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eMethods. The Cochrane Risk-of-Bias Tool for Randomized Trials (RoB 2) eReferences.

This supplementary material has been provided by the authors to give readers additional information about their work.

# eTable 1. Full Search Strategy

Ovid MEDLINE® ALL - 1946 to November 21, 2019 Searched on November 24, 2019 Limited to RCTs via BMJ's study design search filter available from: https://bestpractice.bmj.com/info/toolkit/learn-ebm/study-design-search-filters/

Line # | Search

- 1 Percutaneous Coronary Intervention/
- 2 (percutaneous coronary intervention\* or percutaneous coronary revascularization\* or PCI or percutaneous coronary angioplasty or stent or stents or stenting).tw.
- 3 Angioplasty, Balloon, Coronary/
- 4 (coronary balloon angioplasties or coronary balloon angioplasty or transluminal coronary balloon dilation or coronary artery balloon dilation or percutaneous transluminal coronary angioplasty or coronary angioplasty or coronary angioplasties or PTCA).tw.
- 5 or/1-4
- 6 Coronary Artery Bypass/
- 7 (coronary adj2 (bypass or graft)).tw.
- 8 (CABG or aorticocoronary anastomosis or total arterial revascularization or total arterial revascularisation or Multiple arterial revascularization or multiple arterial revascularisation).tw.
- 9 Coronary Artery Bypass, Off-Pump/
- 10 Internal Mammary-Coronary Artery Anastomosis/
- 11 ((Right Internal Mammary Artery or RIMA or Coronary Internal Mammary Artery or arteria mammaria interna or arteria thoracica interna or internal thoracic artery or mammary internal artery) and (transplant\* or graft\* or anastomosis)).tw.
- 12 (surgical revascularization or cardiac muscle revascularisation or cardiac muscle revascularization or coronary revascularisation or heart muscle revascularisation or heart myocardium revascularisation or heart revascularisation or heart revascularization or internal mammary arterial anastomosis or internal mammary artery graft or internal mammary artery implant or internal mammary artery graft or internal mammary artery anastomosis or myocardial revascularization or myocardial revascularisation or myocardial revascularization or myocardial revascularisation or myocardial laser revascularisation or transmyocardial la
- 13 or/6-12
- 14 "randomized controlled trial".pt.
- 15 (random\$ or placebo\$ or single blind\$ or double blind\$ or triple blind\$).ti,ab
- 16 (retraction of publication or retracted publication).pt.
- 17 or/14-16
- 18 (animals not humans).sh.
- 19 ((comment or editorial or meta-analysis or practice-guideline or review or letter) not "randomized controlled trial").pt.
- 20 (random sampl\$ or random digit\$ or random effect\$ or random survey or random regression).ti,ab. not "randomized controlled trial".pt.

- 21 17 not (18 or 19 or 20)
- 22 5 and 13
- 23 22 and 21

eTable 2. Summary of the Included Randomized Clinical Trials

Trial	Number of centers	Location	Study period	Number of patients randomized	Mean follow-up (years)
ARTS <sup>1</sup>	67	Europe	1997-1998	1205 (PCI: 600, CABG: 605)	5
BEST <sup>2</sup>	27	Asia	2008-2013	880 (PCI: 438, CABG: 442)	4.6
Blazek et al <sup>3</sup>	1	Germany	1997-2001	220 (PCI: 110, CABG: 110)	10.3
Boudriot et al <sup>4</sup>	4	Germany	2003-2009	201 (PCI: 100, CABG: 101)	1
CARDia <sup>5</sup>	24	United Kingdom, Ireland	2002-2007	510 (PCI: 256, CABG: 254)	2
Cisowski et al <sup>6</sup>	1	Poland	2000-2001	100 (PCI: 50, CABG: 50)	1
Drenth et al <sup>7</sup>	1	Netherlands	1997-1999	102 (PCI: 51, CABG: 51)	4
ERACI II <sup>8</sup>	7	North America, Europe, South America	1996-1998	450 (PCI: 225, CABG: 225)	5
EXCEL <sup>9</sup>	126	Europe, North America, Asia, South America	2010-2014	1905 (PCI: 948, CABG: 957)	5
FREEDOM <sup>10</sup>	140	United States	2005-2010	1900 (PCI: 953, CABG: 947)	3.8, 7.5
Hong et al <sup>11</sup>	1	South Korea	2003	189 (PCI: 119, CABG: 70)	0.5
Kim et al <sup>12</sup>	1	South Korea	2000-2001	100 (PCI: 50, CABG: 50)	1
LE MANS <sup>13</sup>	3	Poland	2001-2004	105 (PCI: 52, CABG: 53)	9.8
MASS-II <sup>14</sup>	1	Brazil	1995-2000	408 (PCI: 205, CABG: 203)	11.4
Myoprotect <sup>15</sup>	1	Germany	1998-2001	44 (PCI: 23, CABG: 21)	1
NOBLE <sup>16</sup>	36	Europe	2008-2015	1184 (PCI: 592, CABG: 592)	4.9
Octostent <sup>17</sup>	3	Netherlands	1998-2000	280 (PCI: 138, CABG: 142)	1
PRECOMBAT <sup>18</sup>	13	Korea	2004-2009	600 (PCI: 300, CABG: 300)	5
Stent or Surgery (SoS) <sup>19</sup>	53	Europe, Canada	1996-1999	988 (PCI: 488, CABG: 500)	2
SIMA 20	6	Europe	-	121 (PCI: 62, CABG:59)	10
SYNTAX 21,22	85	Europe, United States	2005-2007	1800 (PCI: 903, CABG: 897)	5, 10
Thiele et al <sup>23</sup>	1	Germany	2003-2007	130 (PCI: 65, CABG: 65)	3.6
VA CARDS 24	22	United States	2006-2010	198 (PCI: 101, CABG: 97)	2

# eTable 3. Details of Patient Characteristics

						1	1						1					I .			1	Т	Т
Trial	Treatme	Age, mean	Fema	BMI (SD)	Smoki	D	Insu	CAD	Sta	HT	HC	PV	Caro	Prio	Pri	Pri	Pri	Pri	Pri	LVEF (SD)	S	UA	AC
	nt	(SD), median	le (%)	[IQR]	ng	Μ	lin	,	tin	Ν	L/	D	tid	r	or	or	or	or	or	[IQR]	А	(%)	S
		[IQR]			(%)	(%)	(%)	fam	(%)	(%)	HL	(%)	arte	Stro	MI	TIA	CH	PCI	CA		(		(%
								ily			D		ry	ke	(%)	(%)	F	(%)	BG		%		)
								hist			(%)		dise	(%)	. ,	. ,	(%)	. ,	(%)		)		
								orv			. ,		ase	. ,			. ,		. ,		ĺ,		
								(%)					(%)										
ARTS <sup>1</sup>	PCI	61 (10)	23	27.2 (3.7)	28	19	-	39	-	45	58	6	-	-	44	-	-	-	-	-	5 7	37	-
	CABG	61 (9)	24	27.4 (3.7)	26	16	-	42	-	45	58	5	-	-	42	-	-	-	-	-	6 0	35	-
BEST <sup>2</sup>	PCI	64.0 (9.3)	30.6	24.7 (2.9)	20.1	40.	4.6	-	-	67.	54.	3.4	-	8.4	5.7	-	3.7	6.8	-	59.1 (8.5)	4	42.	-
						4				6	6										7.	1	
																					9		
	CABG	64.9 (9.4)	26.5	25.0 (2.9)	20.1	42.	4.1	-	-	66.	50.	2.7	-	7.5	6.6	-	2.7	8.6	-	59.9 (8.1)	4	45.	-
						1				7	2										6.	0	
																					2		
Blazek et al <sup>3</sup>	PCI	62.5 (10.2)	28	28.2 (3.8)	25	34	-	18	-	72	70	-	-	-	45	-	-	0	0	62 (15)	-	-	-
	CABG	61.6 (10.0)	15	27.2 (3.4)	25	25	-	17	-	71	73	-	-	-	45	-	-	0	0	63 (11)	-	-	-
Boudriot et	PCI	66 [62-73]	28	27.2 [24.6-	-	40	-	-	-	82	68	-	-	3	19	-	-	-	-	65.0	-	-	-
al. <sup>4</sup>		[]		31.5]										_						[55.0-			
				,																70.01			
	CABG	69 [63-73]	22	27.0 [24.9-	-	33	-	-	-	82	64	-	-	6	14	-	-	-	-	65.0	1_	-	-
	0,100	05 [05 75]	22	30.1]		55				02	01			Ũ	1.					[55.0-			
				50.1]																68.01			
CARDia <sup>5</sup>	PCI	64 3 (8 5)	29.3	29.2 (4.9)	29.3	10	36.5	-	-	76	92	24	-	-	-	-	-	-	-	-	-	-	-
CARDIa	1 01	04.5 (0.5)	25.5	23.2 (4.3)	25.5	0	50.5			6	9	2.4											
	CARG	63.6 (9.1)	22.1	29/1 (5.3)	20.1	10	30.1			80	87	5.2	_	-	_	-	_	_	-		+	+	_
	CADO	05.0 (5.1)	22.1	25.4 (5.5)	23.1	0	55.1	-	_	6	2	J.2	-	_	-	_	-	-	_		_	_	_
Cicowski ot	DCI	E2 2 (10 2)	16		ED	0		40		50								0	0		+		-
al <sup>6</sup>	PCI	55.5 (10.2)	10	-	52	0	-	40	-	52	/0	-	-	-	-	-	-	0	0	-	-	-	-
	CABG	54.1 (9.1)	18	-	48	6	-	44	-	56	76	-	-	-	-	-	-	0	0	-	-	-	-
Drenth et	PCI	61 (1.3)	25	-	58	18	-	50	-	33	45	-	-	0	18	-	-	0	0	-	-	-	-
al <sup>7</sup>		()												-				-	-				
	CABG	60 (1.6)	22	-	62	8	-	46	-	16	41	-	-	0	24	-	-	0	0	-	-	-	-
ERACI II <sup>8</sup>	PCI	62.5 (11.5)	22.7	28.8%	54.3	17.	-	-	-	71.	62.	19.	-	-	28.	-	-	-	-	-	-	92.	-
				above 30		3		1		0	5	1			5							1	
	CABG	61.4 (10.1)	18.6	32.5%	49.5	17.	-	-	-	70.	60.	26.	-	-	27.	-	-	-	-	-	-	90.	-
				above 30		3				5	2	6			7							7	

EXCEL <sup>9</sup>	PCI	66.0 (9.6)	23.8	28.6 (5.0)	23.4	30.	7.7	-	-	74.	70.	10.	-	-	17.	5.5	7.1	18.	0	57.0 (9.6)	5	24.	-
						2				2	5	2			8			4			2. 7	1	
	CABG	65.9 (9.5)	22.5	28.8 (4.9)	20.2	28.	7.7	-	-	73.	68.	8.8	-	-	16.	7.0	6.2	15.	0	57.3 (9.0)	5	24.	-
		()				0				2	1				8			9			2.	5	
FREEDOM <sup>1</sup>	PCI	63.2 (8.9)	26.8	29.6 (5.4)	14.8	10	33.8	-	82.	84.	-	-	-	3.9	26.	-	-	-	-	65.7	-	-	31.
0		~ /		( )		0			1	6					2					(12.1)			9
	CABG	63.1 (9.2)	30.5	29.8 (5.3)	16.6	10 0	30.9	-	82. 6	85. 1	-	-	-	3.0	25. 0	-	-	-	-	66.6 (10.5)	-	-	29. 5
Hong et al <sup>11</sup>	PCI	60.5 (9.6)	36.1	25.5 (2.9)	40.3	37. 0	-	9.3	-	50. 4	54. 6	-	-	2.5	21. 8	-	-	0	0	52.8 (8.8)	-	50. 4	-
	CABG	61.4 (9.9)	35.7	26.6 (3.9)	45.7	48.	-	10.	-	55.	51.	-	-	2.9	22.	-	-	0	0	51.9 (9.1)	-	42.	-
		· · ·		. ,		6		0		7	4				9					. ,		9	
Kim et al <sup>12</sup>	PCI	61 (12)	40	-	45	20	-	-	-	55	60	-	-	2	22	-	0	0	0	51 (11)	-	65	-
	CABG	63 (12)	30	-	55	15	-	-	-	55	70	-	-	2	22	-	0	0	0	49 (13)	-	55	-
LE MANS <sup>13</sup>	PCI	60.6 (10.5)	40	-	-	19	-	-	-	75	65	-	-	-	36	-	-	-	-	53.5 (10.7)	-	-	-
	CABG	61.3 (8.4)	27	-	-	17	-	-	-	70	60	-	-	-	32	-	-	-	-	53.7 (6.7)	-	-	-
MASS-II <sup>14</sup>	PCI	60 (9)	33.0	-	27	23	-	-	-	61	-	-	-	-	52	-	-	-	-	67 (8)	7 8	-	-
	CABG	60 (9)	28.0	-	32	29	-	-	-	63	-	-	-	-	41	-	-	-	-	67 (9)	8 6	-	-
Myoprotec t <sup>15</sup>	PCI	69 (8)	17	-	-	39	-	-	22	96	-	-	-	-	-	-	-	-	-	52	7	-	-
	CABG	71 (7)	43	-	-	38	-	-	48	86	-	-	-	-	-	-	-	-	-	56	5 7	-	-
NOBLE <sup>16</sup>	PCI	66.2 (9.9)	20.0	27.9 (4.5)	19	15	-	58	82	65. 2	-	-	-	-	-	-	-	19. 6	0.7	60 [55-65]	8 2. 1	-	17. 9
	CABG	66.2 (9.4)	24.0	28.1 (4.4)	22	15	-	56	78	65. 7	-	-	-	-	-	-	-	19. 9	0.3	60 [52-64]	8 2. 9	-	16. 9
Octostent <sup>1</sup> 7	PCI	60.3 (9.1)	30	-	25	9	-	60	-	33	59	7	-	1	25	-	-	4	-	-	-	30	-
	CABG	58.9 (10.0)	28	-	19	14	-	62	-	31	60	7	-	2	23	-	-	5	-	-	-	34	-
PRECOMB AT <sup>18</sup>	PCI	61.8 (10.0)	24.0	24.6 (2.7)	-	34	3.3	-	-	54. 3	42. 3	5.0	-	-	3.4	-	0.0	12. 7	-	61.7 (8.3)	5 3.	42. 7	-
	CABG	62.7 (9.5)	23.0	24.5 (3.0)	-	30	3.0	-	-	51. 3	40. 0	2.3	-	-	6.7	-	0.7	12. 7	-	60.6 (8.5)	3 4 5.	48. 0	-
						1				Ĩ								l '			7	Ĭ	

