Supplementary Appendix

Patient-tailored antithrombotic therapy following percutaneous coronary intervention

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Supplementary Table 1. Randomized controlled trials comparing shortened with standard or extended duration of dual antiplatelet therapy

Study (year)	DAPT duration	Sample Size	Primary Endpoint	Secondary Endpoint	Randomization and Design	ACS	Primary and Secondary Results (shortened vs. standard DAPT)
RESET[1] (2012)	3 vs. 12 mo.	2,117	Cardiac death, MI, ST, revascularization or bleeding at 1 year	Major or minor bleeding at 1 year	Randomization at time of PCI; Open-label, non-inferiority study	55%	4.7% vs. 4.7% (P_{NI}<0.001) 0.5% vs. 1.0% (P=0.20)
OPTIMIZE[2] (2014)	3 vs. 12 mo.	3,119	All-cause death, MI, stroke or bleeding at 1 year	Major bleeding at 1 year	Randomization at time of PCI; Single-blind, non-inferiority study	32%	6.0% vs. 5.8% (P_{NI}=0.002) 0.6% vs. 0.9% (P=0.41)
REDUCE[3] (2019)	3 vs. 12 mo.	1,496	All-cause death, MI, ST , stroke, TVR or bleeding at 1 year	N/A	Randomization at time of initial hospitalization; Open-label, non-inferiority study	100%	8.2% vs. 8.4% (P_{NI}<0.001)
EXCELLENT[4] (2011)	6 vs. 12 mo.	1,443	Cardiac death, MI or ischemia driven TVR at 1 year	All-cause death, MI, stroke, ST or TIMI major bleeding at 1 year	Randomization at time of PCI; Open-label, non-inferiority study	51%	4.8% vs. 4.3% (P_{NI}=0.001) 3.3% vs. 3.0% (P=0.64)
ISAR-SAFE[5] (2014)	6 vs. 12 mo.	4,000	All-cause death, MI, ST, stroke and TIMI major bleeding at 9 months	TIMI major bleeding at 9 months	Randomization at DAPT discontinuation; Double-blind, non-inferiority study	40%	1.5% vs. 1.6% (P_{NI}<0.001) 0.2% vs. 0.3% (P=0.74)
I-LOVE-IT 2[6] (2016)	6 vs. 12 mo.	1,829	Cardiac death, target vessel MI or clinically indicated TLR at 1 year	All-cause death, MI, stroke or BARC type ≥3 bleeding at 1 year	Randomization at time of PCI; Single-blind, non-inferiority study	85%	6.8% vs. 5.9% (P_{NI}=0.0065) 7.2% vs. 6.4% (P=0.53)
IVUS-XPL[7] (2016)	6 vs. 12 mo.	1,400	Cardiac death, MI, stroke or TIMI major bleeding at 1 year	TIMI major bleeding at 1 year	Randomization at time of PCI; Open-label, superiority study	49%	2.2% vs. 2.1% (P=0.85) 0.7% vs. 1.0% (P=0.56)
SMART-DATE[8] (2018)	6 vs. 12 mo.	2,712	All-cause death, MI or stroke at 18 months	BARC type 2-5 bleeding at 18 months	Randomization at time of PCI; Open-label, non-inferiority study	100%	4.7% vs. 4.2% (P_{NI}=0.03) 2.7% vs. 3.9% (P=0.09)
DAPT-STEMI[9] (2018)	6 vs. 12 mo.	870	All-cause mortality, revascularization, MI, stroke and TIMI major bleeding at 18 months	All-cause mortality, MI, stroke and TIMI bleeding at 18 months	Randomization at DAPT discontinuation; Single-blind, non-inferiority study	100%	4.8% vs 6.6% (P_{NI}=0.004) 3.2% vs. 4.3% (P=0.40)
SECURITY[10] (2014)	6 vs. 12 mo.	1,399	Cardiac death, MI, stroke, ST, BARC type 3 or 5 bleeding at 1 year	N/A	Randomization at time of PCI; Open-label, non-inferiority study	38%	4.5% vs. 3.7% (P_{NI}<0.05)
PRODIGY[11] (2012)	6 vs. 24 mo.	1,970	All-cause death, MI or stroke at 2 years	N/A	Randomization at time of PCI; Open-label, superiority study	75%	10.0% vs. 10.1% (P=0.91)
ITALIC[12] (2017)	6 vs. 24 mo.	1,850	All-cause death, MI, urgent TVR, stroke or major bleeding at 1 year	Major bleeding at 1 year	Randomization at time of PCI; Open-label, non-inferiority study	44%	1.6% vs. 1.5% (P_{NI}=0.0002) 0.4% vs. 0.0% (P=N/A)

Abbreviations: ACS=acute coronary syndrome; BARC=Bleeding Academic Research Consortium; DAPT=dual antiplatelet therapy; DES=drug-eluting sent; MI=myocardial infarction; PCI=percutaneous coronary intervention; ST=stent thrombosis; TIMI=Thrombolysis in Myocardial Infarction; TLR=target lesion revascularization; TVR=target vessel revascularization

Supplementary Table 2. Randomized controlled trials comparing shortened dual antiplatelet therapy followed by $P2Y_{12}$-inhibitor monotherapy with standard dual antiplatelet therapy

Study (year)	Intervention Strategy	Sample Size	Primary Endpoint	Secondary Endpoint	Design and Randomization	ACS	Primary and Secondary Results ($P2Y_{12}$ monotherapy vs. DAPT)
GLOBAL-LEADERS[13] (2018)	Ticagrelor alone after 1 mo. DAPT	15,968	All-cause death or new Q-wave MI at 2 years	BARC type 3 or 5 bleeding at 2 years	Randomization at time of PCI; Open-label, superiority study	47%	3.8% vs. 4.4% (P=0.07) 2.0% vs. 2.1% (P=0.77)
STOPDAPT-2[14] (2019)	Clopidogrel alone after 1 mo. DAPT	3,009	Cardiac death, MI, stroke, ST, and TIMI major or minor bleeding at 1 year	TIMI major or minor bleeding at 1 year	Randomization at time of PCI; Open-label, non-inferiority study	38%	2.4% vs. 3.7% (P_{NI}<0.001) 0.4% vs. 1.5% (P=0.004)
SMART-CHOICE[15] (2019)	$P2Y_{12}$-inhibitor after 3 mo. DAPT	2,993	All-cause death, MI or stroke at 1 year	BARC type 2-5 bleeding at 1 year	Randomization at time of PCI; Open-label, non-inferiority study	58%	2.9% vs. 2.5% (P_{NI}=0.007) 2.0% vs. 3.4% (P=0.02)
TICO[16] (2020)	Ticagrelor alone after 3 mo. DAPT	3,056	All-cause death, MI, ST, stroke, TVR or TIMI major bleeding at 1 year	TIMI major bleeding at 1 year	Randomization at time of PCI; Open-label, superiority study	100%	3.9% vs. 5.9% (P=0.01) 1.7% vs. 3.0% (P=0.02)
TWILIGHT[17] (2019)	Ticagrelor alone after 3 mo. DAPT	7,119	BARC type 2, 3, or 5 bleeding at 1 year	All-cause death, MI, stroke at 1 year	Randomization after 3 months; Double-blind, superiority study	65%	4.0% vs. 7.1% (P<0.001) 3.9% vs. 3.9% (P_{NI}<0.001)

Abbreviations: ACS=acute coronary syndrome; BARC=Bleeding Academic Research Consortium; DAPT=dual antiplatelet therapy; DES=drug-eluting sent; MI=myocardial infarction; PCI=percutaneous coronary intervention; ST=stent thrombosis; TIMI=Thrombolysis in Myocardial Infarction; TVR=target vessel revascularization

