Short versus long-term dual antiplatelet therapy in patients at high bleeding risk undergoing PCI in contemporary practice. A systemic review and meta-analysis.

Cardiology and Therapy.

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Supplemental Appendix

Supplementary Table 1. Search strategy.

Database	Method	Result
PubMed	(((((short DAPT[Title/Abstract]) OR (Short dual antiplatelet therapy[Title/Abstract]) AND ((clinicaltrial[Filter] OR clinicaltrialphaseii[Filter] OR clinicaltrialphaseiii[Filter] OR clinicaltrialphaseiv[Filter] OR comparativestudy[Filter] OR controlledclinicaltrial[Filter] OR multicenterstudy[Filter] OR observationalstudy[Filter] OR randomizedcontrolledtrial[Filter]) AND (humans[Filter]) AND (2004/1/1:2021/12/31[pdat]) AND (english[Filter]))) AND ((Percutaneous coronary intervention[Title/Abstract]) AND (high bleeding risk[Title/Abstract]) AND ((clinicaltrial[Filter] OR clinicaltrialphaseii[Filter] OR clinicaltrialphaseiii[Filter] OR clinicaltrialphaseiv[Filter] OR comparativestudy[Filter] OR controlledclinicaltrial[Filter] OR multicenterstudy[Filter] OR observationalstudy[Filter] OR randomizedcontrolledtrial[Filter]) AND (humans[Filter]) AND (2004/1/1:2021/12/31[pdat]) AND (english[Filter])))) OR ((PCI[Title/Abstract]) AND (HBR[Title/Abstract]) AND ((clinicaltrial[Filter] OR clinicaltrialphaseii[Filter] OR clinicaltrialphaseiii[Filter] OR clinicaltrialphaseiv[Filter] OR comparativestudy[Filter] OR controlledclinicaltrial[Filter] OR multicenterstudy[Filter] OR observationalstudy[Filter] OR randomizedcontrolledtrial[Filter]) AND (humans[Filter]) AND (2004/1/1:2021/12/31[pdat]) AND (english[Filter])))) OR ((Percutaneous coronary intervention[Title/Abstract]) AND (HBR[Title/Abstract]) AND ((clinicaltrial[Filter] OR clinicaltrialphaseii[Filter] OR clinicaltrialphaseiii[Filter] OR clinicaltrialphaseiv[Filter] OR comparativestudy[Filter] OR controlledclinicaltrial[Filter] OR multicenterstudy[Filter] OR observationalstudy[Filter] OR randomizedcontrolledtrial[Filter]) AND (humans[Filter]) AND (2004/1/1:2021/12/31[pdat]) AND (english[Filter])))) OR ((PCI[Title/Abstract]) AND (high bleeding risk[Title/Abstract]) AND ((clinicaltrial[Filter] OR clinicaltrialphaseii[Filter] OR clinicaltrialphaseiii[Filter] OR clinicaltrialphaseiv[Filter] OR comparativestudy[Filter] OR controlledclinicaltrial[Filter] OR multicenterstudy[Filter] OR observationalstudy[Filter] OR randomizedcontrolledtrial[Filter]) AND (humans[Filter]) AND (2004/1/1:2021/12/31[pdat]) AND (english[Filter]))) AND ((clinicaltrial[Filter] OR clinicaltrialphaseii[Filter] OR clinicaltrialphaseiii[Filter] OR clinicaltrialphaseiv[Filter] OR comparativestudy[Filter] OR controlledclinicaltrial[Filter] OR multicenterstudy[Filter] OR observationalstudy[Filter] OR randomizedcontrolledtrial[Filter]) AND (humans[Filter]) AND (2004/1/1:2021/12/31[pdat]) AND (english[Filter]))	74
Scopus	(TITLE-ABS-KEY(short DAPT) OR TITLE-ABS-KEY(short dual antiplatelet therapy) AND TITLE-ABS-KEY(PCI HBR) OR TITLE-ABS-KEY(Percutaneous coronary intervention high bleeding risk) OR TITLE-ABS-KEY(PCI high bleeding risk) OR TITLE-ABS-KEY(Percutaneous coronary intervention HBR)) AND PUBYEAR > 2003 AND PUBYEAR < 2022 AND (LIMIT-TO (LANGUAGE,"English")) AND (LIMIT-TO (SUBJAREA,"MEDI") OR LIMIT-TO (SUBJAREA,"PHAR")) AND (LIMIT-TO (SRCTYPE,"j"))	195
www.clinicaltrials.gov	Keywords used were “Short DAPT,” “short dual anti-platelet therapy,” “Percutaneous coronary intervention,” “PCI,” "HBR," and “high bleeding risk,”Reports before 01 January 2004 were not searched.	

Supplementary Table 2 Definitions of HBR criteria, inclusion and exclusion criteria, major bleeding, as well as DAPT duration

Study	Short DAPT duration	Long DAPT duration	Inclusion	Exclusion	Major bleeding endpoint definition
Kirtane et al. 2021 EVOLVE Short DAPT	3 Month *except those on chronic anticoagulation in whom aspirin was optional.*	12 Month	Patients with HBR were enrolled if they met at least one of the following inclusion criteria: age ≥75 years; need for chronic anticoagulation; history of major bleeding within 12 months of the index procedure; history of ischemic or haemorrhagic stroke; renal insufficiency (creatinine ≥2.0 mg/dL) or failure (dialysis dependent), and platelet count ≤100,000/μL.	Patients with non–ST-segment–elevation MI or ST-segment–elevation MI, treatment of >3 lesions or >2 major epicardial vessels, ostial or saphenous vein graft lesions, in-stent restenosis, left main disease, or total occlusion.	BARC 3 or 5 Bleeding
Mehran et al. 2021 TWILIGHT-HBR	3 Month	12 Month	Patients were considered as HBR retrospectively (from the main TWILIGHT trial) if they fulfilled at least one major or two minor criteria as defined by the ARC-HBR consensus statement. Major criteria were severe or end-stage CKD [i.e. estimated glomerular filtration rate (eGFR) <30mL/min/1.73 m2 or dialysis], haemoglobin <11 g/dL, moderate or severe thrombocytopenia (i.e.platelet count <100_109/L), previous major bleeding, and liver disease. Minor criteria included age ≥75 years, moderate CKD (i.e. eGFR >_30 and < 60mL/min/1.73m2), haemoglobin ≥11 and <13 g/dL for men and ≥11 and <12 g/dL for women, and non-steroidal anti-inflammatory drug use.	Presentation with ST-elevation MI, cardiogenic shock, prior stroke, or need for oral anticoagulation.	BARC 3 or 5 Bleeding