Stent or Surgery (SoS) <sup>19</sup>	PCI	61 (9.2)	20.0	-	16	13. 9	4	48	-	43	53	6	-	1	44	1	-	-	-	57		-	19	-
	CABG	62 (9.8)	22.0	-	14	14. 8	2	48	-	47	50	7	-	3	47	2	-	-	-	57		-	22	-
SIMA <sup>20</sup>	PCI	59 (57-62)	) 24	-	57	11	-	36	-	46	62	-	-	2	2	-	-	-	-	67 [65-	69]			
	CABG	60 (58-63)	) 17	-	50	13	-	27	-	48	55	-	-	0	2	-	-	-	-	67 [65-	70]			
SYNTAX <sup>21,22</sup>	PCI	65.2 (9.7)	23.6	28.1 (4.8)	18.5	25. 6	24.6	-	-	68. 9	78. 7	-	8.1	1 3.9	31. 9	4.3	4.0	-	-	-		5 6. 9	28. 9	-
	CABG	65.0 (9.8)	21.1	27.9 (4.5)	22.0	24. 6	9.9	-	-	64. 0	77. 2	-	8.4	4.8	33. 8	5.2	5.3	-	-	-		5 7. 2	28. 0	-
Thiele et al <sup>23</sup>	PCI	66 (59-72)	) 31	28.0 (3.7)	14	28	-	-	-	83	55	-	-	3	23	-		0	0	65 [60-	66]	-	-	-
	CABG	66 (59-71)	) 29	26.9 (4.0)	18	25	-	-	-	85	55	-	-	9	23	-		0	0	65 [60-	70]	-	-	-
VA CARDS <sup>24</sup>	PCI	62.7 (7.1)	1.0	32.8 (5.7)	27.7	10 0	47.9	-	-	96. 0	-	10. 9	-	6.9	-	-	-	34. 7	3	-		-	-	-
	CABG	62.1 (7.4)	1.0	33.0 (5.7)	20.6	10 0	47.5	-	-	95. 7	-	17. 0	-	8.5	-	-	-	20. 2	1.1	-		-	-	-
Trial		Treatment	Bifurcation (%)	Bifurcation trifurcation	n or n of the c	distal	Disea	sed no nary art	n-left ı eries (	main 0,1,2,3	)	NYHA Class I	(%)	NYHA Class II (%)	NYH Class	4 ;	NYHA Class I	V (	EuroSC SD) [IC	CORE QR]	SYN [IQ	NTAX R]	score	(SD)
ARTS1		PCI	34	-	(70)		(0.2.6	(02.83				_		-	(70)		-	-			-			
		CABG	31	-			(0.0.6	57.33)				-		-	-		-	-			-			
BEST <sup>2</sup>		PCI	57.5	_			-	,,,,,,,				-		-	-		-	7	9 (2.0	))	24	2 (7.5	5)	
		CABG	58.8	-			-					-		-	-		-	3	3.0 (2.1	1)	24.	6 (8.1	1)	
Blazek et al <sup>3</sup>		PCI	-	-			-				-	-		-	-		-	-		,	-	(	,	
		CABG	-	-			-					-		-	-		-	-			-			
Boudriot et a	al4	PCI	-	-			(28,3	5,26,11	L)			-		-	-		-	-			24.	0 [19	.0-29.	.0]
		CABG	-	-			(29,2	7,28,17	7)			-		-	-		-	-			23.	0 [14	.8-29.	.0]
CARDia⁵		PCI	-	-			-					-		-	-		-	-			-			
		CABG	-	-			-					-		-	-		-	-			-			
Cisowski et a	al <sup>6</sup>	PCI	-	-			-					-		-	-		-	-			-			
		CABG	-	-			-					-		-	-		-	-			-			
Drenth et al <sup>7</sup>	7	PCI	-	-			-							-	-		-	-			-			
		CABG	-	-			-					-		-	-		-	-			-			
ERACI II <sup>8</sup>		PCI	-	-			-					-		-	-		-	-			-			
		CABG	-	-			-					-		-	-		-	-			-			

EXCEL <sup>9</sup>	PCI	-	81.3	(17.2,30.8,34.3,17.)	-	-	-	-	-	32.2% (<22);
										42.8% (23-32);
										25.1% (>33)
	CABG	-	77.4	(17.5,30.5,30.8,19.0)	-	-	-	-	-	39.3% (<22);
										37.3% (23-32);
										23.4% (>33)
FREEDOM <sup>10</sup>	PCI	-	-	-	-	-	-	-	2.7 (2.4)	26.2 (8.4)
	CABG	-	-	-	-	-	-	-	2.8 (2.5)	26.1 (8.8)
Hong et al <sup>11</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
Kim et al <sup>12</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
LE MANS <sup>13</sup>	PCI	-	-	(0,13,27,60)	-	-	-	-	3.3 (2.3)	25.2 (8.7)
	CABG	-	-	(0,6,19,75)	-	-	-	-	3.5 (2.3)	24.7 (6.8)
MASS-II <sup>14</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
Myoprotect <sup>15</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
NOBLE <sup>16</sup>	PCI	-	-	-	53	29.6	13	5	2 [2-4]	22.5 (7.5)
	CABG	-	-	-	43	33.0	17	7	2 [2-4]	22.4 (8.0)
Octostent <sup>17</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
PRECOMBAT <sup>18</sup>	PCI	66.7	-	(9.0,17.7, 33.7,40.7)	-	-	-	-	2.6 (1.8)	24.4 (9.4)
	CABG	61.0	-	(11.3, 17.7, 30.0, 41.0)	-	-	-	-	2.8 (1.9)	25.8 (10.5)
Stent or Surgery	PCI	-	-	-	-	-	-	-	-	-
(SoS) <sup>19</sup>										
	CABG	-	-	-	-	-	-	-	-	-
SIMA <sup>20</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
SYNTAX <sup>21,22</sup>	PCI	72.4	-	-	-	-	-	-	3.8 (2.6)	28.4 (11.5)
	CABG	73.3	-	-	-	-	-	-	3.8 (2.7)	29.1 (11.4)
Thiele et al <sup>23</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
VA CARDS <sup>24</sup>	PCI	-	-	-	5.0	22.8	8.9	0	-	21.5 (8.9)
	CABG	-	-	-	11.7	24.5	7.4	0	-	22.7 (10.6)

ACS- Acute coronary syndrome; BMI- Body mass index; CABG- Coronary artery bypass grafting; CAD- Coronary artery disease; CHF- Chronic heart failure; DM- Diabetes mellitus; HTN- Hypertension; HCL- Hypercholesterolemia; HLD- Hyperlipidemia; MI- Myocardial infarction; ; NYHA- New York Heart Association PCI-Percutaneous coronary intervention; PVD- Peripheral vascular disease; SA- Stable angina pectoris; TIA- Transient ischemic attack; UA- Unstable angina

# eTable 4. Procedural Characteristics

Trial	Treatment	Aspirin (%)	Thienophy ridine (%)	Ticagrelor	GP Inhibitor	Statin (%)	Beta- blocker (%)	ACEI or ARB (%)	Calcium channel	No. of lesions (SD or IOR)	CR (%)	No. of stents (SD) [IOR]	DES use (%)	Type of stent	Total stent length, mm (SD)	Stent diameter, mm (SD) [IQR]	No. of non-LMCA stents (0,1,2, bifurcation ) (%)	Bifurcation technique (1 stent, 2 stent) (%)	Intravascul ar ultrasound , (any, pre-
ARTS <sup>1</sup>	PCI	100	100	-	-	-	-	-	-	2.8 (1.0)	-	2.6 (1.1)	0	BMS	47.5 (21.8)	-	-	-	-
	CABG	100	100	-	-	-	-	-	-	2.8 (1.0)	-	-	-	-	-	-	-	-	-
BEST <sup>2</sup>	PCI	97.0	96.6	-	-	83.1	68.5	44.5	58.0	-	53.9	3.4 (1.4)	100	DES	85.3 (38.2)	3.1 (0.3)	-	-	(76.0,-,-)
	CABG	96.6	89.3	-	-	83.5	42.8	25.3	46.4	-	62.0	-	-	-	-	-	-	-	-
Blazek et al <sup>3</sup>	PCI	-	-	-	-	-	-	-	-	-	-	1.2 (0.4)	0	BMS	15.1 (4.3)	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Boudriot et al <sup>4</sup>	PCI	-	-	-	-	97	99	98	-	-	-	-	100	DES	-	-	-	-	-
	CABG	-	-	-	-	94	95	92	-	-	-	-	-	-	-	-	-	-	-
CARDia <sup>5</sup>	PCI	-	-	-	-	-	-	-	-	3.6	-	-	69	BMS, DES	71	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-
Cisowski et al <sup>6</sup>	PCI	-	-	-	-	-	-	-	-	-	-	-	0	BMS	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Drenth et al <sup>7</sup>	PCI	-	-	-	-	-	-	-	-	-	-	-	0	BMS		-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ERACI II <sup>8</sup>	PCI	-	-	-	-	-	-	-	-	-	-	-	0	BMS	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
EXCEL <sup>9</sup>	PCI	95.9	95.9	6.9	-	94.7	81.8	55.7	5.8	1.9 (1.1)	-	2.4 (1.5)	100	DES	49.1 (35.6)	-	-	-	(76.2,-,-)
	CABG	92.1	31.0	0.2	-	88.0	88.1	40.1	6.8	2.6 (0.8)	-	-	-	-	-	-	-	-	-
FREEDOM <sup>10</sup>	PCI	98.4	97.8	-	-	83.7	79.3	80.2	24.7	5.7 (2.2)	-	3.5 (1.4)	100	DES	26.1 (14.2)	-	-	-	-
	CABG	85.9	23.9	-	-	81.1	76.1	60.2	18.0	5.7 (2.2)	-	-	-	-	-	-	-	-	-
Hong et al <sup>11</sup>	PCI	-	-	-	-	-	-	-	-	-	-	1.2 (0.2)	100	DES	22.6 (4.8)	2.9 (0.3)	-	-	-
	CABG	-	-	-	-	-	-	-	-	-	-	-		-		-	-	-	-
Kim et al <sup>12</sup>	PCI	-	-	-	-	-	-	-	-	-	-	-	0	-	22 (11)	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-	-	-		-		-	-	-	-
LE MANS <sup>13</sup>	PCI	-	-	-	-	-	-	-	-	-	79	-	35	BMS, DES	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-	89	-	-	-	-	-	-	-	-
MASS-II <sup>14</sup>	PCI	-	-	-	-	-	-	-	-	-	41	2.1 (0.7)	0	BMS	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myoprotect <sup>15</sup>	PCI	91	-	-	-	39	70	43	0	1.48	-	-	0	BMS	13.4 (4.0)	-	-	-	-