Supplementary Table 3. Randomized controlled trials comparing extended with standard or shortened duration of dual antiplatelet therapy

Study (year)	DAPT duration	Sample Size	Primary Endpoint	Secondary Endpoint	Design and Randomization	ACS	Primary and Secondary Results (extended vs. standard DAPT)
NIPPON[18] (2017)	6 vs. 18 mo.	3,773	All-cause death, MI, stroke and major bleeding at 18 months	N/A	Randomization at time of PCI; Open-label, non-inferiority study	45%	1.5% vs. 2.1% (P_{NI}<0.05)
PRODIGY[11] (2012)	6 vs. 24 mo.	1,970	All-cause death, MI or stroke at 2 years	N/A	Randomization at time of PCI; Open-label, superiority study	75%	10.1% vs. 10.0% (P=0.91)
ITALIC[12] (2017)	6 vs. 24 mo.	1,850	All-cause death, MI, urgent TVR, stroke or major bleeding at 1 years	Major bleeding at 1 year	Randomization at time of PCI; Open-label, non-inferiority study	44%	1.5% vs. 1.6% (P_{NI}=0.0002) 0.0% vs. 0.4% (P=N/A)
ARCTIC[19] (2014)	12 vs. 18-24 mo.	1,259	All-cause death, MI, ST, stroke or urgent revascularization at 18 months	STEEPLE major bleeding at 18 months	Randomization at 12 months after PCI; Open-label, superiority study	26%	4.0% vs. 4.0% (P=0.58) <0.5% vs. 1.0% (P=0.07)
DAPT[20] (2014)	12 vs. 30 mo.	9,961	All-cause death, MI or stroke at 30 months	GUSTO moderate or severe bleeding at 30 months	Randomization at DAPT discontinuation; Double-blind, superiority study	43%	4.3% vs. 5.9% (P<0.001) 2.5% vs. 1.6% (P<0.001)
DES LATE[21] (2014)	12 vs. 36 mo.	5,045	Cardiac death, myocardial infarction or stroke at 2 years	TIMI major bleeding at 2 years	Randomization at 12 months after PCI; Open-label, superiority study	61%	2.6% vs. 2.4% (P=0.75) 1.4% vs. 1.1% (P=0.20)
OPTIDUAL[22] (2015)	12 vs. 48 mo.	1,385	All-cause death, MI, stroke or major bleeding at 3 years	N/A	Randomization at DAPT discontinuation; Open-label, superiority study	36%	5.8% vs. 7.5% (P=0.17)
PEGASUS-TIMI 54[23] (2016)	0 vs. 33 mo.	21,162	Cardiac death, MI or stroke at 3 years	TIMI major bleeding at 3 years	Randomization 1-3 years after MI; Double-blind, superiority study	100%	7.8% vs. 9.0% (P=0.001) 2.6% vs. 1.1% (P<0.001)
THEMIS[24] (2019)	0 vs. 54 mo.	19,271	Cardiac death, MI or stroke at 4.5 years	TIMI major bleeding at 4.5 years	Randomization at outpatient clinic; Double-blind, superiority study	0%	6.9% vs. 7.6% (P=0.04) 0.89% vs. 0.38% (P<0.001)

Abbreviations: ACS=acute coronary syndrome; BARC=Bleeding Academic Research Consortium; DAPT=dual antiplatelet therapy; DES=drug eluting sent; GUSTO=Global Utilization Of Streptokinase and Tpa for Occluded arteries; MI=myocardial infarction; PCI=percutaneous coronary intervention; ST=stent thrombosis; TIMI=Thrombolysis in Myocardial Infarction; TVR=target vessel revascularization; STEEPLE=Safety and Efficacy of Enoxaparin in PCI Patients, an International Randomized Evaluation.

Supplementary Table 4. Randomized controlled trials comparing factor Xa- or thrombin inhibitor therapy on top of antiplatelet therapy with standard treatment

Study (year)	Intervention Strategy	Sample Size	Primary Endpoint	Secondary Endpoint	Design and Randomization	ACS	Primary and Secondary Results (intervention vs. standard therapy)
RE-DEEM[25]* (2009)	Dabigatran on top of DAPT	1,861	ISTH major or clinically relevant minor bleeding at 6 months	Cardiac death, MI or stroke at 6 months	Randomization at time of MI; Double-blind, superiority study	100%	3.5%, 4.3%, 7.9%, 7.8% vs. 2.2% (P_{trend}<0.001) 4.6%, 4.9%, 3.0%, 3.5% vs. 3.8%
APPRAISE[26]† (2009)	Apixaban on top of DAPT	1,715	ISTH major or clinically relevant minor bleeding at 6 months	Cardiac death, MI, severe recurrent ischemia or stroke at 6 months	Randomization within 7 days of MI; Double-blind, superiority study	100%	5.7%, 7.9% vs. 3.0% (P=0.09, P=0.005) 7.6%, 6.0% vs. 8.7% (P=0.21, P=0.07)
ATLAS ACS-TIMI 46[27]‡ (2009)	Rivaroxaban on top of DAPT	3,491	All-cause death, MI, stroke or revascularization at 6 months	TIMI major or minor bleeding or bleeding requiring medical attention at 6 months	Randomization within 7 days after hospital admission; Double-blind, superiority study	100%	7.0% vs. 5.9% (P=0.10) 8.6% vs. 3.3% (P<0.0001)
APPRAISE-2[28] (2011)	Apixaban on top of DAPT	7,392	Cardiac death, MI or stroke at 15 months	TIMI major bleeding after 15 months	Randomization within 7 days of ACS; Double-blind, superiority study	100%	7.5% vs. 7.9% (P=0.51) 1.3% vs. 0.5% (P=0.001)
ATLAS ACS 2-TIMI 51[29]§ (2012)	Low-dose rivaroxaban on top of DAPT	15,526	Cardiac death, MI or stroke at 2 years	TIMI major bleeding at 2 years	Randomization within 7 days after hospital admission; Double-blind, superiority study	100%	8.9% vs. 10.7% (P=0.008) 2.1% vs. 0.6% (P<0.001)
COMPASS[30]¶ (2017)	Low-dose rivaroxaban on top of aspirin	27,395	Cardiac death, MI or stroke after mean follow-up of 23 months	ISTH major bleeding after mean follow-up of 23 months	Randomization after run-in phase; Double-blind, superiority study	0%	4.1% vs. 5.4% (P<0.001) 3.1% vs. 1.9% (P<0.001)
GEMINI-ACS-1[31] (2017)	Low-dose rivaroxaban plus $P2Y_{12}$-inhibitor	3,037	TIMI major bleeding at 1 year	Cardiac death, MI, stroke or ST at 1 year	Randomization within 10 days of ACS; Double-blind, superiority study	100%	5% vs. 5% (P=0.5840) 5% vs. 5% (P=0.7316)

Abbreviations: ACS=acute coronary syndrome; BARC=Bleeding Academic Research Consortium; DAPT=dual antiplatelet therapy; DES=drug eluting sent; ISTH=International Society of Thrombosis and Haemostasis; MI=myocardial infarction; PCI=percutaneous coronary intervention; ST=stent thrombosis; TIMI=Thrombolysis in Myocardial Infarction; TVR=target vessel revascularization

* Phase II trial investigating different doses of dabigatran which showed a dose-dependent increase in bleeding events (P_{trend}<0.001); Results are for the different doses used (50 mg, 75 mg, 110 mg or 150mg once daily) vs. placebo

† Phase II trial investigating different doses of apixaban; Results are for the different doses used (2.5 mg twice daily and 10 mg once daily) vs. placebo

‡ Phase II trial investigating different doses of rivaroxaban; Results are for the combined rivaroxaban-treated group vs. placebo

§ The ATLAS ACS 2-TIMI 51 trial used both 2.5 mg rivaroxaban twice daily and 5.0 mg rivaroxaban twice daily

¶ The COMPASS trial also looked at low-dose rivaroxaban without aspirin versus aspirin, this analysis is not presented in this table

Supplementary Appendix 5

Methodology and results of pooled hazard ratios for bleeding and ischemic events

Objective

We intended to show the impact of different risk factors for bleeding and/or ischemic events by pooling hazard ratios from previously published studies in patients with coronary artery disease and using antiplatelet therapy.