Mehran et al. 2021 Xience 28	1 Month *For those on long-term anticoagulant agents, dual therapy consisting of an oral anticoagulant agent and a P2Y12 inhibitor, preferably clopidogrel, could be considered per investigator's discretion.*	6 Month	HBR patients undergoing successful PCI exclusively with a fluoropolymer-based cobaltchromium everolimus-eluting stent (XIENCE) in whom, in the opinion of the treating physician, the risk for major bleeding associated with a prolonged DAPT regimen outweighed the benefit were eligible for enrolment. Patients had to meet at least 1 of the following HBR criteria: age ≥75 years, indication for long-term anticoagulant therapy, history of major bleeding in the previous 12 months, history of ischemic or haemorrhagic stroke, renal insufficiency defined as creatinine ≥ 2.0 mg/dL or maintenance dialysis, anemia with hemoglobin <11 g/dL, and systemic conditions associated with an increased risk for bleeding, including hematologic disorders such as thrombocytopenia (platelet count <100,000/mm3) and coagulation disorders.	Presentation with ST-segment elevation MI, implantation of a drug-eluting stent other than a cobalt-chromium everolimus-eluting stent in the previous 12 months, and target lesion treated with overlapping stents.	BARC 3 to 5 Bleeding
Mehran et al. 2021 Xience 90	3 Month *For those on long-term anticoagulant agents, dual therapy consisting of an oral anticoagulant*	12 Month	Eligibility criteria were consistent for both XIENCE 90 and XIENCE 28 trials except for the following: 1. Staged procedures were allowed only in XIENCE 90 trials 2. Target lesions containing thrombus or >32 mm in length were only allowed in XIENCE 28 trials.		BARC 3 to 5 Bleeding

	agent and a P2Y12 inhibitor, preferably clopidogrel, could be considered per investigator's discretion.				
Valgimigli et al. 2021 MASTER DAPT	1 Month	6 Month *(3 months after the index procedure) for those receiving clinically indicated oral anticoagulation with the continuation of single antiplatelet therapy thereafter.*	Post-PCI, patients were at high bleeding risk if at least one of the following criteria applies: 1. Clinical indication for treatment with oral anticoagulant (OAC) for at least 12 months. 2. Recent (<12 months) non-access site bleeding episode(s) that required medical attention. 3. Previous bleeding episode(s) that required hospitalization if the underlying cause had not been definitively treated (i.e. surgical removal of the bleeding source). 4. Age ≥75 years. 5. Systemic conditions associated with an increased bleeding risk (e.g.hematological disorders, including a history of current thrombocytopenia defined as a platelet count <100.00/ mm3 or any known coagulation disorder associated with increased bleeding risk. 6. Documented anemia, defined as repeated hemoglobin levels <11 g/dL or transfusion during the 4 weeks before inclusion. 7. Need for chronic treatment with steroids or nonsteroidal anti-inflammatory drugs.	The implantation of a stent other than the Ultimaster stent within 6 months before the index procedure, the implantation of a bioresorbable scaffold at any time before the index procedure, and treatment for in-stent restenosis or stent thrombosis.	BARC 3 to 5 Bleeding. However , there was no BARC 4 events reported in this trial.

			8. Diagnosed malignancy (other than skin) considered at high bleeding risk including gastrointestinal, genitourethral/renal and pulmonary. 9. Stroke at any time or transient ischemic attack in the previous 6 months. 10. PRECISE-DAPT score ≥25.		
Watanabe et al. 2020 STOPDAPT-2 post-hoc	1 Month	12 Month	Patients were regarded as HBR if having at least one major criterion or two minor criteria. The ARC-HBR definitions were modified, because some criteria of ARC-HBR were not exactly captured in the STOPDAPT-2 trial; The usage of oral anticoagulants was one of the exclusion criteria, but some patients receiving anticoagulation were enrolled (protocol violation) and included in analysis; all previous bleeding history was regarded as minor criterion; liver cirrhosis was considered as major criterion regardless of the presence of portal hypertension; malignancy was excluded from the criteria for HBR; history of stroke was regarded as minor criterion; history of intracranial bleeding was regarded as major criteria regardless of its etiology; planned major surgery was included as major criteria, regardless of whether the procedure was deferrable or not. The information on bleeding	The use of oral anticoagulants, history of intracranial hemorrhage, or known intolerance to clopidogrel.	BARC 3 or 5 Bleeding

			diathesis, brain arterio-venous malformation, and recent major trauma or surgery (major criteria), use of non-steroid anti-inflammatory drugs or steroids (minor criteria) were not captured in this trial, and these criteria were regarded as absent.		

DAPT: dual antiplatelet therapy, HBR: high bleeding risk, MI: myocardial infarction, BARC: bleeding academic research consortium, CKD: chronic kidney disease, eGFR: estimated glomerular filtration rate, PCI: percutaneous coronary intervention.