	CABG	86	-	-	-	10	33	67	14	1.5	-	-	-	-	-	-	-	-	-
NOBLE <sup>16</sup>	PCI	91.0	95.6	-	18.6	-	-	-	-	2 (1-3)	91.7	-	100	DES	-	4.0 [4.0-4.5]	(52.7, 32.3, 9.3, 85.8)	(-, 29.7)	(- ,45.6,72.6)
	CABG	-	-	-	-	-	-	-	-	2 (2-3)	-	-	-	-	-	-	-	-	
Octostent <sup>17</sup>	PCI	-	-	-	-	-	-	-	-	-	-	1.4	0	BMS	201. (10.2)	-	-	-	-
	CABG																		
PRECOMBAT <sup>18</sup>	PCI	98.3	97.7	-	-	71.7	60.7	39.3	61.3	-	68.3	2.7 (1.4)	100	DES	60.0 (24.1)	-	-	(29.0, 32.3)	(83.3,-,-)
	CABG	96.7	90.7	-	-	72.0	40.3	26.7	45.3	-	70.3	-	-	-	-	-	-	-	-
Stent or Surgery (SoS) <sup>19</sup>	PCI	-	-	-	8.2	-	-	-	-	2.7	-	2 [2-3]	0	BMS	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
SIMA <sup>20</sup>	PCI	90	-	-	-	-	56	2	33	-	-	-	-	-	-	-	-	-	-
	CABG	87	-	-	-	-	55	0	33	-	-	-	-	-	-	-	-	-	-
SYNTAX <sup>21,22</sup>	PCI	96.3	96.8	1.9	-	86.7	81.3	78.6	25.8	4.3 (1.8)	61.3	4.6 (2.3)	100	DES	86.1 (47.9)	-	-	-	-
	CABG	88.5	19.5	4.8	-	74.5	78.6	68.4	18.4	4.4 (1.8)	56.3	-	-	-	-	-	-	-	-
Thiele et al <sup>23</sup>	PCI	100	100	-	-	99	99	100	-	-	-	-	95.4	DES, BMS	-	-	-	-	-
	CABG	100	34	-	-	97	97	97	-	-	-	-			-	-	-	-	-
VA CARDS <sup>24</sup>	PCI	-	-	-	-	-	-	-	-	-	-	-	100	DES	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Trial	Treatment	LIMA (%)	BIMA (%)	OPCAB (%)	LIMA+ SV grafting (%)	No. of grafts,	No. of arterial	No. of venous	No. of grafts, (1,2,3,4,5) (%)	Ultrasound (epi-aortic or transesophageal-aortic,
		. ,			с с <i>с</i> ,	mean (SD)	grafts,	grafts,		epi-aortic,
							mean (SD)	mean (SD)		transesophageal)
ARTS <sup>1</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	88.5	-	-	-	2.6 (1.0)	-	-	-	-
BEST <sup>2</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	90.0	-	58.4	-	3.1 (0.9)	2.1 (1.1)	1.0 (0.8)	-	-
Blazek et al <sup>3</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
Boudriot et al <sup>4</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	99.0	-	-	-	-	-	-	-	-
CARDia <sup>5</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	94	-	-	-	2.9	-	-	-	-
Cisowski et al <sup>6</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
Drenth et al <sup>7</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
ERACI II <sup>8</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
EXCEL <sup>9</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	94.9	27.7	28.3	-	2.6 (0.8)	1.4 (0.6)	1.2 (0.9)	-	(43.6, 12.6, 40.8)

FREEDOM <sup>10</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	89.5	-	17.4	-	2.9 (0.8)	-	-	-	-
Hong et al <sup>11</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
Kim et al <sup>12</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
LE MANS <sup>13</sup>	PCI	72%	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
MASS-II <sup>14</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	3.3 (0.8)	-	-	-	-
Myoprotect <sup>15</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	-	-	-	-	-	-	-	-	-
NOBLE <sup>16</sup>	PCI	-	-	-	-	-	-	-	-	-
	PCI	-	-	-	-	-	-	-	-	-
Octostent <sup>17</sup>	CABG	-	-	-	-	1.2	1.2			
	CABG	92.1	7.4	14.9	81.1	-	-	-	(3.9,49.7,37.2,4.2,0.5)	-
PRECOMBAT <sup>18</sup>	PCI	-	-	-	-	-	-	-	-	-
	CABG	77.7	-	51.7	-	2.7 (0.9)	2.1 (0.9)	0.7 (0.8)	-	-
Stent or Surgery	PCI	-	-	-	-	-	-	-	-	-
(303)	CARG	70	10.2			28				
SIN4A20	DCL	75	10.2	-	-	2.0	-	-	-	-
SIIVIA	CARG	-	-	-	-	-	-	-	-	-
SVNITA ¥21,22	PCI	100	-	_			_			_
JINIAA	CARG		2/1	1/1 3		28(07)	_			_
Thiele et al <sup>23</sup>	PCI	98 5	-	95.8	_	2.0 (0.7)	_	_		_
	CARG	50.5		55.0						
VA CARDS <sup>24</sup>	PCI	-	-	-	-	-	-	_		
WI GAILES	CABG	-	-	-	-	-	-	-	-	-

ACEI- Angiotensin-converting enzyme inhibitor; ARB- Angiotensin II receptor blockers; BIMA- Bilateral internal mammary artery; BMS: Bare-metal stent; CR- Complete revascularization; DES- Drugeluting stent; GP- Glycoprotein IIa IIb; LIMA- Left internal mammary artery; LMCA- Left main coronary artery; OPCAB- Off-pump coronary artery bypass grafting; SV- Saphenous vein

### eTable 5. Details of Medical Therapy

Trial	Description of Medical Therapy
ARTS <sup>1</sup>	Antianginal medication (PCI: 78.9%, CABG: 58.5%)
BEST <sup>2</sup>	Aspirin (PCI: 78.2%, CABG: 76.1%)
	Thienopyridine (PCI: 58.8%, CABG: 48.4%)
	Any antiplatelet drug (PCI: 92.0%, CABG: 90.8%)
	Beta-blocker (PCI: 50.0%, CABG: 37.0%)
	Calcium-channel blocker (PCI: 55.2%, CABG: 37.0%)
	ACE inhibitor or ARB (PCI: 34.5%, CABG: 21.7%)
	Statin (PCI: 79.3%, CABG: 75.0%)

Blazek et al <sup>3</sup>	• PCI: aspirin (100 mg/day, indefinitely); ticlopidine or clopidogrel (4 weeks, following a loading dose the day before the
	procedure)
	CABG: aspirin (100 mg/day, indefinitely)
	Beta-blocker (PCI: 74%, CABG: 75%)
	ACE inhibitor/AT-1 antagonist: (PCI: 73%, CABG: 71%)
	Statin (PCI: 68%, CABG: 68%)
	Aspirin (PCI: 74%, CABG: 69%)
	Thienopyridines (PCI: 10%, CABG: 8%)
	Nitrates (PCI: 20%, CABG: 19%)
	Calcium antagonists (PCI: 22%, CABG: 15%)
	Antidiabetic medication (PCI: 21%, CABG: 18%)
Boudriot et al <sup>4</sup>	• PCI: antiplatelet therapy (>100 mg/day, indefinitely); clopidogrel (75 mg/day, ≥12 months); Glycoprotein IIb/IIIa inhibitor use
	was left to the discretion of the operator.
	• CABG: aspirin (100 mg/day, indefinitely)
	BOTH: other pharmacological treatments such as statins, angiotensin-converting enzyme inhibitors, and betablockers were
	recommended based on current practice in both treatment groups.
	At discharge
	Aspirin (PCI: 100%, CABG: 100%)
	Clopidogrel (PCI: 100, CABG: 32%)
	Beta-blocker (PCI: 99, CABG: 95%)
	ACE inhibitor/AT-1 antagonist (PCI: 98%, CABG: 92%)
	Statins (PCI: 97%, CABG: 94%)
CARDia⁵	• Routine administration of abciximab and clopidogrel for 1 to 3 months after BMS placement or 12 months after DES placement.
	Aspirin (PCI: 83.4%, CABG: 87.2%)
	Clopidogrel (PCI: 54.4%, CABG: 10.3%)
	Aspirin and clopidogrel (PCI: 50.9%, CABG: 16.5%)
	Statins (PCI: 83.4%, CABG: 89.3%)
	ACE inhibitors: (PCI: 56.1%, CABG: 60.3%)
	Oral hypoglycemics (PCI: 65.5%, CABG: 61.1%)
	Insulin (PCI: 29.8%, CABG: 40.9%)
Cisowski et al <sup>6</sup>	• PCI: ticlopidine (4 weeks)
Drenth et al <sup>7</sup>	<ul> <li>PCI: aspirin (100 mg/day, indefinitely); ticlopidine (250 mg/day, 1 month); Glycoprotein IIb/IIIa inhibitor was not used.</li> <li>CABG: (100 mg/day, indefinitely)</li> </ul>

	No Beta blocker/Calcium antagonist/Long-acting nitrate (PCI: 24%, CABG: 29%)
	≥1 Beta-blocker/Calcium antagonist/Long-acting nitrate: (PCI: 41%, CABG: 65%)
	≥2 Beta blocker/Calcium antagonist/Long-acting nitrate: (PCI: 35%, CABG: 6%)
ERACI II <sup>8</sup>	Abciximab (PCI: 28.3%, CABG: 0.0%)
EXCEL <sup>9</sup>	Aspirin (PCI: 93.0%, CABG: 93.6%)
	P2Y12 receptor inhibitor (PCI: 61.6%, CABG: 21.0%)
	Clopidogrel or ticlopidine (PCI: 50.0%, CABG: 20.3%)
	Clopidogrel (PCI: 50.0%, CABG: 20.2%)
	Ticlopidine (PCI: 0.0%, CABG: 0.1%)
	Prasugrel or ticagrelor (PCI: 11.6%, CABG: 0.8%)
	Prasugrel (PCI: 8.5%, CABG: 0.4%)
	Ticagrelor (PCI: 3.1%, CABG: 0.4%)
	Beta-blockers (PCI: 86.6%, CABG: 94.3%)
	Calcium channel blockers (PCI: 18.3%, CABG: 19.1%)
	ACE inhibitors or receptor blockers (PCI: 66.7%, CABG: 59.4%)
	Aldosterone antagonist: (PCI: 1.6%, CABG: 1.7%)
	Diuretic: (PCI: 17.1%, CABG: 38.8%)
	Anti-arrhythmic agent: (PCI: 3.1%, CABG: 17.4%)
	Statins: (PCI: 97.5%, CABG: 96.2%)
	Chronic oral anticoagulant (PCI: 5.2%, CABG: 10.8%)
FREEDOM <sup>10</sup>	Aspirin (PCI: 95.3%, CABG: 95.4%)
	Thienopyridine (PCI: 58.7%, CABG: 22.8%)
	Warfarin (PCI: 1.4%, CABG: 1.7%)
	Statin (PCI: 91.4%, CABG: 89.9%)
	Beta blocker (PCI: 82.6%, 82.8%)
	ACE inhibitor (PCI: 67.4%, 66.7%)
	Angiotensin-II receptor antagonist (PCI: 31.6%, CABG: 29.4%)
	Calcium-channel blocker (PCI: 28.4%, CABG: 24.8%)
	H2-receptor blocker (PCI: 19.7%, CABG: 20.8%)
Hong et al <sup>11</sup>	PCI: aspirin (indefinitely); clopidogrel or ticlopidine (6 months)
Kim et al <sup>12</sup>	<ul> <li>PCI: aspirin (100 mg/day, indefinitely), ticlopidine (250 mg/day, indefinitely)</li> </ul>
	• CABG: aspirin (100 mg/day, indefinitely)
LE MANS <sup>13</sup>	• PCI: Acetylsalicylic acid and thienopyridine (clopidogrel or ticlopidine) was initiated at least 2 days before the procedure.
	Intravenous glycoprotein IIb/IIIa blockers were used at the operator's discretion only in procedures performed in patients with
	complex coronary lesions and unstable angina. Unfractionated heparin was used in standard doses.
	• CABG: Double antiplatelet treatment ( $\geq$ 12 months); other pharmacological treatments (e.g., statins, angiotensin-converting
	enzyme inhibitors, beta-blockers) were recommended based on current practice and were left to the discretion of a
	supervising physician.
	Acetylsalicylic acid (PCI: 84%, CABG: 85%)