Study selection

We performed a computerized literature search of the PubMed database between January 6th and February 15th 2020, using the following search terms: "bleeding risk" or "ischemic risk", "coronary artery disease" and "hazard ratio". Per risk factor several additional search terms were added (see below). Citations were screened at the title/abstract level and retrieved as full articles (including supplementary material). Additionally, bibliographies of suitable articles were screened using a snowball approach.

Studies were eligible for inclusion if they i) were performed in patients with (a high risk of) coronary artery disease regardless of treatment, ii) reported multivariable adjusted hazard ratios including the corresponding 95%-confidence interval (CI) for bleeding and/or thrombotic risk depending on the risk factor of interest, and iii) were deemed of sufficient methodological quality. Non-English articles, case reports, reviews, and studies reporting duplicate data were excluded.

Statistical analysis

The statistical analyses were performed with R (version 3.6.1) and RStudio (version 1.2.1335). Pooling was performed at study-level. Due to the expected high heterogeneity between the studies a random-effects model was used. Hazard ratios and 95%-CI were log-transformed to enable the calculation of standard errors. Subsequently, the results were pooled using inverse variance weighting.

Results

Our literature search produced a vast amount of studies per risk factor. In the section below the search results are shown for each risk factors sorted in three categories: i) risk factors both bleeding and/or ischemic events ii) risk factors for ischemic events alone, and iii) risk factors for bleeding events alone. Results are reported as pooled hazard ratio including corresponding 95%-CI. References to all included studies are also provided.

Risk factors for bleeding and ischemic events

1. *Age*

Additional search term(s): "age"

Studies screened: 598 (ischemic risk) and 83 (bleeding risk)

	Ischemic Risk		Bleeding Risk	
Age per 10 yr.	*Study*	*HR (95%-CI)*	*Study*	*HR (95%-CI)*
	Zhang et al. (2015)[32]	1.55 (1.35-1.78)	Ko et al. (2010)[33]	1.41 (1.23-1.61)
	Pepine et al. (2006)[34]	1.63 (1.56-1.71)	Costa et al. (2017)[35]	1.34 (1.11-1.48)
			Yeh et al. (2016)[36]	1.54 (1.34-1.78)
			Kikkert et al. (2015)[37]	1.29 (1.13-1.49)
	Pooled hazard ratio	**1.62 (1.55-1.70)**	**Pooled hazard ratio**	**1.39 (1.30-1.49)**

2. *Diabetes mellitus*

Additional search term(s): "diabetes mellitus"

Studies screened: 268 (ischemic risk) and 31 (bleeding risk)

	Ischemic Risk		Bleeding Risk	
Diabetes mellitus	*Study*	*HR (95%-CI)*	*Study*	*HR (95%-CI)*
	Lemesle et al. (2018)[38]	1.41 (1.11-1.78)	Lemesle et al. (2018)[38]	1.75 (1.05-2.91)
	Hamilos et al. (2018)[39]	1.27 (0.89-1.79)	Hamilos et al. (2018)[39]	1.20 (0.79-1.84)
	Lee et al. (2017)[40]	1.25 (1.12-1.40)	Lin et al. (2013)[41]	1.21 (0.95-1.55)
	Tajik et al. (2017)[42]	1.41 (1.29-1.53)	Palmerini et al. (2013)[43]	1.31 (1.10-1.55)
	Lin et al. (2017)[44]	2.15 (1.03-4.49)		
	Loutfi et al. (2016)[45]	1.82 (1.16-2.84)		
	Mathew et al. (2002)[46]	1.29 (0.99-1.68)		
	Baber et al. (2016)[47]	1.69 (1.14-2.52)		
	Yeh et al. (2016)[36]	1.38 (1.10-1.72)		
	Bavry et al. (2013)[48]	1.73 (1.57-1.90)		
	Bhatt et al. (2010)[49]	1.44 (1.36-1.53)		
	Vanassche et al. (2019)[50]	1.46 (1.31-1.63)		
	Pepine et al. (2006)[34]	1.77 (1.62-1.93)		
	Miao et al. (2020)[51]	1.25 (1.20-1.30)		
	Kikkert et al. (2014)[52]	1.69 (1.18-2.41)		
	Pooled hazard ratio	**1.46 (1.35-1.57)**	**Pooled hazard ratio**	**1.30 (1.14-1.48)**

3. Chronic kidney disease

Additional search term(s): "chronic kidney disease", "renal failure"

Studies screened: 198 (ischemic risk) and 50 (bleeding risk)

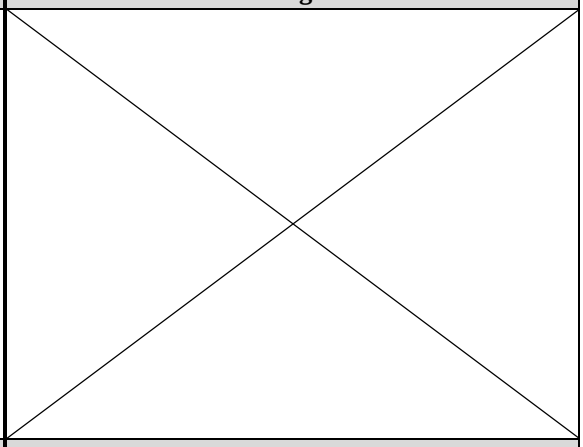
	Ischemic Risk		Bleeding Risk	
Chronic kidney disease	*Study*	*HR (95%-CI)*	*Study*	*HR (95%-CI)*
	Baber et al. (2016)[47]	2.12 (1.46-3.05)	Baber et al. (2016)[47]	1.81 (1.16-2.82)
	Yeh et al. (2016)[36]	1.55 (1.03-2.32)	Yeh et al. (2016)[36]	1.66 (1.04-2.66)
	Tomaniak et al. (2020)[53]	1.55 (1.22-1.96)	Tomaniak et al. (2020)[53]	1.40 (1.22-1.96)
	Bernaudo et al. (2013)[54]	1.77 (1.15-2.73)	Saltzman et al. (2011)[55]	1.43 (1.26-1.62)
	Dan et al. (2012)[56]	2.39 (2.35-4.26)	Ko et al. (2010)[33]	1.93 (1.37-2.74)
	Saltzman et al. (2011)[55]	1.38 (1.20-1.59)	Ninomiva et al. (2005)[57]	1.09 (0.29-4.13)
	Buckley et al. (2009)[58]	1.32 (0.18-9.59)	Manzano et al. (2009)[59]	2.59 (1.00-6.95)
	Chonchol et al. (2007)[60]	1.46 (1.01-2.11)	Lin et al. (2013)[41]	1.58 (1.17-2.13)
	Ninomiya et al. (2005)[57]	2.26 (1.06-4.79)	Honda et al. (2017)[61]	1.56 (1.10-2.42)
	Bavry et al. (2013)[48]	1.62 (1.30-2.01)	Manzano et al. (2008)[62]	3.10 (0.60-16.0)
			Palmerini et al. (2013)[43]	1.24 (1.05-1.47)
	Pooled hazard ratio	**1.68 (1.46-1.92)**	**Pooled hazard ratio**	**1.46 (1.32-1.63)**