Supplementary Table 3 Bias risk assessment of observational studies using the New-Castle-Ottawa scale

Study	Year	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration of the absence of outcome of interest at the start of the study	Comparability (control for important factors) (maximum two stars)	Assessment of outcome	Follow-up adequate for outcomes	Adequacy of follow up	Total score
Kirtane et al. 2021 EVOLVE Short DAPT	2021	*		*	*	*	*	*	*	7
Mehran et al. 2021 TWILIGHT-HBR	2021	*	*	*	*	*	*	*	*	8
Mehran et al. 2021 Xience 28	2021	*		*	*	*	*	*	*	7
Mehran et al. 2021 Xience 90	2021	*		*	*	*	*	*	*	7
Watanabe et al. 2020 STOPDAPT-2 post-hoc	2020	*	*	*	*	*	*	*	*	8

Supplementary Table 4 Bias risk assessment of randomized controlled trials with the revised Cochrane assessment tool (RoB 2)

	Valgimigli et al. 2021 MASTER DAPT
Risk of bias arising from the randomisation process	+
Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	?
Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)	+
Risk of bias due to missing outcome data	+
Risk of bias in measurement of outcomes	+
Risk of bias in selection of the reported results	+

+ = Low risk of bias - = High risk of bias ? = Some concerns

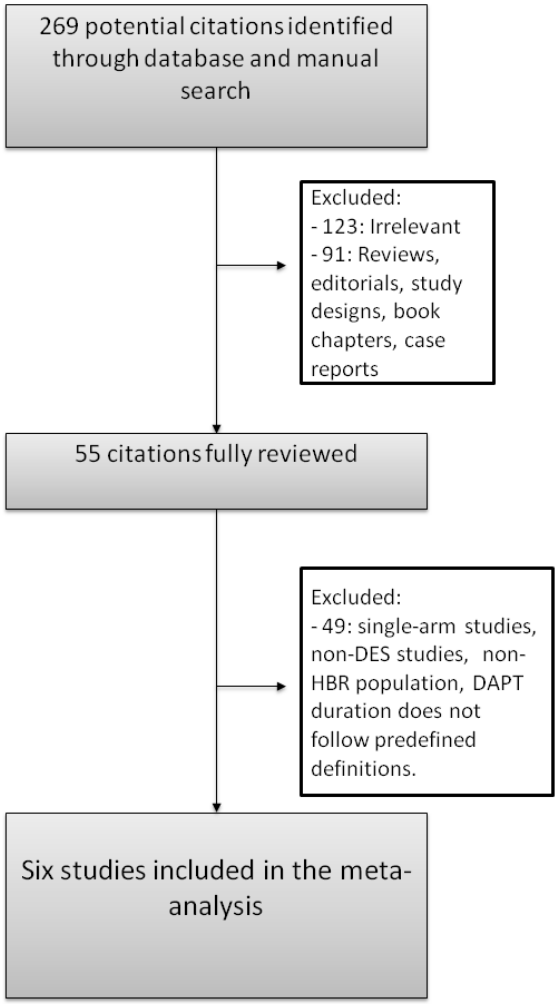
RoB2: Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2).