	Clopidogrel (PCI: 5%, CABG: 5%)
	Angiotensin receptor blocker (PCI: 68%, CABG: 65%)
	ACE inhibitor (PCI: 5%, CABG: 5%)
	Beta-blocker (PCI: 84%, CABG: 80%)
	Statin (PCI: 84%, CABG: 85%)
MASS-II <sup>14</sup>	• All: optimal medical regimen of titrated nitrates, aspirin, beta-blockers, calcium channel blockers, angiotensin-converting
	enzyme inhibitors, or a combination of these drugs unless contraindicated.
	• Lipid-lowering agents, particularly statins, were also prescribed, along with a low-fat diet, on an individual basis.
	Aspirin (PCI: 80%, CABG: 70%, Overall: 77%)
	Long-acting nitrates (PCI: 41%, CABG: 12%, Overall: 42%)
	Beta-blockers (PCI: 61%, CABG: 44%, Overall: 58%)
	Calcium channel antagonists (PCI: 30%, CABG: 44%, Overall: 45%)
	HMG-CoA reductase inhibitors (PCI: 73%, CABG: 49%, Overall: 63%)
	ACE inhibitors (PCI: 30%, CABG: 21%, Overall: 27%)
	Insulin (PCI: 9%, CABG: 11%, Overall: 11%)
	Oral hypoglycemic agents (PCI: 14%, CABG: 35%, Overall: 37%)
Myoprotect <sup>15</sup>	None reported
NOBLE <sup>16</sup>	• All: aspirin (75–150 mg/day, indefinitely); clopidogrel (75 mg/day, 12 months if acute coronary syndrome is present)
	• PCI: clopidogrel (75 mg/day, 12 months); prasugrel or ticagrelor could be substituted for clopidogrel at the discretion of the PCI
	operator.
Octostent <sup>17</sup>	PCI: glycoprotein IIb/IIIa receptor blocker was administered in 16 patients (12.2%).
PRECOMBAT <sup>18</sup>	Beta-blocker (PCI: 55.3%, CABG: 44.0%)
	Calcium channel-blocker (PCI: 61.7%, CABG: 46.3%)
	ACE inhibitor (PCI: 15.1%, CABG: 9.2%)
	Angiotensin II-receptor antagonist (PCI: 24.5%, CABG: 18.0%)
	Statin: (PCI: 72.1%, CABG: 48.0%)
Stent or Surgery (SoS)	Antianginal medications (number of drugs)
19	0 (PCI: 18.5%, CABG: 35.1%)
	1 (PCI: 44.4%, CABG: 44.2%)
	2 (PCI: 28.9%, CABG: 18.3%)
	3 (PCI: 7.9%, CABG: 2.2%)
	4 (PCI: 0.2%, CABG: 0.0%)
SIMA <sup>20</sup>	Antiplatelet therapy (94% PCI and 96% CABG)
	Lipid-lowering therapy increased gradually from 24% at 2 years to 89% (88% PCI and 91% CABG)
	Beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists : more than 50% of the patients without differences
	between the 2 groups
SYNTAX <sup>21,22</sup>	Acetylsalicylic acid (Aspirin) (PCI: 87.1%, CABG: 85.0%)
	Thienopyridine (PCI: 32.0%, CABG: 12.1%)

	Other antiplatelet (PCI: 4.1%, CABG: 3.3%)
	Acetylsalicylic acid (Aspirin) and Antiplatelet (PCI: 27.4%, CABG: 9.1%)
Thiele et al <sup>23</sup>	PCI: aspirin (100 mg/day, indefinitely); clopidogrel (75 mg/day, ≥12 months)
	CABG: aspirin (100 mg/day, indefinitely)
VA CARDS <sup>24</sup>	None reported

ACE: Angiotensin converting enzyme; CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention

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Trial	Primary outcomes	Secondary outcomes
ARTS <sup>1</sup>	freedom from major adverse cardiac and cerebrovascular events including all-cause mortality, transient ischemic attacks, myocardial infarction, repeat revascularization	angina status, use of medications, costs, cost effectiveness, and quality of life; a combined end point of mortality, myocardial infarction, or stroke; and the rates of mortality, myocardial infarction, stroke, and revascularization procedures.
BEST <sup>2</sup>	composite of all-cause mortality, myocardial infarction, or target-vessel revascularization	safety composite of all-cause mortality, myocardial infarction, or stroke and a composite of mortality, myocardial infarction, stroke, or any repeat revascularization
Blazek et al <sup>3</sup>	freedom from major adverse cardiac events, defined as death from any cause, myocardial infarction, and the need for repeated target vessel revascularization	individual component of the primary endpoint
Boudriot et al <sup>4</sup>	all-cause mortality, myocardial infarction, and the need for repeat revascularization within twelve months	individual components of the composite end point
CARDia⁵	composite of all-cause mortality, myocardial infarction, and stroke	repeat revascularization
Cisowski et al <sup>6</sup>	all-cause mortality, myocardial infarction, and reoccurrence of angina pectoris (ie, a major adversecoronary event) that required hospital treatment and repeat revascularization of the target vessel	
Drenth et al <sup>7</sup>	major adverse cardiac and cerebrovascular events, defined as cardiac death, myocardial infarction, stroke, and need for repeat target vessel revascularization	angina pectoris class and need for antianginal medication at four years of follow-up
ERACI II <sup>8</sup>	Composite of all-cause mortality, Q-wave myocardial infarction, stroke, and need for repeat revascularization procedures at 30 days, 1 year, 3 years, and 5 years of follow-up.	angina status and functional class at one, three, and five years of follow-up; completeness of revascularization, determined by stress thallium at one month; and follow-up cost and cost-effectiveness of both technique
EXCEL <sup>9</sup>	composite of all-cause mortality, stroke, myocardial infarction	primary outcome at 30 days and composite of all-cause mortality, stroke, myocardial infarction and repeat revascularization. The cause of mortality was adjudicated as definite cardiovascular, definite noncardiovascular, or undetermined, and undetermined cases were conservatively classified as cardiovascular.
FREEDOM <sup>10</sup>	composite of all-cause mortality, nonfatal myocardial infarction, or nonfatal stroke	major adverse cardiovascular and cerebrovascular events 30 days and 12 months after the procedure (including components of the primary outcome as well as repeat revascularization) and annual all-cause and cardiovascular mortality
Hong et al <sup>11</sup>	cardiac death, myocardial infarction, and the need for repeated revascularization of the target vessel	
Kim et al <sup>11</sup>	Major adverse cardiac events, all-cause mortality, percutaneous coronary intervention, coronary bypass,ST elevation myocardial infarction, non-ST elevation myocardial infarction, intraaortic balloon pump, pulmonary edema, bleeding complication,economic data like admission length, intensive care unit length of stay, post-operative length of stay	Mortality, cause of mortality and target vessel revascularization
LE MANS <sup>13</sup>	left ventricular ejection fraction assessed by 2-dimensional echocardiography at 1 year	all-cause mortality, myocardial infarction, target vessel revascularization, and stroke
MASS-II <sup>14</sup>	all-cause mortality, Q-wave myocardial infarction, or refractory angina that required revascularization	angina status, mortality due to a cardiac cause, and a cerebrovascular accident
Myoprotect <sup>15</sup>	event-free survival including from causes like mortality, myocardial infarction, or need for target lesion revascularization at 1 year	quality-of-life evaluation and total treatment costs
NOBLE <sup>16</sup>	composite of all-cause mortality, non-procedural myocardial infarction, any repeat coronary revascularization	individual components of the primary major adverse cardiac and cerebrovascular endpoint, definite stent thrombosis, and symptomatic graft occlusion

Octostent <sup>17</sup>	freedom from all-cause mortality, stroke, acute MI, and repeat revascularization at 12	survival free of stroke and acute myocardial infarction, freedom from angina and
	months	medication, quality of life, and cost-effectiveness
PRECOMBAT <sup>18</sup>	composite of all-cause mortality, myocardial infarction, stroke, ischemia driven	individual components of the primary endpoint; a composite of mortality, myocardial
	revascularization	infarction, or stroke; and clinically driven target vessel revascularization
Stent or	repeat revascularization	all-cause mortality
Surgery (SoS)		
19		
SIMA <sup>20</sup>	all cause mortality, myocardial infarction, and the need for additional revascularization	angina functional class
SYNTAX <sup>21,22</sup>	all-cause mortality, stroke, myocardial infarction, and repeat revascularization	major adverse cardiac and cerebrovascular event rates at different time intervals
Thiele et al <sup>23</sup>	freedom from major adverse cardiovascular events, which included cardiovascular	each individual component of the composite end point and periprocedural adverse
	mortality, myocardial infarction, and the need for repeated target vessel	events occurring within thirty days after randomization
	revascularization within twelve months.	
VA CARDS <sup>24</sup>	composite of all-cause mortality or nonfatal myocardial infarction	all-cause mortality, cardiac mortality, nonfatal myocardial infarction, and stroke

Trial	Adjudication process
ARTS <sup>1</sup>	An independent committee adjudicated clinical events and electrocardiograms.
BEST <sup>2</sup>	All the clinical end points were assessed by the event-adjudication committee, whose members were unaware of the study-group assignments.
Blazek et al <sup>3</sup>	All events were adjudicated by an event monitoring committee consisting of an experienced cardiologist and cardiovascular surgeon.
Boudriot et al <sup>4</sup>	All clinical outcomes were adjudicated by a clinical event committee consisting of a cardiothoracic surgeon and a cardiologist blinded to treatment allocation.
CARDia <sup>5</sup>	All major events including death, myocardial infarction, stroke, bleeding, and repeat revascularization were reviewed by the Critical Events Adjudication Committee, which consisted of cardiologists and surgeons who were blinded to treatment allocation. There were 2 adjudicators for each event, with a third used if required. An independent Data and Safety Monitoring Board comprising 2 cardiologists and 1 surgeon reviewed trial data according to protocol.
Cisowski et al <sup>6</sup>	The same committee consisting of cardiac surgeon and cardiologist, who were not involved into the study, assessed the angiograms.
Drenth et al <sup>7</sup>	Clinical events were checked by contact with the treating physicians and adjudicated by an event-monitoring committee of an experienced cardiologist and cardiac surgeon.
ERACI II <sup>8</sup>	The Clinical Events Committee reviewed the major adverse events and was blinded to the initial treatment strategy received.
EXCEL <sup>9</sup>	Trial monitors collected source documents of all primary and secondary outcome events for adjudication by an independent events committee.
FREEDOM <sup>10</sup>	An events committee provided central independent adjudication of all occurrences of the primary end points in an unblinded fashion.
Hong et al <sup>11</sup>	None reported
Kim et al <sup>12</sup>	None reported
LE MANS <sup>13</sup>	All clinical outcomes were analyzed by the clinical events committee. Information on any adverse event (including cardiac and noncardiac death, myocardial infarction, stroke, or repeated revascularization) was confirmed with hospital discharge files where the adverse event took place and was analyzed by the Clinical Events Committee.
MASS-II <sup>14</sup>	None reported
Myoprotect <sup>15</sup>	None reported

NOBLE <sup>16</sup>	An independent clinical events committee consisting of cardiologists and a cardiac surgeon adjudicated all possible events concerning cause of death, stroke, myocardial infarction, revascularisation, graft occlusion, and stent thrombosis
Octostent <sup>17</sup>	An independent committee blinded to the treatment allocation evaluated all events.
PRECOMBAT <sup>18</sup>	The event adjudication committee, whose members were blind to the study group assignments, assessed all clinical endpoints.
Stent or Surgery (SoS) <sup>19</sup>	Deaths were reported by the clinical events committee.
SIMA <sup>20</sup>	None reported
SYNTAX <sup>1,21</sup>	An independent clinical events committee adjudicated all primary clinical events, and patient safety was assessed at prespecified intervals by an independent data monitoring committee. An independent clinical events committee (including cardiologists, cardiac surgeons, and a neurologist (list in the Supplementary Appendix) adjudicated all primary clinical end points, staged procedures, and cases in which the sternum was reopened.
Thiele et al <sup>23</sup>	All clinical outcomes were adjudicated by a clinical event committee consisting of a cardiothoracic surgeon and a cardiologist.
VA CARDS <sup>24</sup>	A data monitoring committee reviewed safety and outcome measures semiannually. A 3-member endpoint committee blinded to treatment assignment adjudicated all MIs and strokes. Where records related to a death in follow-up were available, the endpoint committee reviewed them to assign a presumed cardiac versus noncardiac cause.