Risk factors for ischemic events

1. *ACS at presentation*

Additional search term(s): "acute coronary syndrome", "ACS"

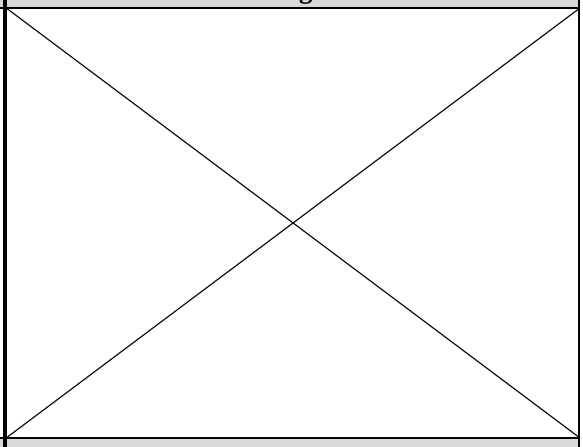
Studies screened: 43

	Ischemic Risk		Bleeding Risk
ACS at presentation	*Study*	*HR (95%-CI)*	
	Baber et al. (2016)[47]	2.09 (1.24-3.53)	
	Yeh et al. (2016)[36]	1.79 (1.43-2.23)	
	Pooled hazard ratio	**1.84 (1.49-2.25)**	

2. *Prior myocardial infarction*

Additional search term(s): "prior myocardial infarction", "history of myocardial infarction"

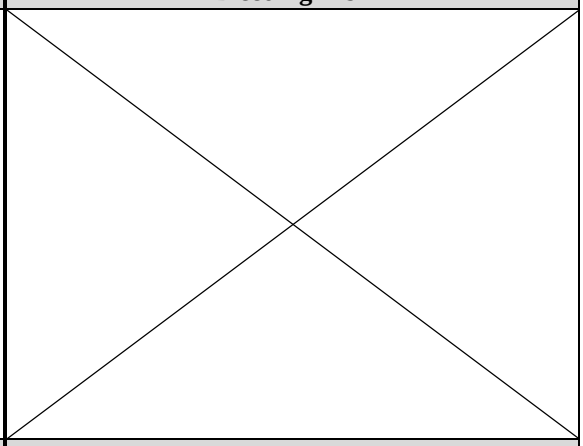
Studies screened: 299

	Ischemic Risk		Bleeding Risk
Prior myocardial infarction	*Study*	*HR (95%-CI)*	
	Lin et al. (2017)[44]	3.17 (1.80-5.57)	
	Yeh et al. (2016)[36]	1.79 (1.43-2.23)	
	Bavry et al. (2013)[48]	1.48 (1.35-1.63)	
	Bhatt et al. (2010)[49]	1.71 (1.57-1.85)	
	Pepine et al. (2006)[34]	1.34 (1.23-1.46)	
	Kikkert et al. (2014)[52]	1.47 (1.03-2.10)	
	Pooled hazard ratio	**1.60 (1.39-1.82)**	

3. Multivessel disease

Additional search term(s): "extensive coronary artery disease", "multivessel coronary artery disease"

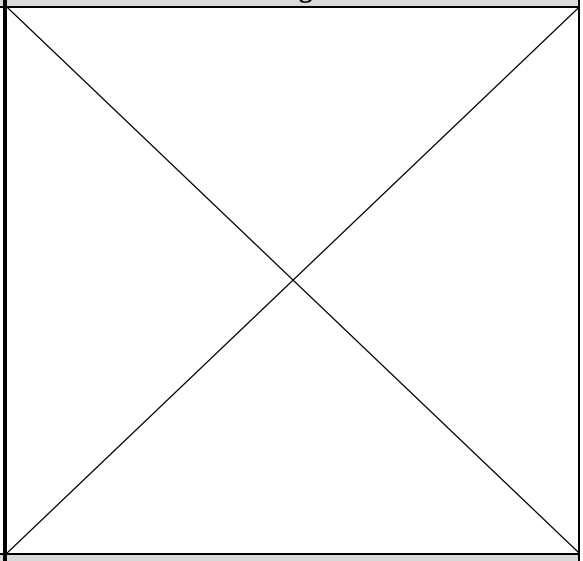
Studies screened: 139

	Ischemic Risk		Bleeding Risk
Extensive CAD	*Study*	*HR (95%-CI)*	
	Lee et al. (2017)[40]	1.14 (1.08-1.21)	
	Lemesle et al. (2017)[63]	1.53 (1.08-2.15)	
	Arnold et al. (2015)[64]	2.89 (1.90-4.39)	
	Sorajja et al. (2007)[65]	1.80 (1.27-2.54)	
	Kikkert et al. (2014)[52]	1.52 (1.12-2.06)	
	Pooled hazard ratio	**1.63 (1.21-2.18)**	

4. Smoking

Additional search term(s): "smoking"

Studies screened: 137

	Ischemic Risk		Bleeding Risk
Smoking	*Study*	*HR (95%-CI)*	
	Lin et al. (2017)[44]	1.48 (1.16-1.89)	
	Buckley et al. (2009)[58]	1.94 (1.31-2.89)	
	Baber et al. (2016)[47]	1.69 (1.14-2.52)	
	Yeh et al. (2016)[36]	1.40 (1.11-1.76)	
	Lemesle et al. (2017)[63]	1.87 (1.27-2.77)	
	Bavry et al. (2013)[48]	1.42 (1.29-1.57)	
	Bhatt et al. (2010)[49]	1.30 (1.20-1.41)	
	Vanassche et al. (2019)[50]	1.15 (1.01-1.31)	
	Khan et al. (2017)[66]	1.49 (0.97-2.29)	
	Zhang et al. (2015)[32]	1.80 (1.34-2.54)	
	Satoh et al. (2006)[67]	2.47 (0.86-7.10)	
	Pepine et al. (2006)[34]	1.41 (1.29-1.54)	
	Miao et al. (2020)[51]	1.56 (1.47-1.65)	
	Pooled hazard ratio	**1.45 (1.34-1.57)**	

5. Peripheral artery disease

Additional search term(s): "peripheral artery disease"

Studies screened: 172

	Ischemic Risk		Bleeding Risk
Peripheral Artery Disease	*Study*	*HR (95%-CI)*	
	Buckley et al. (2009)[58]	1.01 (0.50-2.01)	
	Yeh et al. (2016)[36]	1.49 (1.05-2.13)	
	Ostman et al. (2017)[68]	2.10 (1.34-3.27)	
	Bavry et al. (2013)[48]	1.20 (1.06-1.36)	
	Zhang et al. (2015)[32]	1.85 (1.34-2.54)	
	Pepine et al. (2006)[34]	1.27 (1.14-1.42)	
	Miao et al. (2020)[51]	1.28 (1.22-1.35)	
	Inohara et al. (2018)[69]	1.63 (1.48-1.78)	
	Franzone et al. (2016)[70]	1.70 (1.17-2.48)	
	Inglis et al. (2013)[71]	1.26 (1.09-1.44)	
	Kikkert et al. (2014)[52]	1.89 (1.22-2.92)	
	Pooled hazard ratio	**1.42 (1.28-1.58)**	

1. Complex PCI

Additional search term(s): "complex PCI", "complex lesions"

Studies screened: 83

	Ischemic Risk		Bleeding Risk
ACS at presentation	*Study*	*HR (95%-CI)*	
	Giustino et al. (2016)[72]	1.98 (1.50-2.60)	
	Yeh et al. (2017)[73]	2.05 (1.60-2.61)	
	Wang et al. (2020)[74]	1.63 (1.38-1.92)	
	Pooled hazard ratio	**1.82 (1.55-2.14)**	

