Madhavan et al. Meta-Analysis

Long-term follow-up after ultrathin vs. conventional 2nd-generation drug-eluting stents: a systematic review and meta-analysis of randomized controlled trials[1]

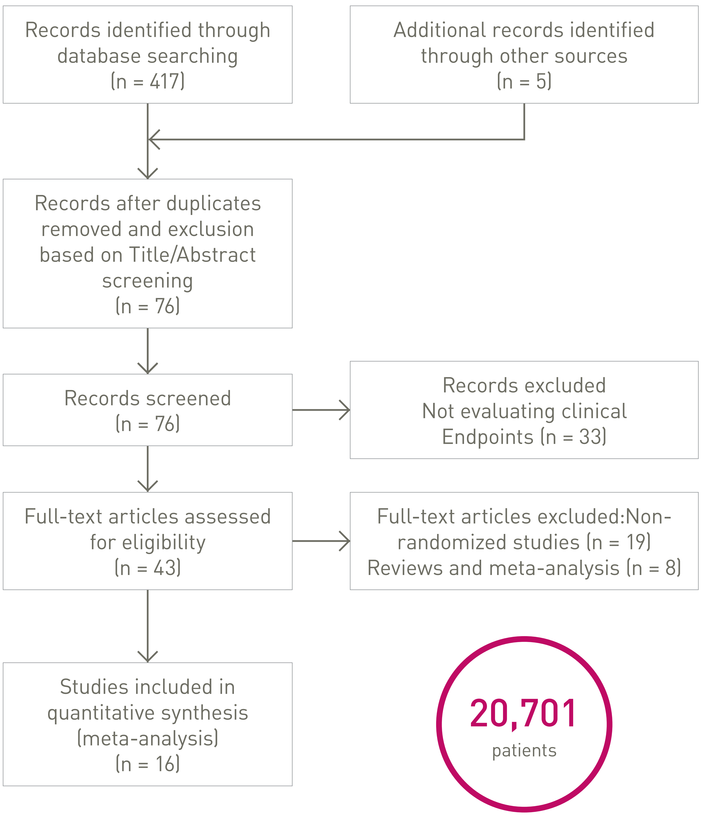
Conclusions

- Out of 16 trials randomizing 20,701 patients and with a mean follow-up of 2.5 years, Ultrathin strut DES (U-TS) (Strut thickness ⩽70 µm) demonstrated a 15% relative risk (RR) reduction for the 1° EP of TLF as compared to Thin strut DES (TS), primarily driven by 25% RR reduction in CD-TLR.
- Similar observations were made for TVF with 15% RR reduction, primarily driven by 16% RR reduction in CD-TVR; similar risks observed for MI, ST, cardiac death, and all-cause mortality.
- The performance of Orsiro SES was assessed in majority (12 out of 16) of the RCTs with U-TS compared to TS.
- The present report confirms that further reducing strut thickness to < 70 µm has a favorable effect on freedom from repeat revascularization.§

Study design

Random-effects meta-analysis of 16 randomized controlled trials (RCT) comparing Orsiro and three other ultrathin strut DES (Strut thickness ⩽ 70 µm) to conventional 2nd-generation DES.

Search strategy**,[2]



Endpoints

Primary endpoint

Target Lesion Failure (TLF) at latest follow-up reported, composite of:

- Cardiac death
- Target-vessel myocardial infarction (TV-MI)
- Clinically-driven target lesion revascularization (CD-TLR)

Secondary endpoints

- Individual components of the primary endpoint
- Target Vessel Failure (TVR)
- Clinically-driven target vessel revascularization (CD-TVR)
- Stent Thrombosis – definite and definite or probable (ST)*
- Any Myocardial Infarction (MI)
- Non-Cardiac death
- All-cause death

Selected Stent characteristics[2]

Category	Stent name	Stent manufacturer	Metallic alloy	Strut thickness	Polymer type	Drug name
U-TS	Orsiro	BIOTRONIK	Cobalt-chromium	60 µm	Bioabsorbable	Sirolimus
U-TS	MiStent	MiCell Technologies	Cobalt-chromium	64 µm	Bioabsorbable	Sirolimus
U-TS	BioMime	Meril Life Sciences	Cobalt-chromium	65 µm	Bioabsorbable	Sirolimus
U-TS	Supraflex	Sahajanand Medical Technologies	Cobalt-chromium	60 µm	Bioabsorbable	Sirolimus
TS	Xience Prime/ Xpedition	Abbott	Cobalt-chromium	81 µm	Durable	Everolimus
TS	Resolute Integrity	Medtronic	Cobalt-chromium	91 µm	Durable	Zotarolimus
TS	Resolute Onyx	Medtronic	Cobalt-chromium	81 µm	Durable	Zotarolimus
TS	BioFreedom	Biosensors	Stainless steel	120 µm	None	Biolimus A9
TS	Endeavor	Medtronic	Cobalt-chromium-nickel	91 µm	Durable	Zotarolimus
TS	Nobori	Terumo	Stainless steel	120 µm	Bioabsorbable	Biolimus A9
TS	Nobori	Terumo	Stainless steel	120 µm	Bioabsorbable	Biolimus A9

List of studies included[2]