**eTable 8.** Details of Noncardiac Mortality in Percutaneous Coronary Intervention (PCI) vs Coronary Artery Bypass Grafting (CABG) Randomized Clinical Trials

Trial Name	PCI	CABG
ARTS <sup>1</sup>	Reported cardiac and non-cardiac deaths	Reported cardiac and non-cardiac deaths
BEST <sup>2</sup>	Reported "non-cardiac death" but did not specify cause	Reported "non-cardiac death" but did not specify cause
Blazek et al <sup>3</sup>	Reported cardiac death from which non-cardiac death was calculated	Reported cardiac death from which non-cardiac death was calculated
Drenth et al <sup>7</sup>	Reported cardiac and non-cardiac death	Reported cardiac and non-cardiac death
ERACI II 8	Four non-cardiac deaths were due to renal insufficiency, lung cancer,	Causes of non-cardiac deaths were pulmonary emphysema, stroke, renal
	pulmonary emphysema, and mesenteric infarction	insufficiency, and prostate and lung cancer
EXCEL <sup>9</sup>	Pulmonary: 8	Pulmonary: 5
	infection: 14	infection: 7
	gastrointestinal: 1	gastrointestinal: 2
	malignancy: 29	malignancy: 23
	accident/trauma:3	accident/trauma:2
	non-cardiovascular organ failure: 2	non-cardiovascular organ failure: 0
	other non-cardiovascular cause: 0	other non-cardiovascular cause: 2
	undetermined cause: 16	undetermined cause: 9
FREEDOM <sup>10</sup>	Reported cardiac death from which non-cardiac death was calculated	Reported cardiac death from which non-cardiac death was calculated
Kim et al <sup>12</sup>	cancer deaths: 1; CVA death: 1; unknown cause: 0	cancer deaths: 0; CVA death: 0; unknown cause: 1
MASS-II <sup>14</sup>	Reported cardiac death from which non-cardiac death was calculated	Reported cardiac death from which non-cardiac death was calculated
NOBLE <sup>16</sup>	Vascular death: 2	Vascular death: 1
	Reported cardiac and vascular death from which non-cardiac death was	Reported cardiac and vascular death from which non-cardiac death was
	calculated	calculated
PRECOMBAT	Reported "non-cardiac death" but did not specify cause	Reported "non-cardiac death" but did not specify cause
18		
Octostent <sup>7</sup>	Reported all-cause mortality, cardiovascular mortality and other mortality	Reported all-cause mortality, cardiovascular mortality and other mortality
Stent or	Other vascular: 2	Other vascular: 1
Surgery	cancer: 9	cancer: 3
(SoS) <sup>19</sup>	unknown: 2	unknown: 0
SIMA <sup>20</sup>	Reported all-cause, cardiac and non-cardiac mortality	Reported all-cause, cardiac and non-cardiac mortality
SYNTAX <sup>21,22</sup>	Reported cardiac death from which non-cardiac death was calculated	Reported cardiac death from which non-cardiac death was calculated
VA CARDS <sup>24</sup>	Reported cardiac death from which non-cardiac death was calculated	Reported cardiac death from which non-cardiac death was calculated

eFigure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flowchart of Our Analysis





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eFigure 5. Leave-One-Out Analysis for All-Cause Mortality for Fixed-Effects Model (A) and Random-Effects Model

Α.

Incidence Rate					
Study	Ra	l	IRR	95%-CI	
Omitting EXCEL		<b>_</b>	1.14	[1.02; 1.27]	
Omitting NOBLE		— — — — — — — — — — — — — — — — — — —	1.17	[1.06; 1.30]	
Omitting PRECOMBAT			1.18	[1.07; 1.31]	
Omitting BEST			1.16	[1.05; 1.29]	
Omitting Stent or Surgery (SoS)			1.15	[1.04; 1.27]	
Omitting ARTS		<b>i</b>	1.17	[1.06; 1.30]	
Omitting ERACI II			1.19	[1.07; 1.31]	
Omitting LE MANS		— <b>—</b>	1.18	[1.06; 1.30]	
Omitting Boudriot et al.		— <b>—</b>	1.17	[1.06; 1.29]	
Omitting MASS-II			1.18	[1.06; 1.31]	
Omitting VA CARDS			1.16	[1.05; 1.28]	
Omitting CARDIa			1.17	[1.06; 1.29]	
Omitting FREEDOM			1.12	[1.00; 1.25]	
Omitting SYNTAX		— <b>-</b>	1.17	[1.04; 1.32]	
Omitting Cisowski et al.			1.16	[1.05; 1.28]	
Omitting Blazek et al.			1.17	[1.06; 1.30]	
Omitting Drenth et al.			1.17	[1.06; 1.29]	
Omitting Kim et al.			1.17	[1.05; 1.29]	
Omitting Myoprotect I			1.17	[1.05; 1.29]	
Omitting Octostent			1.17	[1.06; 1.29]	
Omitting SIMA		— <mark>•</mark> —	1.17	[1.05; 1.29]	
Omitting Hong et al.		<mark></mark> -	1.17	[1.06; 1.29]	
Fixed effect model			1.17	[1.05; 1.29]	
	0.0	1 105			
	0.0	1 1.25			
	Favors PCI	Favors CA	BG		

	Incide	ence Rate		
Study	F	Ratio	IRR	95%-CI
Study Omitting EXCEL Omitting NOBLE Omitting PRECOMBAT Omitting BEST Omitting Stent or Surgery (SoS) Omitting ARTS Omitting ERACI II Omitting ERACI II Omitting Boudriot et al. Omitting Boudriot et al. Omitting VA CARDS Omitting CARDIa Omitting CARDIa Omitting FREEDOM Omitting FREEDOM Omitting FREEDOM Omitting SYNTAX Omitting Disewski et al. Omitting Disewski et al. Omitting Disenth et al. Omitting Kim et al. Omitting Kim et al. Omitting SIMA Omitting SIMA Omitting SIMA			IRR 	<b>95%-Cl</b> [0.93; 1.29] [0.96; 1.32] [0.99; 1.34] [0.95; 1.30] [0.96; 1.27] [0.96; 1.27] [0.96; 1.33] [1.01; 1.34] [0.99; 1.33] [0.97; 1.34] [0.93; 1.29] [0.97; 1.28] [0.93; 1.28] [0.93; 1.31] [0.96; 1.31] [0.96; 1.31] [0.96; 1.31] [0.96; 1.31] [0.96; 1.31] [0.96; 1.31] [0.96; 1.31]
Random effects model	Γ	+	1.13	[0.97; 1.31]
	0.8	1 1	.25	
	Favors PCI	Favors	CABG	

Α.

Study	Incider Ra	ice Rate atio	IRR 95%-CI
Omitting EXCEL Omitting NOBLE Omitting PRECOMBAT Omitting BEST Omitting FREEDOM Omitting SYNTAX Omitting Stent or Surgery (SoS) Omitting ARTS Omitting ERACI II Omitting MASS-II Omitting VA CARDS Omitting Blazek et al. Omitting Drenth et al. Omitting Cotostent Omitting SIMA Omitting SIMA Omitting Thiele et al.	_		$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Fixed effect model	0.75	1 1.	<b>1.24 [1.05; 1.45]</b> 5
	Favors PCI	Favors CAE	3G

	Incidence Rate				
Study		Ratio	IRR	95%-CI	
Study Omitting EXCEL Omitting NOBLE Omitting PRECOMBAT Omitting BEST Omitting FREEDOM Omitting SYNTAX Omitting Stent or Surgery (SoS) Omitting ARTS Omitting ERACI II Omitting MASS-II Omitting VA CARDS Omitting Blazek et al. Omitting Drenth et al. Omitting Kim et al. Omitting Cotostent			IRR - 1.15 - 1.17 - 1.23 - 1.16 1.12 1.09 1.13 - 1.23 1.15 - 1.23 1.14 1.11 - 1.17 - 1.17 - 1.17 - 1.17 - 1.17	<b>95%-CI</b> [0.88; 1.52] [0.90; 1.53] [0.97; 1.56] [0.89; 1.51] [0.85; 1.48] [0.85; 1.41] [0.88; 1.46] [0.88; 1.50] [0.97; 1.56] [0.87; 1.49] [0.89; 1.39] [0.91; 1.52] [0.92; 1.50] [0.92; 1.50]	
Omitting SIMA			1.15	[0.89; 1.48]	
Random effects model			1.19	[0.94; 1.51] [0.91; 1.48]	
	0.75	1 1	.5		
	Favors	PCI Favors CA	BG		

eFigure 7. Leave-One-Out Analysis for Noncardiac Mortality for Fixed-Effects Model (A) and Random-Effects Model (B)

#### Α.

Incidence Rate						
Study	R	Ratio	IRR	95%-CI		
Omitting EXCEL Omitting NOBLE Omitting PRECOMBAT Omitting PREEDOM Omitting FREEDOM Omitting SYNTAX Omitting Stent or Surgery (SoS) Omitting ARTS Omitting ERACI II Omitting MASS-II Omitting MASS-II Omitting Blazek et al. Omitting Kim et al.			1.11 1.19 1.18 1.17 1.17 - 1.26 1.16 1.22 1.20 1.23 1.18 1.19 1.19 1.18	[0.92; 1.34] [1.00; 1.42] [0.99; 1.40] [0.99; 1.39] [0.97; 1.40] [1.04; 1.52] [0.98; 1.38] [1.02; 1.46] [1.01; 1.42] [1.03; 1.47] [0.99; 1.39] [1.00; 1.42] [1.01; 1.41] [1.01; 1.41]		
Omitting Octostent Omitting SIMA			1.19 1.19	[1.00; 1.40] [1.01; 1.41] [1.00; 1.41]		
Fixed effect model	0.75		1.19	[1.00; 1.41]		
	U.75 Favors PCI	Favors CAE	.5 3G			

Β.

	Incider	nce Rate		
Study	Ra	atio	IRR	95%-CI
Omitting EXCEL Omitting NOBLE Omitting PRECOMBAT Omitting BEST Omitting FREEDOM Omitting SYNTAX Omitting Stent or Surgery (SoS) Omitting ARTS Omitting ERACI II Omitting MASS-II Omitting MASS-II Omitting Blazek et al. Omitting Drenth et al. Omitting Ctostent Omitting SIMA			1.11 1.19 1.18 1.17 1.26 1.16 1.22 1.20 1.23 1.18 1.19 1.19 1.19 1.19	[0.92; 1.34] [0.98; 1.46] [0.98; 1.41] [0.98; 1.41] [0.96; 1.43] [1.04; 1.52] [0.98; 1.38] [1.01; 1.48] [1.00; 1.44] [1.03; 1.47] [0.99; 1.39] [0.98; 1.45] [1.00; 1.43] [0.98; 1.43] [1.09; 1.44]
Random effects model	[		1.19	[1.00; 1.42]
	0.75	1 1.	5	
	Favors PCI	Favors CAE	3G	

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eFigure 8. Subgroup Analysis for All-Cause Mortality for Trials Including Patients With Left Main Disease vs Non–Left Main Disease

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		Incide	nce Ra	ate			
Study		F	Ratio		IRR	95	5%-CI
Left Main Disease			á				
EXCEL			÷		1.12	[0.73;	1.72]
NOBLE			- <b>H</b>		1.00	[0.57;	1.74]
PRECOMBAT			<b>⊢</b> ¦		0.55	[0.26;	1.15]
Fixed effect model			<b>+</b>		0.96	[0.70;	1.30]
Random effects model			+		0.93	[0.64;	1.35]
Heterogeneity: $l^2 = 27\%$ , $\tau^2 = 0.0306$ , $p =$	0.25						
Others							
BEST					1.12	[0.57;	2.21]
FREEDOM			<b></b>		1.40	[0.98;	2.00]
SYNTAX			j <del>e -</del>		1.81	[1.25;	2.63]
Stent or Surgery (SoS)				_	2.25	[0.69;	7.31]
ARTS		_	-		1.24	[0.65;	2.34]
ERACIII					0.57	[0.28;	1.16]
MASS-II					1.32	[0.76;	2.29]
VA CARDS					4.20	[1.58;	11.14
Blazek et al.		. –			0.90	[0.37,	2.21]
Dienin et al.					0.20	[0.01,	4.17]
Cotostont			i i		0.00	10.01	0.10j 4 171
SIMA		-			2.00	[0.01,	22 061
Thiele et al					0.20	10 02	1 711
Fixed effect model			5		1.36	[1.13:	1.641
Random effects model			-		1.27	[0.95:	1.701
Heterogeneity: $l^2 = 41\% \tau^2 = 0.0996 \rho =$	0.05						1
notorogeneity. 1110, 1 0.00000, p	0.00		1				
Fixed effect model			٠		1.24	[1.05;	1.45]
Random effects model					1.16	[0.91;	1.48]
Heterogeneity: $l^2 = 44\%$ , $\tau^2 = 0.0940$ , $p = 0.03$			1	10			
	0.01	0.1	1	10	100		
	Favors	PCI		Favors	CABG		