Risk factors for bleeding events

1. *History of bleeding*

Additional search term(s): "history of bleeding", "previous bleeding"

Studies screened: 55

	Ischemic Risk	Bleeding Risk	
History of bleeding		*Study*	*HR (95%-CI)*
		Ko et al. (2010)[33]	2.42 (1.70-3.46)
		Costa et al. (2017)[35]	4.14 (1.22-14.0)
		Bonaca et al. (2018)[75]	3.51 (2.08-5.90)
		Lin et al. (2013)[41]	3.70 (2.82-4.85)
		Honda et al. (2017)[61]	3.49 (2.03-5.79)
		Manzano et al. (2008)[62]	1.10 (0.20-4.40)
		Kikkert et al. (2015)[37]	2.07 (1.14-3.73)
		Pooled hazard ratio	**3.00 (2.41-3.78)**

2. *Triple therapy*

Additional search term(s): "triple therapy", "oral anticoagulants"

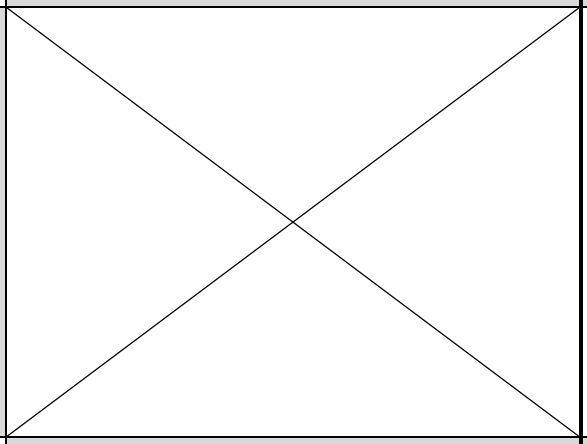
Studies screened: 43

	Ischemic Risk	Bleeding Risk	
Triple Therapy		*Study*	*HR (95%-CI)*
		Ko et al. (2010)[33]	3.12 (2.50-3.90)
		Manzano et al. (2009)[59]	3.29 (1.23-8.84)
		Baber et al. (2016)[47]	1.93 (1.08-3.43)
		Inohara et al. (2019)[76]	2.27 (1.38-3.73)
		Honda et al. (2017)[61]	2.94 (1.83-4.61)
		Choi et al. (2017)[77]	4.48 (1.81-11.1)
		Lopes et al. (2016)[78]	1.55 (0.44-5.47)
		Mennuni et al. (2015[79]	1.79 (1.11-2.89)
		Manzano et al. (2008)[62]	7.10 (1.50-32.4)
		Pooled hazard ratio	**2.64 (2.16-3.25)**

3. Anemia

Additional search term(s): "anemia", "low hemoglobin"

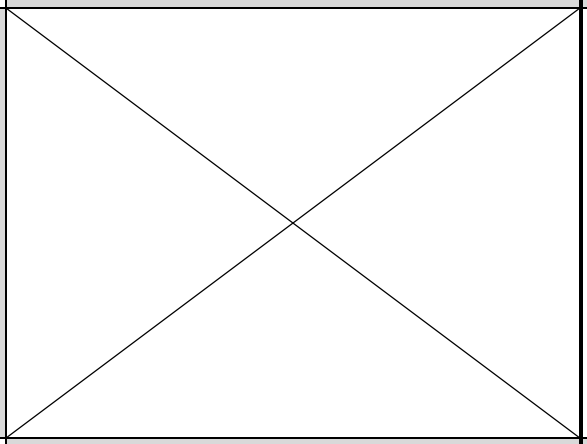
Studies screened: 15

	Ischemic Risk	Bleeding Risk	
Anemia		*Study*	*HR (95%-CI)*
		Kalra et al. (2017)[80]	2.06 (1.23-3.44)
		Manzano et al. (2009)[59]	2.36 (1.00-5.54)
		Baber et al. (2016)[47]	2.72 (1.83-4.04)
		Bonaca et al. (2018)[75]	1.56 (1.22-1.98)
		Honda et al. (2017)[61]	1.75 (1.10-2.73)
		Manzano et al. (2008)[62]	3.80 (1.20-12.5)
		Wester et al. (2019)[81]	1.30 (1.00-1.60)
		Kikkert et al. (2015)[37]	1.87 (1.26-2.79)
		Faggioni et al. (2019)[82]	2.32 (1.67-3.20)
		Pooled hazard ratio	**1.90 (1.55-2.29)**

4. Malignancy

Additional search term(s): "malignancy", "cancer"

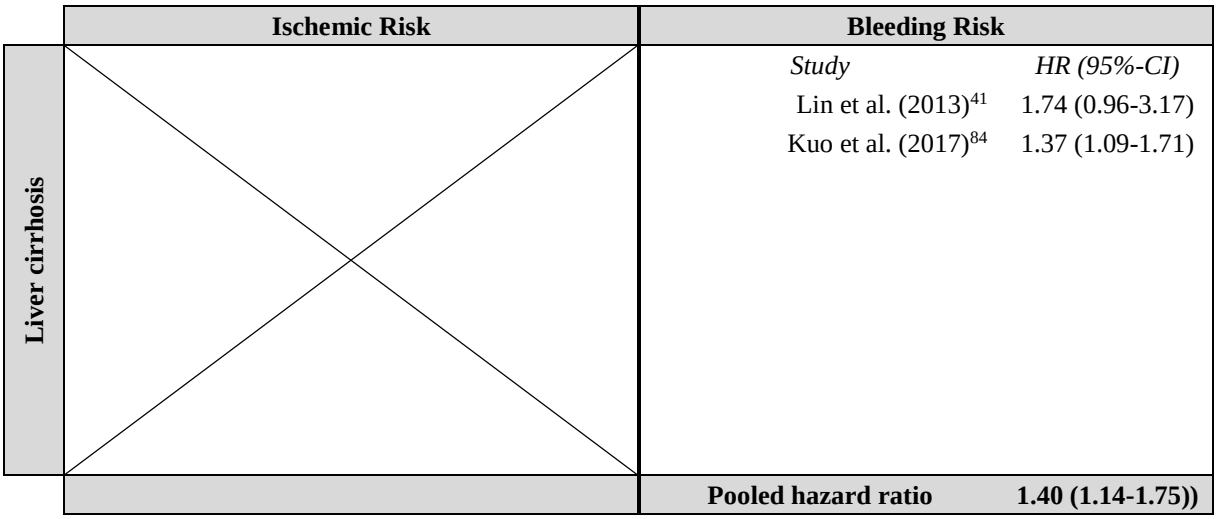
Studies screened: 10

	Ischemic Risk	Bleeding Risk	
Malignancy		*Study*	*HR (95%-CI)*
		Ko et al. (2010)[33]	1.80 (1.09-2.96)
		Nakatsuma et al. (2018)[83]	1.28 (1.08-1.51)
		Pooled hazard ratio	**1.58 (1.15-2.18)**

5. Liver cirrhosis

Additional search term(s): "liver cirrhosis", "liver failure"