Supplementary Table 5 Baseline Characteristics as reported by individual studies

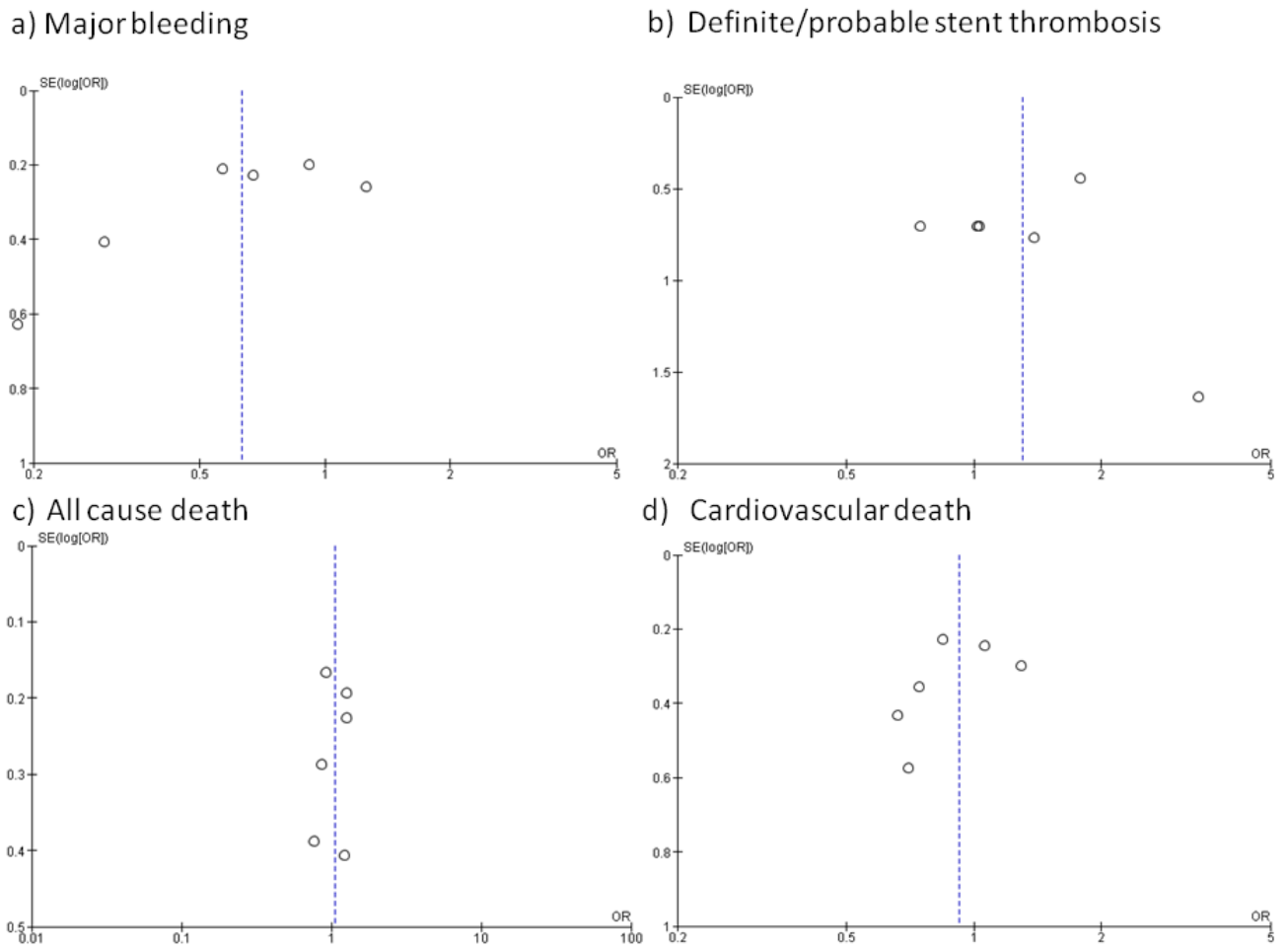
Short DAPT/Long DAPT	Number of patients	Age (years) (mean)	Male (%)	Diabetes (%)	Hypertension (%)	Hyperlipidaemia (%)	Smoking (%)	Prior MI (%)	Prior PCI (%)	Prior CABG (%)	ACS (%)	CSS (%)
Kirtane et al. 2021 EVOLVE Short DAPT	1487 / 1948	75.2±8.5/ 74.8±8.8	65.2 / 64.9	32.9/ 33.0	88.2/ 87.9	--	7.6/ 8.2	20.6/ 21.5	35.1/ 36.2	13.6 / 13.9	24.4/ 24.6	75.8 /75.4
Mehran et al. 2021 TWILIGHT-HBR	521 / 543	71.7±10.7/ 72.0±10.0	67.9 / 65.6	45.9/ 48.6	81.4/ 81.2	65.6/ 68.3	10.0/ 10.7	28.0/ 29.5	44.5/ 46.2	15.5/ 16.2	61.8/ 62.4	38.2/ 37.6
Mehran et al. 2021 Xience 28	1392 / 1411	75.9 ±8.4/ 72.6 ±10.4	67.5 / 59.2	37.0 / 42.3	84.7 / 91.5	67.5 / 90.7	--	16.4/ 30.3	28.0/ 37.9	8.0/ 14.8	34.1/ 35.8	65.9/ 64.2
Mehran et al. 2021 Xience 90	1693 / 1280	75.3 ±9.3/ 72.7 ± 10.3	64.8 / 59.1	39.2 / 42.9	89.5 / 91.7	82.8 / 90.7	--	15.8 / 30.1	30.7 / 38.8	12.1 / 14.1	34.7/ 33.9	65.3/ 66.1
Valgimigli et al. 2021 MASTER DAPT	2295/ 2284	76.1±8.7/ 76.0± 8.8	69.3/ 69.2	32.9/ 34.3	76.9/ 78.2	67.2/ 68.1	10.0/ 8.1	18.9/ 18.8	25.9/ 26.0	7.4/ 7.5	49.1/ 47.4	50.7/ 52.6
Watanabe et al. 2020 STOPDAPT-2 post-hoc	496/ 558	75.8±9.0/ 75.8±8.2	70.0/ 69.7	45.6/ 43.0	79.2/ 82.8	73.2/ 72.0	16.3/ 11.5	16.9/ 14.3	45.2/ 43.0	1.8/ 4.7	28.8/ 29.9	71.2/ 70.1

MI: myocardial infarction; PCI: percutaneouse coronary intervention; CABG: coronary artery bypass graft; ACS: acute coronary syndrome; CCS: chronic coronary syndrome.

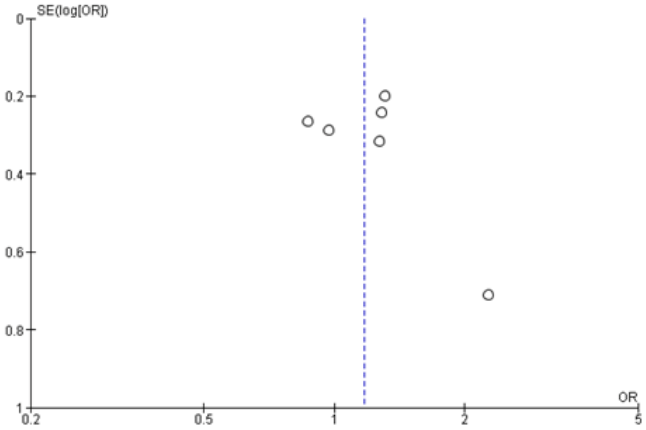
Supplementary Figure 1 The study selection process



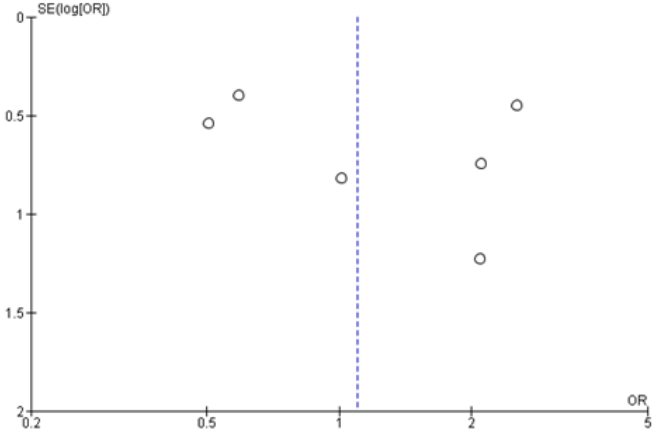
Supplementary Figure 2 Publication bias assessment



