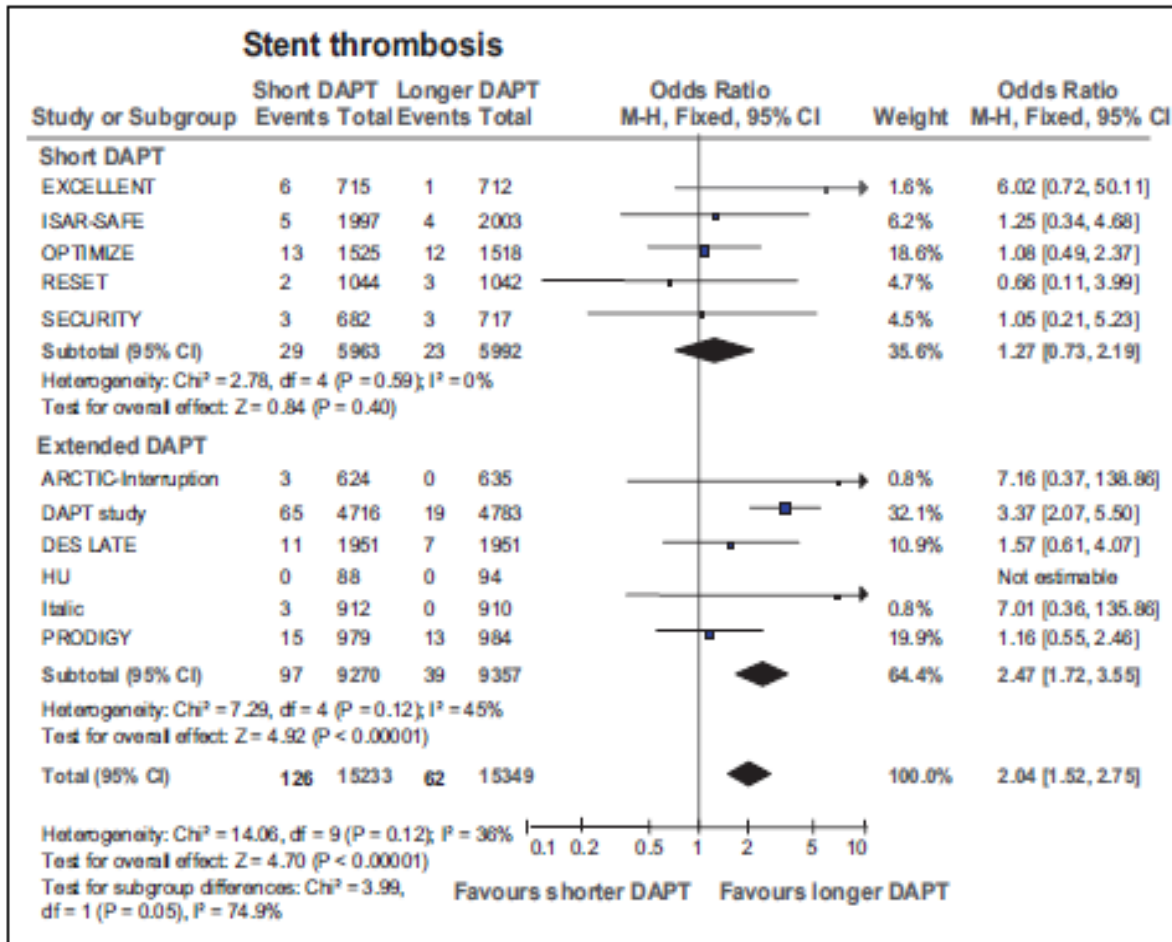


Figure 6. Shorter versus longer dual antiplatelet therapy (DAPT) duration on stent thrombosis (definite/probable) with odds ratios and 95% confidence intervals (CIs). The size of the data markers (squares) is approximately proportional to the statistical weight of each trial.