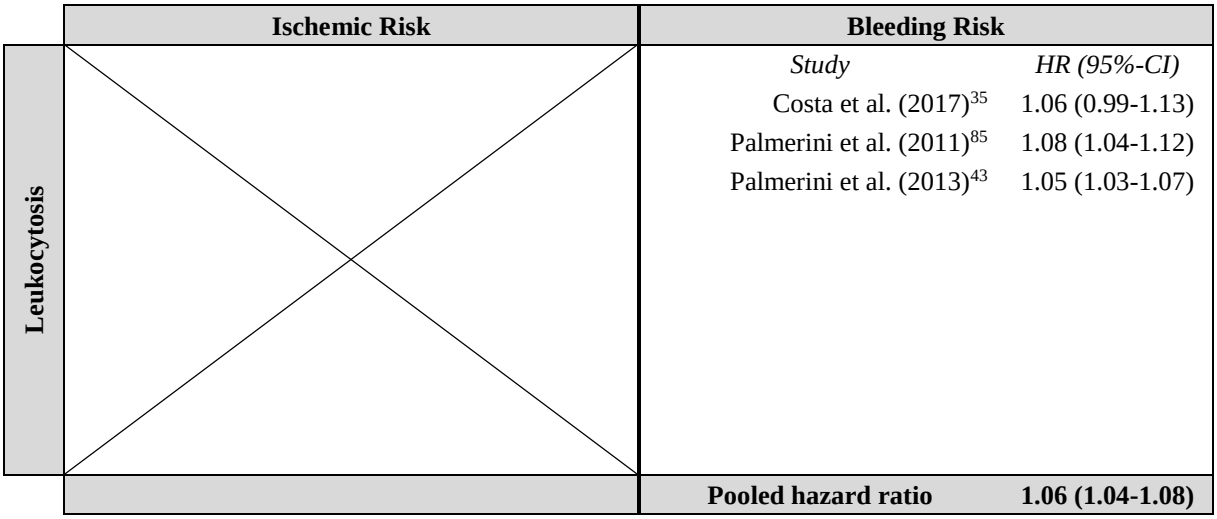
Studies screened: 49



6. Leukocytosis

Additional search term(s): "leukocytes", "white blood cells", "leukocytosis"

Studies screened: 29



7. Thrombocytopenia

Additional search term(s): "thrombocytopenia"

Studies screened: 62

	Ischemic Risk	Bleeding Risk	
Thrombocytopenia		*Study*	*HR (95%-CI)*
		Kikkert et al. (2015)[37]	2.07 (1.10-3.91)
		Morici et al. (2019)[86]	1.34 (0.64-2.81)
		Ito et al. (2018)[87]	2.35 (1.80-3.08)
		Hakim et al. (2011)[88]	1.65 (1.03-2.67)
		Pooled hazard ratio	**1.99 (1.55-2.59)**

Supplementary Table 6. Derivation cohorts of risk scores developed to guide decision-making surrounding dual antiplatelet therapy duration after percutaneous coronary intervention

	PRECISE-DAPT score[35]	**DAPT score[36]**
Size derivation cohort	14,963	11,648
Age (years ±SD)	65.0*	61.3 ±10.3
Sex (male %)	10,549 (70.5)	8,723 (74.9)
Active smoking (%)	3,757 (28.0)	3,142 (27.0)
Hypertension (%)	10,739 (71.9)	8,522 (73.2)
Hypercholesterolemia (%)	9,080 (61.3)	N/A
Diabetes Mellitus (%)	4,168 (27.9)	3,391 (30.4)
Prior MI (%)	2,946 (19.8)	2,456 (21.1)
Prior PCI (%)	2,392 (16.0)	3,368 (30.1)
Prior CABG (%)	893 (6.0)	1,249 (10.7)
Clinical presentation (%)		
CCS	6,299 (42.1)	4,149 (35.6)
ACS, troponin negative	3,215 (21.5)	1,821 (15.6)
ACS, troponin positive	4,669 (31.2)	3,576 (30.7)
Unknown	780 (5.2)	2,102 (18.0)
Follow-up	7 days until 12 months	12 until 30 months
Derivation cohort	BIOSCIENCE COMFORTABLE AMI EXCELLENT OPTIMIZE PRODIGY RESET SECURITY ZEUS	DAPT
Validation cohort	PLATO BernPCI registry	DAPT† PROTECT

Abbreviations: ACS=acute coronary syndrome; CABG=coronary bypass grafting; CCS=chronic coronary syndrome; MI=myocardial infarction; PCI=percutaneous coronary intervention; SD=standard deviation

Results are reported as mean ±SD or number of patients (%) unless mentioned otherwise

* Median value

† Validation of the DAPT score occurred through bootstrap resampling of the derivation cohort

Supplementary Table 7. Validation studies of the PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy (PRECISE-DAPT) score showing cohort characteristics, score discrimination (C-statistic) and calibration

Study (cohort)	Population (n)	Cohort type	ACS	Period	Bleeding endpoint	Bleeding definition	Event rate	C-statistic (95% CI)	Calibration
Costa et al. 2017[35] *(derivation cohort)*	PCI, DAPT (14,963)	RCT	56%	2007-2014	Out-of-hospital bleeding at 1 year	TIMI major or minor TIMI major BARC type 2, 3 or 5 BARC type 3 or 5	1.5% 0.8% 2.4% 1.6%	0.73 (0.61-0.85) 0.71 (0.57-0.85) 0.68 (0.63-0.72) 0.68 (0.63-0.73)	Adequate
Costa et al. 2017[35] *(PLATO)*	ACS (8,595)	RCT	100%	2006-2008	Out-of-hospital bleeding at 1 year	TIMI major or minor TIMI major	1.7% 1.1%	0.70 (0.65-0.74) 0.68 (0.63-0.74)	Underestimated
Costa et al. 2017[35] *(BernPCI)*	PCI (6,172)	Registry	55%	2009-2014	Out-of-hospital bleeding at 1 year	TIMI major or minor TIMI major	1.5% 1.0%	0.66 (0.61-0.71) 0.65 (0.58-0.71)	Adequate
Abu-Assi et al. 2018[89] *(Cardio-CHUVI)*	ACS, PCI, DAPT (2,064)	Registry	100%	2012-2015	Out-of-hospital bleeding at 1 year	BARC type 2, 3 or 5 BARC type 3 or 5	7.1% 2.8%	0.61 (0.56-0.66) 0.73 (0.67-0.79)	Adequate
Choi et al. 2018[90] *(Korean cohort)*	PCI, DAPT (904)	Registry	34%	2008-2016	Bleeding at 1 year	TIMI major or minor BARC type 3-5	13.2% 17.0%	0.75 (0.72-0.78) 0.81 (0.78-0.84)	Adequate
Morici et al. 2019[86] *(Italian cohort)*	ACS (1,000)	Cohort study	100%	2014-2017	Bleeding during follow-up (median follow-up 496 days)	BARC type 2-5	7.2%	0.83 (0.76-0.90)	N/A
Pavasini et al. 2019[91] *(FRASER)*	ACS, DAPT, ≥70yrs (402)	Cohort study	100%	2014-2016	Bleeding at 1 year	BARC type 3 or 5	4.0%	0.79 (0.66-0.91)	N/A
Bianco et al. 2020[92] *(RENAMI)*	ACS, PCI, DAPT (4,434)	Registry	100%	2012-2016	Bleeding on DAPT (median follow-up 14 months)	BARC type 3 or 5	1.9%	0.65 (0.59-0.71)	Adequate
Ueki et al. 2020[93] *(BernPCI)*	PCI (12,121)	Registry	56%	2009-2016	Bleeding at 1 year	BARC type 3 or 5	3.7%	0.67 (0.65-0.70)	N/A
Marti et al. 2020[94] *(Spanish cohort)*	PCI, DAPT, ≥75yrs (448)	Cohort study	53%	2012-2017	Bleeding at 1 year (non-access related)	BARC type 3 or 5	7.3%	0.67 (0.62-0.71)	Adequate
Choi et al. 2020[95] *(SMART-DATE)*	ACS, PCI, DAPT (2,712)	RCT	100%	2012-2015	Out-of-hospital bleeding at 18 months	BARC type 3 or 5	0.5%	0.75 (0.66-0.85)	N/A
Gragnano et al. 2020[96] *(GLOBAL-LEADERS)*	PCI, DAPT (14,928)	RCT	50%	2013-2015	Bleeding at 1 year Bleeding at 2 years	BARC type 3 or 5 BARC type 3 or 5	1.6% 2.2%	0.65 (0.61-0.68) 0.65 (0.62-0.68)	Adequate
Rozemeijer et al. 2020[97] *(ReCre8)*	PCI, DAPT (1,491)	RCT	58%	2014-2017	Out-of-hospital bleeding at 1 year	BARC type 2, 3 or 5	2.3%	0.59 (0.48-0.69)	Adequate
Marquis et al. 2020[98] *(TRILOGY-ACS)*	ACS, DAPT, medical management (9,326)	RCT	100%	2008-2012	Bleeding at 1 year Bleeding at 2 years	TIMI major or minor TIMI major or minor	1.3% 1.7%	0.62 (0.58-0.67) 0.62 (0.58-0.66)	Adequate