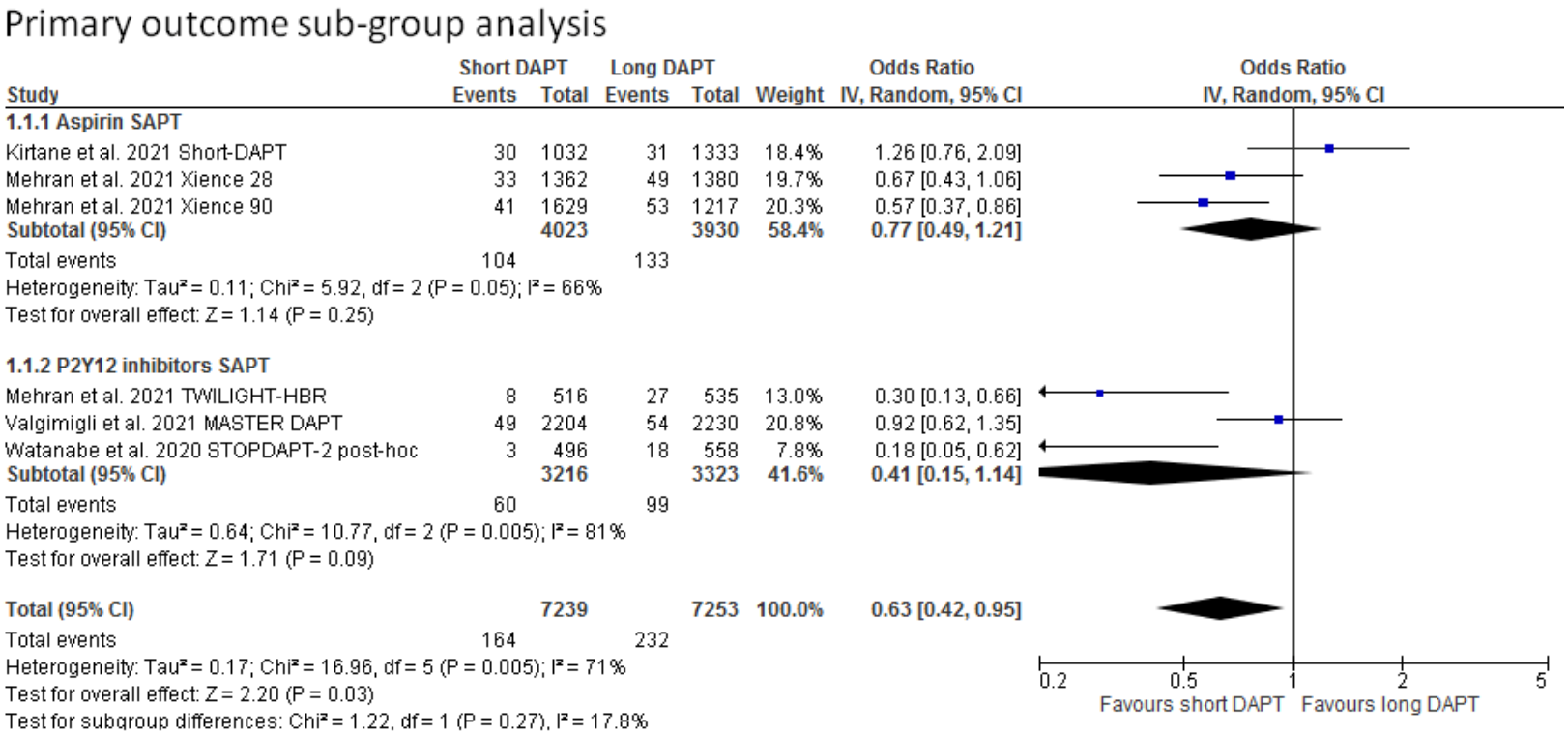
e) Myocardial infarction



f) Ischemic stroke



Supplementary Figure 3 Primary outcome sub-group analysis, aspirin vs. P2Y12 inhibitor SAPT after DAPT

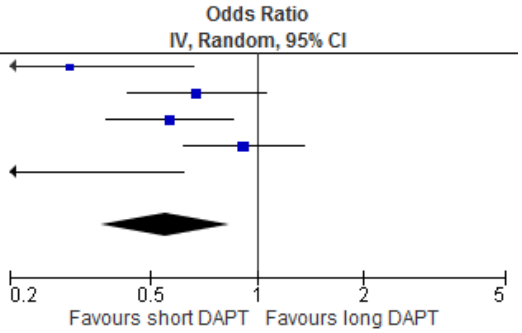


Supplementary Figure 4 Sensitivity analysis including only studies that included patients primary presenting with myocardial infarction

a) Major bleeding

Study	Short DAPT Events	Short DAPT Total	Long DAPT Events	Long DAPT Total	Weight	Odds Ratio IV, Random, 95% CI
Mehran et al. 2021 TWILIGHT-HBR	8	516	27	535	15.1%	0.30 [0.13, 0.66]
Mehran et al. 2021 Xience 28	33	1362	49	1380	24.5%	0.67 [0.43, 1.06]
Mehran et al. 2021 Xience 90	41	1629	53	1217	25.5%	0.57 [0.37, 0.86]
Valgimigli et al. 2021 MASTER DAPT	49	2204	54	2230	26.3%	0.92 [0.62, 1.35]
Watanabe et al. 2020 STOPDAPT-2 post-hoc	3	496	18	558	8.6%	0.18 [0.05, 0.62]
Total (95% CI)		**6207**		**5920**	**100.0%**	**0.55 [0.36, 0.84]**
Total events	134		201			