Study acronym	Year	n	Follow-up**§	Ultrathin stent type	Control stent type
BIOFLOW-IV	2019	575	12	Orsiro	Xience
BIOFLOW-V	2020	1,334	36	Orsiro	Xience
BIOFLOW-II	2018	452	60	Orsiro	Xience
BIO-RESORT	2019	3,514	36	Orsiro	Resolute
BIOSCIENCE	2018	2,119	60	Orsiro	Xience
DESSOLVE III	2020	1,398	36	MiStent	Xience
ORIENT	2019	372	36	Orsiro	Resolute Integrity
PRISON-IV	2019	330	36	Orsiro	Xience
SORT OUT VII	2020	2,525	36	Orsiro	Nobori
meriT-V	2018	256	9	BioMime	Xience
BIOFLOW-VI	2020	440	12	Orsiro	Xience
BIONYX	2020	2,488	24	Orsiro	Resolute Onyx
BIOSTEMI	2019	1,300	24	Orsiro	Xience
SORT OUT IX	2020	3,151	12	Orsiro	BioFreedom
TALENT	2019	1,435	24	Supraflex	Xience
DESSOLVE II	2015	184	9	MiStent	Endeavor

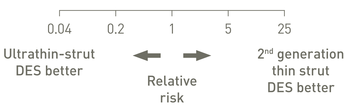
12 out of 16 studies

Orsiro

* According to Academic Research Consortium criteria
** Systematic search of the MEDLINE, Cochrane Central Register of Controlled Trials, and Embase databases from December 2010 through March 2021 for all RCTs comparing ultrathin-strut DES to conventional 2nd-generation thin-strut DES for the treatment of CAD.
*** Follow-up in months (longest follow-up provided if multiple analyses).

Risk of target lesion failure at latest follow-up – Mean 2.5-year

Study	Year	Active Events	N	Control Events	N	Weight	Relative risk [95% CI]
DESSOLVE II	2015	11	123	5	61	1.3%	1.09 (0.40, 3.00)
BIOFLOW-II	2018	30	298	19	154	4.0%	0.82 (0.48, 1.40)
BIOSCIENCE	2018	198	1,063	189	1,056	17.2%	1.04 (0.87, 1.25)
BIOFLOW-IV	2019	14	385	8	190	1.8%	0.86 (0.37, 2.02)
BIO-RESORT	2019	77	1,169	96	1,173	10.5%	0.80 (0.60, 1.07)
ORIENT	2019	11	250	9	122	1.8%	0.60 (0.25, 1.40)
BIOFLOW-V	2020	70	884	59	450	8.8%	0.60 (0.44, 0.84)
DESSOLVE III	2020	72	703	79	695	9.9%	0.90 (0.67, 1.22)
SORT OUT VII	2020	114	1,261	115	1,264	12.6%	0.99 (0.78, 1.27)
BIOFLOW-VI	2020	5	220	3	220	0.7%	1.67 (0.40, 6.89)
BIONYX	2020	71	1,245	76	1,243	9.4%	0.93 (0.68, 1.28)
SORT OUT IX	2020	59	1,579	79	1,572	8.7%	0.74 (0.53, 1.03)
TALENT	2021	49	720	56	715	7.4%	0.87 (0.60, 1.26)
BIOSTEMI	2021	33	649	53	651	6.1%	0.62 (0.41, 0.95)
REML model for all studies (Q = 15.24, df = 13, p for heterogenity = 0.29; I2 = 27.1%) Prediction interval -0.40 - 0.09							0.85 (0.76, 0.96) p for overall effect = 0.008



U-TS showed 15% relative risk reduction (RRR) in TLF as compared to TS, primarily driven by 25% RRR in CD-TLR.

Outcomes with TS are excellent and **have not been improved upon by various iterative designs** [...], in contrast, U-TS have potential advantages in terms of deliverability, are less likely to disturb flow in side-branches, and may promote more rapid endothelialization.°

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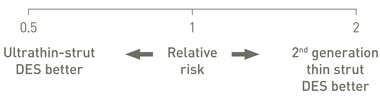
** Systematic search of the MEDLINE, Cochrane Central Register of Controlled Trials, and Embase databases from December 2010 through March 2021 for all RCTs comparing ultrathin-strut DES to conventional 2nd-generation thin-strut DES for the treatment of CAD.
*** Follow-up in months (longest follow-up provided if multiple analyses).

Summary of pooled estimates for key clinical endpoints at latest follow-up

Endpoint	Relative risk [95% CI]	p
Target lesion failure	0.85 (0.76, 0.96)	0.008
Target vessel failure	0.85 (0.75, 0.96)	0.010
All myocardial infarction	0.94 (0.82, 1.08)	0.374
Target-vessel myocardial infarction	0.87 (0.74, 1.02)	0.078
Definite or probable stent thrombosis	0.86 (0.70, 1.06)	0.162
Definite stent thrombosis	0.82 (0.61, 1.10)	0.175
Clinically-driven target lesion revascularization	0.75 (0.62, 0.92)	0.005
Clinically-driven target-vessel revascularization	0.84 (0.74, 0.95)	0.006
Cardiac death	1.07 (0.90, 1.27)	0.424
Non-cardiac death	1.10 (0.88, 1.38)	0.397
All-cause death	1.11 (0.98, 1.26)	0.114



There were no significant differences between stent types in the risks of MI, ST, cardiac death, or all-cause mortality.§

Principal investigator

Mahesh V. Madhavan, Columbia University Irving Medical Center, New York-Presbyterian Hospital; Cardiovascular Research Foundation, New York, NY, USA

§ as per investigators' interpretation of the results; ° as per author's interpretation.

1. Mahesh V. Madhavan, Martin B. Leon, Sripal Bangalore, Gregg W. Stone et al. European Heart Journal (2021) 00, 1–12, doi:10.1093/eurheartj/ehab280; 2. Supplementary Data

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BIOTRONIK AG
Ackerstrasse 6
8180 Bülach,
Switzerland

Tel +41 (0) 44 8645111
Fax +41 (0) 44 8645005
info.vi@biotronik.com
www.biotronik.com

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