		Incide	ence	Rate				
Study		F	Ratio			IRR	95	5%-CI
Left Main Disease								
EXCEL			<u>+</u>			1.51	[1.05;	2.17]
NOBLE			+			1.16	0.68;	1.98]
PRECOMBAT						2.00	[0.50;	8.00]
Fixed effect model			٠			1.41	[1.05;	1.89]
Random effects model			•			1.41	[1.05;	1.89]
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ , $p = 0.64$								
Others								
BEST			∦∎	_		1.83	[0.68;	4.96]
FREEDOM			+			1.32	[0.83;	2.11]
SYNTAX			<b>.</b>			0.92	[0.62;	1.37]
Stent or Surgery (SoS)			-	•		3.67	[1.02;	13.14]
ARTS			+			0.96	[0.57;	1.64]
ERACI II			-			0.80	[0.21;	2.98]
MASS-II			<b>+</b>			0.86	[0.50;	1.47]
VA CARDS				•		21.00	[1.23; 3	58.37]
Blazek et al.			+			1.14	[0.56;	2.34]
Drenth et al.		+				0.33	[0.01;	8.18]
Kim et al.						2.00	[0.18;	22.06]
Octostent		•				0.33	[0.01;	8.18]
SIMA			1	_		1.00	[0.20;	4.95]
Fixed effect model			Ī			1.09	[0.88;	1.34]
Random effects model			1			1.09	[0.88;	1.36]
Heterogeneity: $l^2 = 4\%$ , $\tau^2 = 0.0072$ , $p = 0.40$								
Fixed effect model			•			1.19	[1.00;	1.41]
Random effects model			è			1.19	[1.00;	1.42]
Heterogeneity: $l^2 = 3\% \tau^2 = 0.0040 \ \rho = 0.42$								-
	0.01	0.1	1	10	100			
F	Favors	PCI		Favors	S CABG			

Study of	details					
Refer	ence	Park S-J, Ahn J-M, Kim Y-H, Park D-W, Yun S-C, Lee J-Y, et al. Trial of everolimus-eluting stents or bypass surgery for coronary disease. N Engl J Med. 2015 Mar 26;372(13):1204–12.				
Study o X	<b>design</b> Individua Cluster-r Individua	ally-randomized parallel-group trial randomized parallel-group trial ally randomized cross-over (or other matched) trial				
For the	e purpose:	s of this assessment, the interventions being compared are	defined as			
Exper	imental:	PCI Comparator: CABG				
Specif	fy which c	outcome is being assessed for risk of bias	Non-cardiac mortality			
<b>Specif</b> altern = 1.52 parag	Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.Manuscript results					
ls the r	eview tea	m's aim for this result?				
√ □	to assess to assess	s the effect of <i>assignment to intervention</i> (the 'intention-to s the effect of <i>adhering to intervention</i> (the 'per-protocol' e	-treat' effect) ffect)			
If the aim is to assess the effect of adhering to intervention, select the deviations from intended intervention that should be addressed (at least one must be checked):          occurrence of non-protocol interventions         failures in implementing the intervention that could have affected the outcome         non-adherence to their assigned intervention by trial participants						

Which of the following sources were obtained to help inform the risk-of-bias assessment? (tick as many as apply) Journal article(s) with results of the trial  $\checkmark$ Trial protocol Statistical analysis plan (SAP) Non-commercial trial registry record (e.g. ClinicalTrials.gov record) Company-owned trial registry record (e.g. GSK Clinical Study Register record) "Grey literature" (e.g. unpublished thesis) Conference abstract(s) about the trial Regulatory document (e.g. Clinical Study Report, Drug Approval Package) Research ethics application Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research) Personal communication with trialist Personal communication with the sponsor

Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising from the randomization process

Comments	Response options
	<u>Y</u>
1	<u>Y</u>
	<u>N</u>
	Low
	Unpredictable
	Comments

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y
2.2. Were carers and people delivering the interventions aware of participants' assigned	Y	
--	---------------	
intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose	Y	
because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	<u>PY</u>	
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between	<u>Y</u>	
groups?		
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	<u>Y</u>	
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the	PY	
failure to analyse participants in the group to which they were randomized?		
Risk-of-bias judgement	Some concerns	
Optional: What is the predicted direction of bias due to deviations from intended	Unpredictable	
interventions?		

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during		N/A
the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across	N/A	N/A
intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the	N/A	N/A
outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected	N/A	Y
participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of	N/A	N/A
adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from intended interventions?	N/A	N/A

Domain 3: Missing outcome data

Signalling questions	Comments	Response options

3.1 Were data for this outcome available for all, or nearly all, participants randomized?		<u>Y</u>
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	N/A	N/A
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome data?		NA

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study		<u>PN</u>
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of		N/A
intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of		N/A
intervention received?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan		<u>PY</u>
that was finalized before unblinded outcome data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions, time points) within the		<u>N</u>
outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low

Optional: What is the predicted direction of bias due to selection of the reported result? NA	Optional: What is the predicted direction of bias due to selection of the reported result?		NA
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Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall predicted	NA
direction of bias for this outcome?	

Study details			
Rodriguez AE, Baldi J, Fernández Pereira C, Navia J, Rodriguez Alemparte M, Delacasa A, et al. Five-year follow-up of the Argentine randomized trial of coronary angioplasty with stenting versus coronary bypass surgery in patients with multiple vessel disease (ERACI II). J Am Coll Cardiol. 2005 Aug 16;46(4):582–8.			
Study design X Individu Cluster-i	ally-randomized parallel-group trial randomized parallel-group trial ally randomized cross-over (or other matched) trial		
For the purpose Experimental:	s of this assessment, the interventions being compared are PCI Comparator: CABG	defined as	
Specify which c	outcome is being assessed for risk of bias	Non-cardiac mortality	
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.Manuscript results			
<ul> <li>Is the review team's aim for this result?</li> <li>✓ to assess the effect of assignment to intervention (the 'intention-to-treat' effect)</li> <li>□ to assess the effect of adhering to intervention (the 'per-protocol' effect)</li> </ul>			
If the aim is to assess the effect of adhering to intervention, select the deviations from intended intervention that should be addressed (at least one must be checked):          occurrence of non-protocol interventions         failures in implementing the intervention that could have affected the outcome         non-adherence to their assigned intervention by trial participants			

Which of the following sources were obtained to help inform the risk-of-bias assessment? (tick as many as apply) Journal article(s) with results of the trial  $\checkmark$ Trial protocol Statistical analysis plan (SAP) Non-commercial trial registry record (e.g. ClinicalTrials.gov record) Company-owned trial registry record (e.g. GSK Clinical Study Register record) "Grey literature" (e.g. unpublished thesis) Conference abstract(s) about the trial Regulatory document (e.g. Clinical Study Report, Drug Approval Package) Research ethics application Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research) Personal communication with trialist Personal communication with the sponsor

Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising from the randomization process

Comments	Response options
	<u>Y</u>
1	<u>Y</u>
	<u>N</u>
	Low
	Unpredictable
	Comments

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y

2.2. Were carers and people delivering the interventions aware of participants' assigned	Y
intervention during the trial?	
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose	Y
because of the trial context?	
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	<u>PY</u>
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between	<u>Y</u>
groups?	
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	<u>Y</u>
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the	PY
failure to analyse participants in the group to which they were randomized?	
Risk-of-bias judgement	Some concerns
Optional: What is the predicted direction of bias due to deviations from intended	Unpredictable
interventions?	

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during		N/A
the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across	N/A	N/A
intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the	N/A	N/A
outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected	N/A	Υ
participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of	N/A	N/A
adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from intended interventions?	N/A	N/A

Domain 3: Missing outcome data

Signalling questions	Comments	Response options

3.1 Were data for this outcome available for all, or nearly all, participants randomized?		<u>Y</u>
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	N/A	N/A
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome data?		NA

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		N
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study		<u>PN</u>
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of		N/A
intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of		N/A
intervention received?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

### Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan		<u>PY</u>
that was finalized before unblinded outcome data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions, time points) within the		<u>N</u>
outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall predicted	NA
direction of bias for this outcome?	

Study details		
Reference	Stone GW, Kappetein AP, Sabik JF, Pocock SJ, Morice M-C Main Coronary Disease. N Engl J Med. 2019 Sep 28;0(0).	, Puskas J, et al. Five-Year Outcomes after PCI or CABG for Left
Study design X Individu □ Cluster- □ Individu	ally-randomized parallel-group trial randomized parallel-group trial ally randomized cross-over (or other matched) trial	
For the purpose	s of this assessment, the interventions being compared are	defined as
Experimental:	PCI Comparator: CABG	
Specify which o	outcome is being assessed for risk of bias	Non-cardiac mortality
<b>Specify the nur</b> alternative ana = 1.52 (95% Cl paragraph) tha	nerical result being assessed. In case of multiple lyses being presented, specify the numeric result (e.g. RR 0.83 to 2.77) and/or a reference (e.g. to a table, figure or t uniquely defines the result being assessed.	Manuscript results
<ul> <li>Is the review team's aim for this result?</li> <li>✓ to assess the effect of assignment to intervention (the 'intention-to-treat' effect)</li> <li>□ to assess the effect of adhering to intervention (the 'per-protocol' effect)</li> </ul>		
If the aim is to assess the effect of adhering to intervention, select the deviations from intended intervention that should be addressed (at least one must be checked):          occurrence of non-protocol interventions         failures in implementing the intervention that could have affected the outcome         non-adherence to their assigned intervention by trial participants		
Which of the fol ✓ Journal a	<b>lowing sources were <u>obtained</u> to help inform the risk-of-bia</b> article(s) with results of the trial	as assessment? (tick as many as apply)

Trial protocol
Statistical analysis plan (SAP)
Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Company-owned trial registry record (e.g. GSK Clinical Study Register record)
"Grey literature" (e.g. unpublished thesis)
Conference abstract(s) about the trial
Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
Research ethics application
Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
Personal communication with trialist
Personal communication with the sponsor

## Risk of bias assessment

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Domain 1: Risk of bias arising	from the randomization process
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Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to		<u>Y</u>
interventions?		
1.3 Did baseline differences between intervention groups suggest a problem with the randomization		<u>N</u>
process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y
2.2. Were carers and people delivering the interventions aware of participants' assigned		Y
intervention during the trial?		

2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose	Y
because of the trial context?	
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	<u>PY</u>
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between	<u>Y</u>
groups?	
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	<u>Y</u>
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the	PY
failure to analyse participants in the group to which they were randomized?	
Risk-of-bias judgement	Some concerns
Optional: What is the predicted direction of bias due to deviations from intended	Unpredictable
interventions?	

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during		N/A
the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across	N/A	N/A
intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the	N/A	N/A
outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected	N/A	Y
participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of	N/A	N/A
adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from intended interventions?	N/A	N/A

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?		<u>Y</u>

3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	N/A	N/A
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome data?		NA

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study		<u>PN</u>
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of		N/A
intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of		N/A
intervention received?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

# Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan		PY
that was finalized before unblinded outcome data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions, time points) within the		<u>N</u>
outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall predicted	NA
direction of bias for this outcome?	

Study details		
Reference	Farkouh ME, Domanski M, Sleeper LA, Siami FS, Dangas G Patients with Diabetes. N Engl J Med. 2012 Dec 20;367(25	, Mack M, et al. Strategies for Multivessel Revascularization in 5):2375–84.
Study design X Individu □ Cluster- □ Individu	ally-randomized parallel-group trial randomized parallel-group trial ally randomized cross-over (or other matched) trial	
For the purpose	s of this assessment, the interventions being compared are	defined as
Experimental:	PCI Comparator: CABG	
Specify which c	outcome is being assessed for risk of bias	Non-cardiac mortality
<b>Specify the nur</b> alternative ana = 1.52 (95% Cl paragraph) tha	nerical result being assessed. In case of multiple lyses being presented, specify the numeric result (e.g. RR 0.83 to 2.77) and/or a reference (e.g. to a table, figure or t uniquely defines the result being assessed.	Manuscript results
Is the review tea ✓ to asses □ to asses	a <b>m's aim for this result?</b> s the effect of <i>assignment to intervention</i> (the 'intention-to s the effect of <i>adhering to intervention</i> (the 'per-protocol' e	o-treat' effect) effect)
If the aim is to assess the effect of adhering to intervention, select the deviations from intended intervention that should be addressed (at least one must be checked):		
Which of the fol ✓ Journal a	lowing sources were <u>obtained</u> to help inform the risk-of-bia article(s) with results of the trial	as assessment? (tick as many as apply)

Trial protocol
Statistical analysis plan (SAP)
Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Company-owned trial registry record (e.g. GSK Clinical Study Register record)
"Grey literature" (e.g. unpublished thesis)
Conference abstract(s) about the trial
Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
Research ethics application
Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
Personal communication with trialist
Personal communication with the sponsor

## Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising	from the randomization process
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Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to		<u>Y</u>
interventions?		
1.3 Did baseline differences between intervention groups suggest a problem with the randomization		<u>N</u>
process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y
2.2. Were carers and people delivering the interventions aware of participants' assigned		Y
intervention during the trial?		

2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose	Y
because of the trial context?	
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	<u>PY</u>
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between	<u>Y</u>
groups?	
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	<u>Y</u>
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the	PY
failure to analyse participants in the group to which they were randomized?	
Risk-of-bias judgement	Some concerns
Optional: What is the predicted direction of bias due to deviations from intended	Unpredictable
interventions?	

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during		N/A
the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across	N/A	N/A
intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the	N/A	N/A
outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected	N/A	Y
participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of	N/A	N/A
adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from intended interventions?	N/A	N/A

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?		<u>Y</u>

3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	N/A	N/A
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome data?		NA

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study		<u>PN</u>
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of		N/A
intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of		N/A
intervention received?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

# Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan		PY
that was finalized before unblinded outcome data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions, time points) within the		<u>N</u>
outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall predicted	NA
direction of bias for this outcome?	