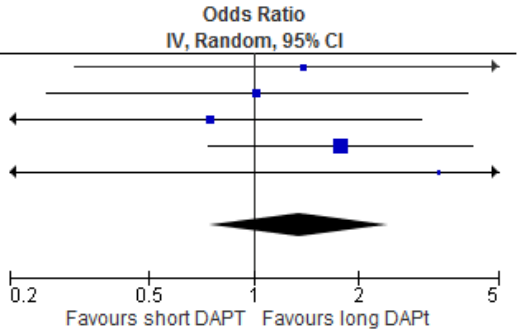
Heterogeneity: Tau² = 0.13; Chi² = 11.19, df = 4 (P = 0.02); I² = 64%
Test for overall effect: Z = 2.80 (P = 0.005)



b) Definite/probable stent thrombosis

Study	Short DAPT Events	Short DAPT Total	Long DAPT Events	Long DAPT Total	Weight	Odds Ratio IV, Random, 95% CI
Mehran et al. 2021 TWILIGHT-HBR	4	516	3	535	15.3%	1.39 [0.31, 6.22]
Mehran et al. 2021 Xience 28	4	1361	4	1387	17.9%	1.02 [0.25, 4.08]
Mehran et al. 2021 Xience 90	4	1635	4	1225	17.9%	0.75 [0.19, 3.00]
Valgimigli et al. 2021 MASTER DAPT	14	2204	8	2230	45.5%	1.78 [0.74, 4.24]
Watanabe et al. 2020 STOPDAPT-2 post-hoc	1	496	0	558	3.4%	3.38 [0.14, 83.20]
Total (95% CI)		**6212**		**5935**	**100.0%**	**1.35 [0.75, 2.44]**
Total events	27		19			

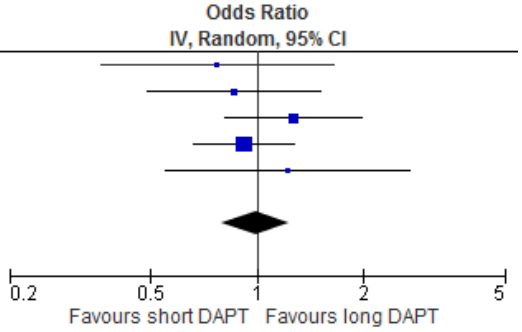
Heterogeneity: Tau² = 0.00; Chi² = 1.55, df = 4 (P = 0.82); I² = 0%
Test for overall effect: Z = 1.01 (P = 0.31)



c) All cause death

Study	Short DAPT Events	Short DAPT Total	Long DAPT Events	Long DAPT Total	Weight	Odds Ratio IV, Random, 95% CI
Mehran et al. 2021 TWILIGHT-HBR	12	516	16	535	8.3%	0.77 [0.36, 1.65]
Mehran et al. 2021 Xience 28	23	1380	27	1399	15.1%	0.86 [0.49, 1.51]
Mehran et al. 2021 Xience 90	54	1672	32	1246	24.1%	1.27 [0.81, 1.97]
Valgimigli et al. 2021 MASTER DAPT	72	2204	79	2230	45.0%	0.92 [0.66, 1.27]
Watanabe et al. 2020 STOPDAPT-2 post-hoc	13	496	12	558	7.5%	1.22 [0.55, 2.71]
Total (95% CI)		**6268**		**5968**	**100.0%**	**0.99 [0.80, 1.23]**
Total events	174		166			

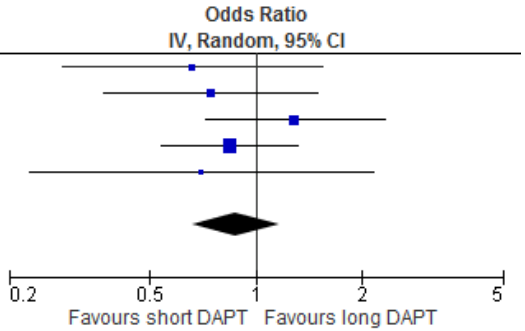
Heterogeneity: Tau² = 0.00; Chi² = 2.30, df = 4 (P = 0.68); I² = 0%
Test for overall effect: Z = 0.08 (P = 0.93)



d) Cardiovascular death

Study	Short DAPT Events	Short DAPT Total	Long DAPT Events	Long DAPT Total	Weight	Odds Ratio IV, Random, 95% CI
Mehran et al. 2021 TWILIGHT-HBR	9	516	14	535	11.5%	0.66 [0.28, 1.54]
Mehran et al. 2021 Xience 28	14	1380	19	1399	17.0%	0.74 [0.37, 1.49]
Mehran et al. 2021 Xience 90	31	1672	18	1246	23.9%	1.29 [0.72, 2.31]
Valgimigli et al. 2021 MASTER DAPT	36	2204	43	2230	41.1%	0.84 [0.54, 1.32]
Watanabe et al. 2020 STOPDAPT-2 post-hoc	5	496	8	558	6.5%	0.70 [0.23, 2.15]
Total (95% CI)		**6268**		**5968**	**100.0%**	**0.88 [0.66, 1.17]**
Total events	95		102			

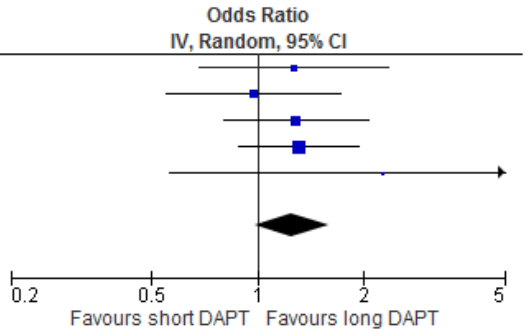
Heterogeneity: Tau² = 0.00; Chi² = 2.49, df = 4 (P = 0.65); I² = 0%
Test for overall effect: Z = 0.89 (P = 0.38)



e) Myocardial infarction

Study	Short DAPT Events	Short DAPT Total	Long DAPT Events	Long DAPT Total	Weight	Odds Ratio IV, Random, 95% CI
Mehran et al. 2021 TWILIGHT-HBR	23	516	19	535	15.0%	1.27 [0.68, 2.36]
Mehran et al. 2021 Xience 28	24	1380	25	1399	18.1%	0.97 [0.55, 1.71]
Mehran et al. 2021 Xience 90	48	1672	28	1246	25.9%	1.29 [0.80, 2.06]
Valgimigli et al. 2021 MASTER DAPT	59	2204	46	2230	38.0%	1.31 [0.88, 1.93]
Watanabe et al. 2020 STOPDAPT-2 post-hoc	6	496	3	558	3.0%	2.27 [0.56, 9.11]
Total (95% CI)		**6268**		**5968**	**100.0%**	**1.25 [0.98, 1.59]**
Total events	160		121			