Drug Eluting Stents

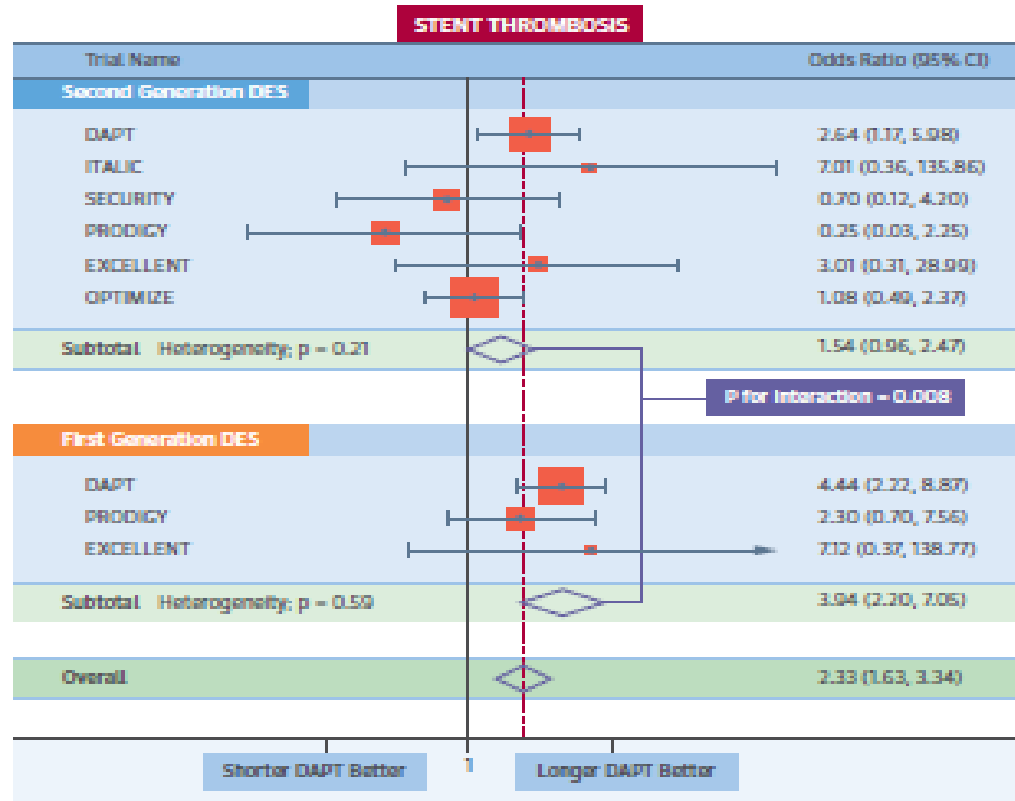
First Generation

- Sirolimus (Cypher)
- Paclitaxel (Taxus)

Second Generation

- Zotarolimus (Endeavor[®])
- Everolimus (Xience V[®])

CENTRAL ILLUSTRATION Stent Thrombosis With First- and Second-Generation Drug-Eluting Stents



Guarino, G. et al. *J Am Coll Cardiol.* 2015; 65(13):1298-310.

A statistically significant interaction was observed between drug-eluting stent (DES) generation and dual antiplatelet therapy (DAPT) duration on risk of stent thrombosis. The mean weighted exposure time to shorter DAPT was 7.8 months for second-generation DES and 20.9 months for first-generation DES. The mean weighted exposure time to longer DAPT was 20.3 months for second-generation DES and 28 months for first-generation DES. Size of central markers reflects the weight of each study. CI = confidence interval; DAPT = Dual Antiplatelet Therapy trial; EXCELLENT = Efficacy of Xience/Pronus Versus Cypher to Reduce Late Loss After Stenting; ITALIC = Is There A Life for DES After Discontinuation of Clopidogrel; OPTIMIZE = Optimized Duration of Clopidogrel Therapy Following Treatment With the Zotarolimus-Eluting Stent in Real-World Clinical Practice; PRODIGY = Prolonging Dual Antiplatelet Treatment After Grading Stent-Induced Intimal Hyperplasia Study; SECURITY = Second Generation Drug-Eluting Stent Implantation Followed by Six- Versus Twelve-Month Antiplatelet Therapy.