Study details		
Reference	Hueb W, Lopes N, Gersh BJ, Soares PR, Ribeiro EE, Pereira AC, et al. Ten-year follow-up survival of the Medicine, Angioplasty, or Surgery Study (MASS II): a randomized controlled clinical trial of 3 therapeutic strategies for multivessel coronary artery disease. Circulation. 2010 Sep 7;122(10):949–57.	
Study design X Individu Cluster-I I Individu	ally-randomized parallel-group trial randomized parallel-group trial ally randomized cross-over (or other matched) trial	
For the purpose Experimental:	s of this assessment, the interventions being compared are PCI Comparator: CABG	defined as
Specify which c	outcome is being assessed for risk of bias	Non-cardiac mortality
<b>Specify the nur</b> alternative ana = 1.52 (95% Cl paragraph) tha	nerical result being assessed. In case of multiple lyses being presented, specify the numeric result (e.g. RR 0.83 to 2.77) and/or a reference (e.g. to a table, figure or t uniquely defines the result being assessed.	Manuscript results
Is the review tea ✓ to asses □ to asses	a <b>m's aim for this result?</b> s the effect of <i>assignment to intervention</i> (the 'intention-to s the effect of <i>adhering to intervention</i> (the 'per-protocol' e	-treat' effect) :ffect)
If the aim is to assess the effect of adhering to intervention, select the deviations from intended intervention that should be addressed (at least one must be checked): <ul> <li>occurrence of non-protocol interventions</li> <li>failures in implementing the intervention that could have affected the outcome</li> </ul>		
non-adherence to their assigned intervention by trial participants		
Which of the fol ✓ Journal a	lowing sources were <u>obtained</u> to help inform the risk-of-bia article(s) with results of the trial	is assessment? (tick as many as apply)

Trial protocol
Statistical analysis plan (SAP)
Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Company-owned trial registry record (e.g. GSK Clinical Study Register record)
"Grey literature" (e.g. unpublished thesis)
Conference abstract(s) about the trial
Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
Research ethics application
Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
Personal communication with trialist
Personal communication with the sponsor

## Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising	from the randomization process
--------------------------------	--------------------------------

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to		<u>Y</u>
interventions?		
1.3 Did baseline differences between intervention groups suggest a problem with the randomization		<u>N</u>
process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y
2.2. Were carers and people delivering the interventions aware of participants' assigned		Y
intervention during the trial?		

2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose	γ
because of the trial context?	
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	<u>PY</u>
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between	<u>Y</u>
groups?	
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the	PY
failure to analyse participants in the group to which they were randomized?	
Risk-of-bias judgement	Some concerns
Optional: What is the predicted direction of bias due to deviations from intended	Unpredictable
interventions?	

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during		N/A
the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across	N/A	N/A
intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the	N/A	N/A
outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected	N/A	Υ
participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of	N/A	N/A
adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from intended interventions?	N/A	N/A

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?		<u>Y</u>

3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	N/A	N/A
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome data?		NA

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study		<u>PN</u>
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of		N/A
intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of		N/A
intervention received?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

# Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan		PY
that was finalized before unblinded outcome data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions, time points) within the		<u>N</u>
outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall predicted	NA
direction of bias for this outcome?	

Study details	· · · · · · · · · · · · · · · · · · ·	
Reference	Holm NR, Mäkikallio T, Lindsay MM, Spence MS, Erglis A, Menown IBA, et al. Percutaneous coronary angioplasty versus coronary artery bypass grafting in the treatment of unprotected left main stenosis: updated 5-year outcomes from the randomised, non-inferiority NOBLE trial. The Lancet. 2019	
Study design X Individu Cluster-	ually-randomized parallel-group trial -randomized parallel-group trial ually randomized cross-over (or other matched) trial	
For the purpose	es of this assessment, the interventions being compared are de	fined as
Experimental.		
Specify which o	outcome is being assessed for risk of bias	on-cardiac mortality
Specify the nur alternative ana = 1.52 (95% Cl paragraph) tha	merical result being assessed. In case of multiple alyses being presented, specify the numeric result (e.g. RR 0.83 to 2.77) and/or a reference (e.g. to a table, figure or at uniquely defines the result being assessed.	1anuscript results
Is the review tea ✓ to asses □ to asses	<b>am's aim for this result?</b> ss the effect of <i>assignment to intervention</i> (the 'intention-to-tre ss the effect of <i>adhering to intervention</i> (the 'per-protocol' effe	eat' effect) cct)
If the aim is to assess the effect of adhering to intervention, select the deviations from intended intervention that should be addressed (at least one must be checked):          occurrence of non-protocol interventions         failures in implementing the intervention that could have affected the outcome         non-adherence to their assigned intervention by trial participants		
Which of the fol ✓ Journal a	<b>llowing sources were <u>obtained</u> to help inform the risk-of-bias a</b> article(s) with results of the trial	ssessment? (tick as many as apply)

Trial protocol
Statistical analysis plan (SAP)
Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Company-owned trial registry record (e.g. GSK Clinical Study Register record)
"Grey literature" (e.g. unpublished thesis)
Conference abstract(s) about the trial
Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
Research ethics application
Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
Personal communication with trialist
Personal communication with the sponsor

## Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising	from the randomization process
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Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to		<u>Y</u>
interventions?		
1.3 Did baseline differences between intervention groups suggest a problem with the randomization		<u>N</u>
process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y
2.2. Were carers and people delivering the interventions aware of participants' assigned		Y
intervention during the trial?		

2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose	γ
because of the trial context?	
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	<u>PY</u>
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between	<u>Y</u>
groups?	
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the	PY
failure to analyse participants in the group to which they were randomized?	
Risk-of-bias judgement	Some concerns
Optional: What is the predicted direction of bias due to deviations from intended	Unpredictable
interventions?	

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during		N/A
the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across	N/A	N/A
intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the	N/A	N/A
outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected	N/A	Υ
participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of	N/A	N/A
adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from intended interventions?	N/A	N/A

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?		<u>Y</u>

3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	N/A	N/A
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome data?		NA

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study		<u>PN</u>
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of		N/A
intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of		N/A
intervention received?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

# Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan		PY
that was finalized before unblinded outcome data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions, time points) within the		<u>N</u>
outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall predicted	NA
direction of bias for this outcome?	

Study details		
Reference	Cisowski M, Drzewiecki J, Drzewiecka-Gerber A, Jaklik A, Kruczak W, Szczeklik M, et al. Primary stenting versus MIDCAB: preliminary report–Comparision of two methods of revascularization in single left anterior descending coronary artery stenosis. Ann Thorac Surg. 2002 Oct;74(4):1334–9	
Study design X Individu Cluster-I	ally-randomized parallel-group trial randomized parallel-group trial ally randomized cross-over (or other matched) trial	
For the purpose	s of this assessment, the interventions being compared are	defined as
Experimental:	PCI Comparator: CABG	
Specify which c	outcome is being assessed for risk of bias	Non-cardiac mortality
<b>Specify the num</b> alternative ana = 1.52 (95% Cl ( paragraph) that	nerical result being assessed. In case of multiple lyses being presented, specify the numeric result (e.g. RR 0.83 to 2.77) and/or a reference (e.g. to a table, figure or t uniquely defines the result being assessed.	Manuscript results
Is the review tea ✓ to assess □ to assess	m <b>'s aim for this result?</b> s the effect of <i>assignment to intervention</i> (the 'intention-to s the effect of <i>adhering to intervention</i> (the 'per-protocol' e	o-treat' effect) effect)
If the aim is to anleast one must boccurrenfailures innon-adhe	ssess the effect of adhering to intervention, select the devia be checked): ice of non-protocol interventions n implementing the intervention that could have affected t erence to their assigned intervention by trial participants	ations from intended intervention that should be addressed (at he outcome
Which of the fol ✓ Journal a	<b>lowing sources were <u>obtained</u> to help inform the risk-of-bia</b> rticle(s) with results of the trial	as assessment? (tick as many as apply)

Trial protocol
Statistical analysis plan (SAP)
Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Company-owned trial registry record (e.g. GSK Clinical Study Register record)
"Grey literature" (e.g. unpublished thesis)
Conference abstract(s) about the trial
Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
Research ethics application
Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
Personal communication with trialist
Personal communication with the sponsor

## Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising	from the randomization process
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Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to		<u>Y</u>
interventions?		
1.3 Did baseline differences between intervention groups suggest a problem with the randomization		<u>N</u>
process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y
2.2. Were carers and people delivering the interventions aware of participants' assigned		Y
intervention during the trial?		

2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose	γ
because of the trial context?	
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	<u>PY</u>
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between	<u>Y</u>
groups?	
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the	PY
failure to analyse participants in the group to which they were randomized?	
Risk-of-bias judgement	Some concerns
Optional: What is the predicted direction of bias due to deviations from intended	Unpredictable
interventions?	

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during		N/A
the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across	N/A	N/A
intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the	N/A	N/A
outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected	N/A	Υ
participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of	N/A	N/A
adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from intended interventions?	N/A	N/A

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?		<u>Y</u>
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	N/A	N/A
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3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome data?		NA

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study		<u>PN</u>
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of		N/A
intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of		N/A
intervention received?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan		PY
that was finalized before unblinded outcome data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions, time points) within the		<u>N</u>
outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall predicted	NA
direction of bias for this outcome?	

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Study details		
Reference	SoS Investigators. Coronary artery bypass surgery versus patients with multivessel coronary artery disease (the Ste Engl. 2002 Sep 28;360(9338):965–70.	percutaneous coronary intervention with stent implantation in nt or Surgery trial): a randomised controlled trial. Lancet Lond
Study design X Individu Cluster-I	ally-randomized parallel-group trial randomized parallel-group trial ally randomized cross-over (or other matched) trial	
For the purpose	s of this assessment, the interventions being compared are	defined as
Experimental:	PCI Comparator: CABG	
Specify which c	outcome is being assessed for risk of bias	Non-cardiac mortality
<b>Specify the num</b> alternative ana = 1.52 (95% Cl ( paragraph) that	nerical result being assessed. In case of multiple lyses being presented, specify the numeric result (e.g. RR 0.83 to 2.77) and/or a reference (e.g. to a table, figure or t uniquely defines the result being assessed.	Manuscript results
Is the review tea ✓ to assess □ to assess	m <b>'s aim for this result?</b> s the effect of <i>assignment to intervention</i> (the 'intention-to s the effect of <i>adhering to intervention</i> (the 'per-protocol' e	o-treat' effect) effect)
If the aim is to an is the antice of the antis antice of the antice of the antice of the an	ssess the effect of adhering to intervention, select the devia be checked): ice of non-protocol interventions n implementing the intervention that could have affected t erence to their assigned intervention by trial participants	ations from intended intervention that should be addressed (at he outcome
Which of the fol ✓ Journal a	lowing sources were <u>obtained</u> to help inform the risk-of-bia rticle(s) with results of the trial	as assessment? (tick as many as apply)

Trial protocol
Statistical analysis plan (SAP)
Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Company-owned trial registry record (e.g. GSK Clinical Study Register record)
"Grey literature" (e.g. unpublished thesis)
Conference abstract(s) about the trial
Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
Research ethics application
Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
Personal communication with trialist
Personal communication with the sponsor

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Domain 1: Risk of bias arising	from the randomization process
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Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to		<u>Y</u>
interventions?		
1.3 Did baseline differences between intervention groups suggest a problem with the randomization		<u>N</u>
process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y
2.2. Were carers and people delivering the interventions aware of participants' assigned		Y
intervention during the trial?		

2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose	γ
because of the trial context?	
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	<u>PY</u>
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between	<u>Y</u>
groups?	
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the	PY
failure to analyse participants in the group to which they were randomized?	
Risk-of-bias judgement	Some concerns
Optional: What is the predicted direction of bias due to deviations from intended	Unpredictable
interventions?	

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of adhering to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during		N/A
the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across	N/A	N/A
intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the	N/A	N/A
outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected	N/A	Υ
participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of	N/A	N/A
adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from intended interventions?	N/A	N/A

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?		<u>Y</u>

3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	N/A	N/A
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome data?		NA

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study		<u>PN</u>
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of		N/A
intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of		N/A
intervention received?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan		PY
that was finalized before unblinded outcome data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions, time points) within the		<u>N</u>
outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall predicted	NA
direction of bias for this outcome?	