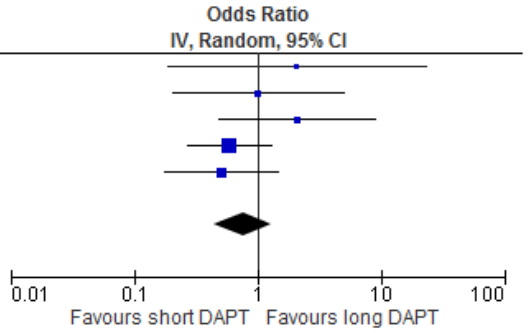
Heterogeneity: Tau² = 0.00; Chi² = 1.52, df = 4 (P = 0.82); I² = 0%
Test for overall effect: Z = 1.81 (P = 0.07)



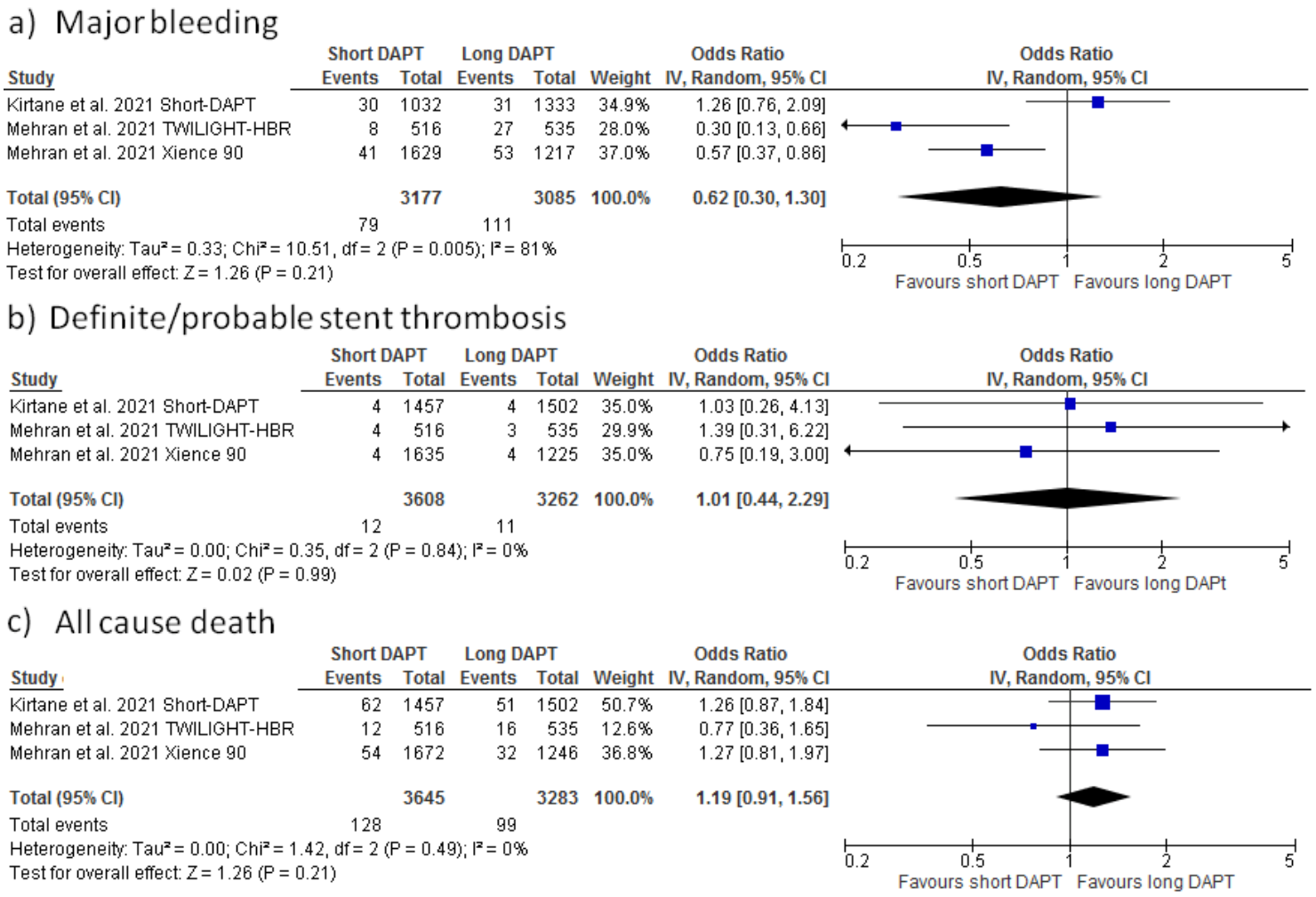
f) Ischemic stroke

Study	Short DAPT Events	Short DAPT Total	Long DAPT Events	Long DAPT Total	Weight	Odds Ratio IV, Random, 95% CI
Mehran et al. 2021 TWILIGHT-HBR	2	516	1	535	4.9%	2.08 [0.19, 22.98]
Mehran et al. 2021 Xience 28	3	1357	3	1373	11.0%	1.01 [0.20, 5.02]
Mehran et al. 2021 Xience 90	19	1624	2	355	13.2%	2.09 [0.48, 9.01]
Valgimigli et al. 2021 MASTER DAPT	10	2204	17	2230	46.0%	0.59 [0.27, 1.30]
Watanabe et al. 2020 STOPDAPT-2 post-hoc	5	496	11	558	24.9%	0.51 [0.17, 1.47]
Total (95% CI)		**6197**		**5051**	**100.0%**	**0.76 [0.45, 1.29]**
Total events	39		34			