Meta Analysis

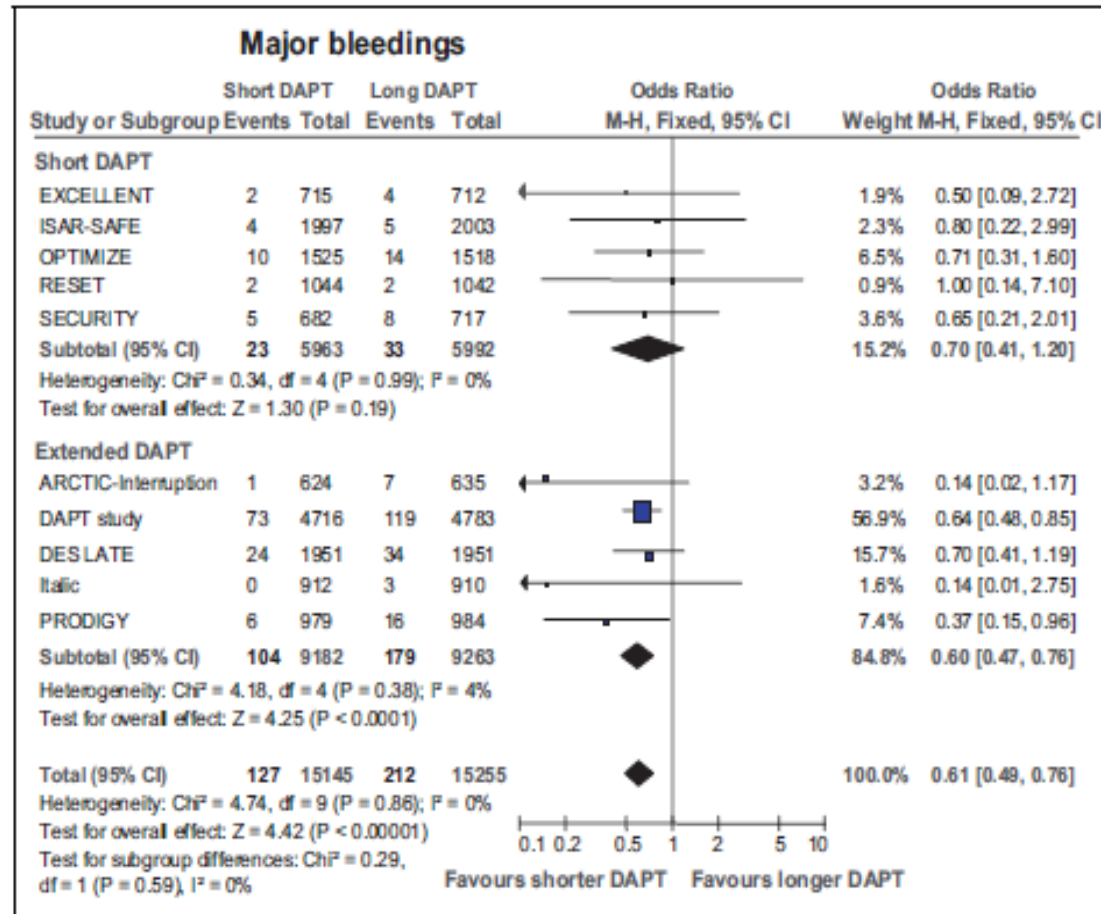


Figure 7. Shorter versus longer dual antiplatelet therapy (DAPT) duration on major bleedings with odds ratios and 95% confidence intervals (CIs). The size of the data markers (squares) is approximately proportional to the statistical weight of each trial.

The Bottom Line

- 3 to 6 months of DAPT appears as safe and effective as 12 months
 - Issues with medical treatment for ACS, low risk population and generation of stent
- Extended therapy (beyond 12 months) is associated with increased bleeding and trend for increased mortality despite a decrease in thrombotic events

The Bottom Line



References

- Basaraba J, Barry A. What is the optimal duration of dual antiplatelet therapy after percutaneous coronary intervention with drug-eluting stent implantation? *Am J Health-Syst Pharm* 2016;73:e229-37.
- Verdoia M, Schaffer A, Barbieri L et al. Optimal duration of dual antiplatelet therapy after DES implantation: A meta-analysis of 11 randomized trials. *Angiology* 2016;67(3):224-238.
- Giustino G, Usman B, Sartori S et al. Duration of dual antiplatelet therapy after drug-eluting stent implantation. A systematic review and meta-analysis of randomized controlled trials. *J Am Coll Cardiol* 2015;65:1298-310.
- Navarese BP, Andreotti F, Schulze V et al. Optimal duration of dual antiplatelet therapy after percutaneous coronary intervention with drug eluting stents: meta-analysis of randomized controlled trials. *BMJ* 2015;350:h1618.