Abbreviations: ACS=acute coronary syndrome; BARC=Bleeding Academic Research Consortium; DAPT=dual antiplatelet therapy; PCI=percutaneous coronary intervention; RCT=randomized controlled trial; TIMI=Thrombolysis in Myocardial Infarction.

Supplementary Table 8. Validation studies of the Dual Antiplatelet Therapy (DAPT) score as a decision tool, with cohort characteristics and absolute risk differences of ischemic and bleeding events of prolonged DAPT compared to standard DAPT, stratified to DAPT score outcome

								Absolute risk differences of prolonged versus standard DAPT (95% CI)				
Study (cohort)	Population (n)	DAPT duration	Cohort type	ACS	Period	DAPT score	Ischemic Endpoint	Event rate	P-value	Bleeding endpoint	Event rate	P-value
Yeh et al. 2016[36] *(DAPT)*	PCI (11,648)	12 vs. 30 months	RCT	74%	2009-2014	≥2	Definite or probable ST or MI at 30 months	-3.0% (-4.1%, -2.0%)	<0.001	GUSTO moderate or severe bleeding at 30 months	+0.4% (-0.3%, +1.0%)	0.26
						<2		-0.7% (-1.4%, +0.1%)	0.07		+1.6% (+0.8%, +2.3%)	<0.001
Harada et al. 2017[99] *(ISAR-SAFE)*	PCI (3,976)	6 vs. 12 months	RCT	40%	2009-2014	≥2	Death, MI, ST or stroke at 15 months	-0.1% (N/A)	0.96	TIMI major bleeding at 15 months	0.0% (N/A)	0.44
						<2		+0.4% (N/A)	0.43		0.0% (N/A)	0.65
Piccolo et al. 2017[100] *(PRODIGY)*	PCI (1,970)	6 vs. 24 months	RCT	74%	2006-2011	≥2	Definite or probable ST or MI at 24 months	-0.6% (-2.8%, +1.6%)	N/A	GUSTO moderate or severe bleeding at 24 months	+0.2% (-1.0%, +1.4%)	N/A
						<2		+1.2% (-0.8%, +3.1%)	N/A		+2.6% (-0.8%, +4.4%)	N/A
Yoshikawa et al. 2018[101] *(CREDO-Kyoto, RESET&NEXT)*	PCI (1,590)	<13 vs. ≥13 months	RCT, registry	22%	2005-2011	≥2	Definite or probable ST or MI at 36 months	-1.0% (N/A)	0.10	GUSTO moderate or severe bleeding at 36 months	-0.3% (N/A)	0.76
						<2		-0.2% (N/A)	0.51		+0.9% (N/A)	0.08
Witberg et al. 2020[102] *(Israeli cohort)*	PCI (4,471)	12 vs. >12 months	Registry	58%	2008-2018	≥2	MI at 36 months	-1.6% (N/A)	0.11	Actionable bleeding at 36 months	+0.2% (N/A)	0.80
						≥2		-0.4% (N/A)	0.66		+0.8% (N/A)	0.31
Jang et al. 2020[103] *(EXCELLENT, RESET, IVUS-XPL, OPTIMA-C)*	PCI (5,131)	≤6 vs. ≥12 months	RCT	57%	2008-2014	≥2	Cardiac death, MI, ST, stroke or revascularization at 12 months	-2.9% (N/A)	0.02	TIMI major or minor bleeding at 12 months	+0.3% (N/A)	0.47
						<2		+0.1% (N/A)	0.91		+0.4% (N/A)	0.09
Gao et al. 2020[104] *(Chinese cohort)*	PCI (10,724)	<13 vs. ≥13 months	Registry	62%	2013	≥2	Definite or probable ST or MI at 24 months	-0.2% (N/A)	0.51	GUSTO moderate or severe bleeding at 24 months	-0.1% (N/A)	0.65
						≥2		-0.1% (N/A)	0.66		-0.1% (N/A)	0.32

Abbreviations: ACS=acute coronary syndrome; DAPT=dual antiplatelet therapy; GUSTO=Global Utilization Of Streptokinase and Tpa for Occluded arteries; MI=myocardial infarction; PCI=percutaneous coronary intervention; RCT=randomized controlled trial; ST=stent thrombosis; TIMI=Thrombolysis in Myocardial Infarction.

Supplementary Table 9. Validation studies of the Dual Antiplatelet Therapy (DAPT) score, showing cohort characteristics, score discrimination (C-statistic) and calibration

Study (cohort)	Population (n)	Cohort type	ACS	Period	Endpoint definition	Event rate	C-statistic (95% CI)	Calibration
Harada et al. 2017[100] *(ISAR-SAFE)*	PCI, event free at 6 months (3,976)	RCT	40%	2009-2014	Death, MI, definite ST or stroke at 15 months	1.4%	0.57 (0.52-0.64)	N/A
					TIMI major or minor bleeding at 15 months	0.5%	0.63 (0.53-0.72)	N/A
Brener et al. 2018[105] *(ADAPT-DES)*	PCI, event free at 12 months (5,397)	Registry	55%	2008-2010	Definite ST or MI at 24 months	1.3%	0.71 (N/A)	Adequate
					Bleeding requiring medical attention at 24 months	2.2%	0.62 (N/A)	Adequate
Song et al. 2018[106] *(Chinese cohort)*	PCI, ACS, event free on DAPT at 12 months (6,088)	Registry	100%	2013	Probable or definite ST or MI at 24 months	2.6%	0.53 (N/A)	N/A
					Major bleeding at 24 months	0.5%	0.71 (N/A)	N/A
Ueda et al. 2018[107] *(SWEDEHEART)*	PCI, event free at 12 months (41,101)	Registry	65%	2006-2013	Definite ST or MI at 30 months	3.1%	0.58 (0.56-0.60)	Overestimated
					Fatal or nonfatal major bleeding at 30 months	0.7%	0.49 (0.45-0.53)	Overestimated
Veron-Esquivel et al. 2019[108] *(Mexican cohort)*	PCI, MI (230)	Registry	100%	2010-2016	Definite ST, MI, TVR or ISR at end of follow-up	17.0%	0.59 (0.50-0.69)	Adequate
					GUSTO moderate or severe bleed at end of follow-up	4.8%	0.79 (0.66-0.93)	Adequate
Witberg et al. 2020[102] *(Israeli cohort)*	PCI, event free at 12 months (4,471)	Registry	58%	2008-2016	MI at 36 months	7.2%	0.50 (0.47-0.53)	N/A
					Actionable bleeding at 36 months	2.3%	0.46 (0.41-0.52)	N/A

Abbreviations: ACS=acute coronary syndrome; DAPT=dual antiplatelet therapy; GUSTO=Global Utilization Of Streptokinase and Tpa for Occluded arteries; ISR=in-stent restenosis; MI=myocardial infarction; PCI=percutaneous coronary intervention; RCT=randomized controlled trial; ST=stent thrombosis; TIMI=Thrombolysis in Myocardial Infarction; TVR=target vessel revascularization.