Heterogeneity: Tau² = 0.00; Chi² = 3.58, df = 4 (P = 0.47); I² = 0%
Test for overall effect: Z = 1.02 (P = 0.31)



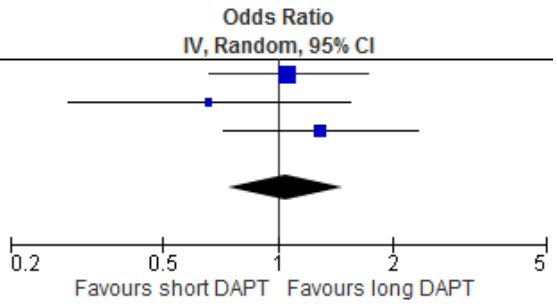
Supplementary Figure 5 Sensitivity analysis including only studies comparing 3-month versus 12 months DAPT duration



d) Cardiovascular death

Study	Short DAPT Events	Short DAPT Total	Long DAPT Events	Long DAPT Total	Weight	Odds Ratio IV, Random, 95% CI
Kirtane et al. 2021 Short-DAPT	35	1457	34	1502	50.4%	1.06 [0.66, 1.71]
Mehran et al. 2021 TWILIGHT-HBR	9	516	14	535	16.1%	0.66 [0.28, 1.54]
Mehran et al. 2021 Xience 90	31	1672	18	1246	33.5%	1.29 [0.72, 2.31]
Total (95% CI)		**3645**		**3283**	**100.0%**	**1.05 [0.75, 1.47]**
Total events	75		66			

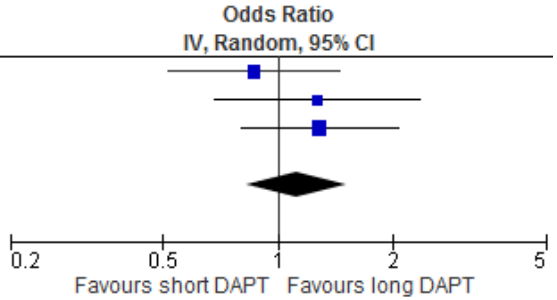
Heterogeneity: Tau² = 0.00; Chi² = 1.62, df = 2 (P = 0.44); I² = 0%
Test for overall effect: Z = 0.28 (P = 0.78)



e) Myocardial infarction

Study	Short DAPT Events	Short DAPT Total	Long DAPT Events	Long DAPT Total	Weight	Odds Ratio IV, Random, 95% CI
Kirtane et al. 2021 Short-DAPT	27	1457	32	1502	34.5%	0.87 [0.52, 1.46]
Mehran et al. 2021 TWILIGHT-HBR	23	516	19	535	24.0%	1.27 [0.68, 2.36]
Mehran et al. 2021 Xience 90	48	1672	28	1246	41.5%	1.29 [0.80, 2.06]
Total (95% CI)		**3645**		**3283**	**100.0%**	**1.12 [0.83, 1.52]**
Total events	98		79			

Heterogeneity: Tau² = 0.00; Chi² = 1.42, df = 2 (P = 0.49); I² = 0%
Test for overall effect: Z = 0.72 (P = 0.47)



f) Ischemic stroke

Study	Short DAPT Events	Short DAPT Total	Long DAPT Events	Long DAPT Total	Weight	Odds Ratio IV, Random, 95% CI
Kirtane et al. 2021 Short-DAPT	17	1457	7	1502	66.7%	2.52 [1.04, 6.10]
Mehran et al. 2021 TWILIGHT-HBR	2	516	1	535	9.0%	2.08 [0.19, 22.98]
Mehran et al. 2021 Xience 90	19	1624	2	355	24.3%	2.09 [0.48, 9.01]
Total (95% CI)		**3597**		**2392**	**100.0%**	**2.37 [1.15, 4.87]**
Total events	38		10			

Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 2 (P = 0.97); I² = 0%
Test for overall effect: Z = 2.34 (P = 0.02)

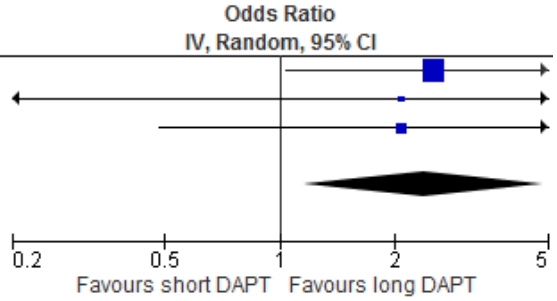


Figure legends

Supplementary fig. 1 The study selection process

Supplementary fig. 2 Publication bias assessment

a) Major Bleeding, b) Probable/definite stent thrombosis, c) All cause death, d) Cardiovascular death, e) Myocardial infarction, f) Ischemic stroke

Supplementary fig. 3 Primary outcome sub-group analysis, aspirin vs. P2Y12 inhibitor SAPT after DAPT

SAPT, single anti-platelet therapy; DAPT, double anti-platelet therapy.

Supplementary fig. 4 Sensitivity analysis including only studies that included patients primarily presenting with myocardial infarction

a) Major Bleeding, b) Probable/definite stent thrombosis, c) All cause death, d) Cardiovascular death, e) Myocardial infarction, f) Ischemic stroke

DAPT, double anti-platelet therapy.

Supplementary fig. 5 Sensitivity analysis including only studies comparing 3-month versus 12 months DAPT duration

a) Major Bleeding, b) Probable/definite stent thrombosis, c) All cause death, d) Cardiovascular death, e) Myocardial infarction, f) Ischemic stroke

DAPT, double anti-platelet therapy.