Supplementary Table 10. Randomized controlled trials comparing platelet function-guided dual antiplatelet therapy with standard antiplatelet therapy

Study (year)	Intervention Strategy	Sample Size	Primary Endpoint	Secondary Endpoint	Design and Randomization	ACS	Primary and Secondary Results (guided vs. non-guided therapy)
Bonello et al.[109] (2009)	Escalation of clopidogrel LD if HPR after initial dose *(max. 3 LDs in guided group)*	429	Definite ST at 1 month	TIMI major or minor bleeding at 1 month	Randomization at time of PCI; Single-blind, superiority study	52%	0.5% vs. 4.7% (P=0.01) 3.7% vs. 2.8% (P=0.80)
3T/2R[110] (2009)	Escalation with additional tirofiban on top of clopidogrel and aspirin if HPR	263	Periprocedural MI within 48 hours	TIMI major or minor bleeding	Randomization at time of PCI; Double-blind; superiority study	0%	20.4% vs. 35.1% (P=0.009) 1.5% vs. 0.8% (P=0.99)
GRAVITAS[111] (2011)	Escalation of clopidogrel to high-dose clopidogrel if HPR	2,214	Cardiac death, MI or ST at 6 months	Severe or moderate GUSTO bleeding at 6 months	Randomization at time of PCI; Double-blind, superiority study	40%	2.3% vs. 2.3% (P=0.97) 1.4% vs. 2.3% (P=0.10)
Wang et al.[112] (2011)	Escalation of clopidogrel MD if HPR at multiple time points *(max. 375 mg once daily)*	306	Cardiac death, ST, recurrent ACS or revascularization at 12 months	TIMI major or minor bleeding at 12 months	Randomization 1 mo. after PCI; Single-blind, superiority study	20%	9.3% vs. 20.4% (P=0.008) 12.9% vs. 16.6% (P=0.06)
TRIGGER[113] (2012)	Escalation of clopidogrel to prasugrel if HPR	423	Cardiac death or MI at 6 months	TIMI major bleeding at 6 months	Randomization at time of PCI; Double-blind, superiority study	0%	Prematurely terminated for lack of futility
ARCTIC[114] (2012)	Escalation of treatment at physician's discretion	2,440	All-cause death, MI, ST, stroke or urgent revascularization at 1 year	STEEPLE major bleeding at 1 year	Randomization at time of PCI; Open-label, superiority study	27%	34.6% vs. 31.1% (P=0.10) 2.3% vs. 3.3% (P=0.15)
ANTARCTIC[115] (2016)	Escalation and de-escalation of prasugrel based on PFT	877	Cardiac death, MI, stroke, ST, urgent revascularization or BARC type 2-5 bleeding at 1 year	BARC type 2-5 bleeding at 1 year	Randomization at time of PCI; Open-label, superiority study	100%	28% vs. 28% (P=0.98) 21% vs. 20% (P=0.77)
TROPICAL-ACS[116] (2017)	De-escalation of prasugrel to clopidogrel based on PFT	2,610	Cardiac death, MI, stroke or BARC type 2-5 bleeding at 1 year	BARC type 2-5 bleeding at 1 year	Randomization at time of PCI; Open-label, non-inferiority study	100%	7.3% vs. 9.0% (P_{NI}<0.0004) 4.9% vs. 6.1% (P=0.23)
CREATIVE[117]* (2018)	Escalation of clopidogrel to high-dose clopidogrel or adjunctive cilostazol if HPR	1,078	All-cause death, MI, TVR or stroke at 18 months	BARC type 3 or 5 bleeding at 18 months	Randomization at time of PCI; Open-label, superiority study	60%	8.5% vs. 14.4% (P<0.05) 2.53% vs. 1.93% (P>0.05)

Abbreviations: ACS=acute coronary syndrome; BARC=Bleeding Academic Research Consortium; DAPT=dual antiplatelet therapy; GUSTO=Global Utilization Of Streptokinase and Tpa for Occluded arteries; HPR=high platelet reactivity; LD=loading dose; MD=maintenance dose; MI=myocardial infarction; PCI=percutaneous coronary intervention; PFT=platelet function testing; ST=stent thrombosis; STEEPLE=Safety and Efficacy of Enoxaparin in PCI Patients, an International Randomized Evaluation; TIMI=Thrombolysis in Myocardial Infarction; TVR=target vessel revascularization

* Results are from the comparison between the adjunctive cilostazol group versus normal-dose clopidogrel group, results for the high-dose clopidogrel group were not statistically different from normal-dose clopidogrel and are not presented in this table.

Supplementary Table 11. Randomized controlled trials comparing genotype-guided dual antiplatelet therapy with standard antiplatelet therapy

Study (year)	Intervention Strategy	Sample Size	Primary Endpoint	Secondary Endpoint	Design and Randomization	ACS	Primary and Secondary Results (guided vs. non-guided therapy)
RAPID GENE[118]* (2012)	Escalation of clopidogrel to prasugrel for CYP2C19*2 carriers	187	HPR (defined as PRU > 234) at 7 days after PCI	N/A	Randomization at time of PCI; Open-label, superiority study	37%	0% vs. 30% (P=0.0092)
IAC-PCI[119]† (2013)	Escalation of clopidogrel to high-dose clopidogrel based on genotype	600	All-cause death, MI, stroke or TVR at 180 days	Bleeding event at 180 days	Randomization at time of PCI; Single-blind, superiority study	N/A	2.66% vs. 9.03% (P<0.01) 1.33% vs. 3.68% (P=0.073)
PHARMCLO[120]‡ (2018)	Treatment at physician's discretion based on genetic and clinical characteristics	888	Cardiac death, MI, stroke or BARC type 3-5 major bleeding at 1 year	N/A	Randomization at time of ACS diagnosis; Single-blind, superiority study	100%	15.9% vs. 25.9% (P<0.001)
POPular Genetics[121] (2019)	De-escalation of ticagrelor or prasugrel to clopidogrel for CYP2C19*2 or *3 carriers	2,488	Cardiac death, MI, ST, stroke or PLATO major bleeding at 1 year	PLATO major or minor bleeding at 1 year	Randomization within 2 days of PCI; Open-label, non-inferiority study	100%	5.1% vs. 5.9% (P_{NI}<0.001) 9.8% vs. 12.5% (P=0.04)
TAILOR PCI[122] (2020)	Escalation of clopidogrel to ticagrelor for CYP2C19*2 or *3 carriers	5,302	Cardiac death, MI, stroke, ST and severe recurrent ischemia at 1 year	TIMI major or minor bleeding at 1 year	Randomization at time of PCI; Open-label, superiority study	84%	4.0% vs. 5.9% (P=0.056) 1.9% vs. 1.6% (P>0.05)

Abbreviations: ACS=acute coronary syndrome; BARC=Bleeding Academic Research Consortium; DAPT=dual antiplatelet therapy; DES=drug-eluting sent; HPR=high platelet reactivity; MI=myocardial infarction; PCI=percutaneous coronary intervention; PRU=$P2Y_{12}$ reactivity unit; ST=stent thrombosis; TIMI=Thrombolysis in Myocardial Infarction; TVR=target vessel revascularization

* Results for the CYP2C19*2 carriers within the total population

† Homozygous CYP2C19*2 or *3 received 200 mg loading dose of cilostazol and 100 mg twice daily for maintenance on top of high-dose clopidogrel

‡ The PHARMCLO trial was prematurely stopped after enrollment of only 25% of the original goal

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