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Study details	5		
Reference	Mohr FW, Morice M-C, Kappetein AP, Feldman TE, Ståhle E, Colombo A, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. The Lancet. 2013 Feb;381(9867):629–38.		
Study design X Individu Cluster-I I Individu	i vidually-randomized parallel-group trial ter-randomized parallel-group trial vidually randomized cross-over (or other matched) trial		
For the purpose Experimental:	oses of this assessment, the interventions being compared are defined as cal: PCI Comparator: CABG		
Specify which c	ch outcome is being assessed for risk of bias Non-cardiac mortality		
<b>Specify the num</b> alternative ana = 1.52 (95% Cl paragraph) that	numerical result being assessed. In case of multiple analyses being presented, specify the numeric result (e.g. RR 6 CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or that uniquely defines the result being assessed.Manuscript results		
Is the review tea ✓ to assess □ to assess	<b>y team's aim for this result?</b> ssess the effect of <i>assignment to intervention</i> (the 'intention-to-treat' effect) ssess the effect of <i>adhering to intervention</i> (the 'per-protocol' effect)		
If the aim is to an is to	<b>to assess the effect of <i>adhering to intervention</i>,</b> select the deviations from intended intervention that should ust be checked): rrence of non-protocol interventions res in implementing the intervention that could have affected the outcome adherence to their assigned intervention by trial participants	l be addressed (at	
Which of the fol ✓ Journal a	e following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply) nal article(s) with results of the trial		

Trial protocol
Statistical analysis plan (SAP)
Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Company-owned trial registry record (e.g. GSK Clinical Study Register record)
"Grey literature" (e.g. unpublished thesis)
Conference abstract(s) about the trial
Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
Research ethics application
Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
Personal communication with trialist
Personal communication with the sponsor

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising	from the randomization process
--------------------------------	--------------------------------

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to		<u>Y</u>
interventions?		
1.3 Did baseline differences between intervention groups suggest a problem with the randomization		<u>N</u>
process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y
2.2. Were carers and people delivering the interventions aware of participants' assigned		Y
intervention during the trial?		

2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose	Y
because of the trial context?	
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	<u>PY</u>
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between	<u>Y</u>
groups?	
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	<u>Y</u>
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the	PY
failure to analyse participants in the group to which they were randomized?	
Risk-of-bias judgement	Some concerns
Optional: What is the predicted direction of bias due to deviations from intended	Unpredictable
interventions?	
<ul> <li>2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?</li> <li>2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?</li> <li>Risk-of-bias judgement</li> <li>Optional: What is the predicted direction of bias due to deviations from intended interventions?</li> </ul>	Y       PY       Some concerns       Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of adhering to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during		N/A
the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across	N/A	N/A
intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the	N/A	N/A
outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected	N/A	Υ
participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of	N/A	N/A
adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from intended interventions?	N/A	N/A

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?		<u>Y</u>

3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	N/A	N/A
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome data?		NA

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study		<u>PN</u>
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of		N/A
intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of		N/A
intervention received?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan		PY
that was finalized before unblinded outcome data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions, time points) within the		<u>N</u>
outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall predicted	NA
direction of bias for this outcome?	

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Study details		
Reference	Kamalesh M, Sharp TG, Tang XC, Shunk K, Ward HB, Wals bypass surgery in United States veterans with diabetes. J	h J, et al. Percutaneous coronary intervention versus coronary Am Coll Cardiol. 2013 Feb 26;61(8):808–16.
Study design X Individu Cluster Individu	ually-randomized parallel-group trial -randomized parallel-group trial ually randomized cross-over (or other matched) trial	
For the purpose Experimental:	PCI Compared are	e defined as
Specify which	outcome is being assessed for risk of bias	Non-cardiac mortality
<b>Specify the nu</b> alternative and = 1.52 (95% Cl paragraph) tha	<b>merical result being assessed.</b> In case of multiple alyses being presented, specify the numeric result (e.g. RR 0.83 to 2.77) and/or a reference (e.g. to a table, figure or at uniquely defines the result being assessed.	Manuscript results
Is the review te ✓ to asses □ to asses	<b>am's aim for this result?</b> ss the effect of <i>assignment to intervention</i> (the 'intention-to ss the effect of <i>adhering to intervention</i> (the 'per-protocol'	o-treat' effect) effect)
If the aim is to a one must be ch ccurre failures non-adh	assess the effect of <i>adhering to intervention,</i> select the devi ecked): nce of non-protocol interventions in implementing the intervention that could have affected the nerence to their assigned intervention by trial participants	ations from intended intervention that should be addressed (at least the outcome
Which of the fo ✓ Journal	<b>llowing sources were <u>obtained</u> to help inform the risk-of-bi</b> article(s) with results of the trial	as assessment? (tick as many as apply)

Trial protocol
Statistical analysis plan (SAP)
Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Company-owned trial registry record (e.g. GSK Clinical Study Register record)
"Grey literature" (e.g. unpublished thesis)
Conference abstract(s) about the trial
Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
Research ethics application
Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
Personal communication with trialist
Personal communication with the sponsor

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising	from the randomization process
--------------------------------	--------------------------------

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to		<u>Y</u>
interventions?		
1.3 Did baseline differences between intervention groups suggest a problem with the randomization		<u>N</u>
process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y
2.2. Were carers and people delivering the interventions aware of participants' assigned		Y
intervention during the trial?		

2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose	Y
because of the trial context?	
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	<u>PY</u>
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between	<u>Y</u>
groups?	
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	<u>Y</u>
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the	PY
failure to analyse participants in the group to which they were randomized?	
Risk-of-bias judgement	Some concerns
Optional: What is the predicted direction of bias due to deviations from intended	Unpredictable
interventions?	

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of adhering to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during		N/A
the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across	N/A	N/A
intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the	N/A	N/A
outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected	N/A	Υ
participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of	N/A	N/A
adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from intended interventions?	N/A	N/A

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?		<u>Y</u>

3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	N/A	N/A
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome data?		NA

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study		<u>PN</u>
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of		N/A
intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of		N/A
intervention received?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan		PY
that was finalized before unblinded outcome data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions, time points) within the		<u>N</u>
outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall predicted	NA
direction of bias for this outcome?	

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Study details				
Refere	ence	Serruys PW, Ong ATL, van Her Stenting Versus Bypass Surger	werden LA, Sousa JE, Jatene y for the Treatment of Mult	e A, Bonnier JJRM, et al. Five-Year Ou ivessel Disease. J Am Coll Cardiol. 20
Study d X	<b>lesign</b> Individua Cluster-r Individua	ally-randomized parallel-group randomized parallel-group trial ally randomized cross-over (or o	trial other matched) trial	
<b>For the</b> Experi	<b>purposes</b> mental:	s of this assessment, the interve PCI	entions being compared are Comparator: CABG	defined as
Specif	y which o	outcome is being assessed for ri	sk of bias	Non-cardiac mortality
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.Manuscript results				Manuscript results
Is the r ✓	eview tea to assess to assess	m's aim for this result…? s the effect of assignment to int s the effect of adhering to inter	<i>tervention</i> (the 'intention-to vention (the 'per-protocol' e	-treat' effect) effect)
If the a that sho	<b>im is to as</b> ould be a occurren failures ir non-adhe	ssess the effect of adhering to in ddressed (at least one must be ice of non-protocol intervention n implementing the interventio erence to their assigned interve	<i>ntervention</i> , select the devia checked): ns n that could have affected t ention by trial participants	ations from intended intervention he outcome
Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)				
	Journal a Trial prot Statistica Non-com Company "Grey lite Conferen Regulato Research Grant dat Personal Personal	rticle(s) with results of the trial tocol II analysis plan (SAP) Imercial trial registry record (e. y-owned trial registry record (e. erature" (e.g. unpublished thesi nce abstract(s) about the trial ry document (e.g. Clinical Study of ethics application tabase summary (e.g. NIH RePC communication with trialist communication with the spons	g. ClinicalTrials.gov record) g. GSK Clinical Study Registe s) / Report, Drug Approval Pac DRTER or Research Councils	er record) kage) UK Gateway to Research)

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Signalling questions	Comments	Response
		options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled		<u>Y</u>
and assigned to interventions?		
1.3 Did baseline differences between intervention groups suggest a problem		<u>N</u>
with the randomization process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the		Unpredictable
randomization process?		

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during		Y
the trial?		
2.2. Were carers and people delivering the interventions aware of		Y
participants' assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the		Y
intended intervention that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the		<u>PY</u>
outcome?		
2.5. If <u>Y/PY/NI to 2.4</u> : Were these deviations from intended		<u>Y</u>
intervention balanced between groups?		
2.6 Was an appropriate analysis used to estimate the effect of		<u>Y</u>
assignment to intervention?		
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact		PY
(on the result) of the failure to analyse participants in the group to		
which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias due to deviations		Unpredictable
from intended interventions?		
		1

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of adhering to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A

2.2. Were carers and people delivering the interventions aware of participants'		N/A
assigned intervention during the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol	N/A	N/A
interventions balanced across intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that	N/A	N/A
could have affected the outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention	N/A	Y
regimen that could have affected participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis	N/A	N/A
used to estimate the effect of adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from	N/A	N/A
intended interventions?		,,,,

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants		<u>Y</u>
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by	N/A	N/A
missing outcome data?		
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true	N/A	N/A
value?		
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended		N/A
on its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome		NA
data?		

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 <u>If N/PN/NI to 4.1 and 4.2</u> : Were outcome assessors aware of the intervention received by study participants?		<u>PN</u>
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		N/A
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a		<u>PY</u>
pre-specified analysis plan that was finalized before unblinded outcome		
data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the		
basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions,		<u>N</u>
time points) within the outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

# Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall	NA
predicted direction of bias for	
this outcome?	

Study c	letails			
Refere	ence	Boudriot E, Thiele H, Walther T Coronary Intervention With Sir Stem Stenosis. J Am Coll Cardio	Γ, Liebetrau C, Boeckstegers rolimus-Eluting Stents Versu ol. 2011 Feb;57(5):538–45.	s P, Pohl T, et al. Randomized Compa is Coronary Artery Bypass Grafting ii
Study o X	<b>lesign</b> Individua Cluster-r Individua	ally-randomized parallel-group t andomized parallel-group trial ally randomized cross-over (or c	trial other matched) trial	
<b>For the</b> Experi	<b>purposes</b> imental:	s of this assessment, the interve	entions being compared are Comparator: CABG	defined as
Specif	y which o	utcome is being assessed for ris	sk of bias	Non-cardiac mortality
<b>Specif</b> altern = 1.52 parag	<b>y the nun</b> ative anal (95% CI ( raph) that	nerical result being assessed. In yses being presented, specify th 0.83 to 2.77) and/or a reference cuniquely defines the result being	case of multiple ne numeric result (e.g. RR e (e.g. to a table, figure or ng assessed.	Manuscript results
Is the r ✓	eview tea to assess to assess	<b>m's aim for this result?</b> s the effect of <i>assignment to int</i> s the effect of <i>adhering to interv</i>	<i>ervention</i> (the 'intention-to <i>vention</i> (the 'per-protocol' e	-treat' effect) effect)
If the a that sh □ □	<b>im is to as</b> ould be a occurren failures ir non-adhe	ssess the effect of adhering to in ddressed (at least one must be o ce of non-protocol intervention n implementing the interventior erence to their assigned interven	n <b>tervention</b> , select the devia checked): s n that could have affected tl ntion by trial participants	ations from intended intervention he outcome
Which	of the foll	owing sources were <u>obtained</u> to	o help inform the risk-of-bia	as assessment? (tick as many as
	Journal a Trial prot Statistica Non-com Company "Grey lite Conferen Regulato Research Grant dat Personal Personal	rticle(s) with results of the trial cocol I analysis plan (SAP) mercial trial registry record (e.g -owned trial registry record (e.g rature" (e.g. unpublished thesis ce abstract(s) about the trial ry document (e.g. Clinical Study ethics application tabase summary (e.g. NIH RePO communication with trialist communication with the sponse	g. ClinicalTrials.gov record) g. GSK Clinical Study Registe s) Report, Drug Approval Pacl RTER or Research Councils or	er record) kage) UK Gateway to Research)

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Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising from the randomization	n process
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Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		<u>Y</u>
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during		Υ
the trial?		
2.2. Were carers and people delivering the interventions aware of		Y
participants' assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the		Υ
intended intervention that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the		<u>PY</u>
outcome?		
2.5. If Y/PY/NI to 2.4: Were these deviations from intended		<u>Y</u>
intervention balanced between groups?		
2.6 Was an appropriate analysis used to estimate the effect of		<u>Y</u>
assignment to intervention?		
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact		PY
(on the result) of the failure to analyse participants in the group to		
which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias due to deviations		Unpredictable
from intended interventions?		
<ul> <li>participants' assigned intervention during the trial?</li> <li>2.3. <u>If Y/PY/NI to 2.1 or 2.2</u>: Were there deviations from the intended intervention that arose because of the trial context?</li> <li>2.4 <u>If Y/PY to 2.3</u>: Were these deviations likely to have affected the outcome?</li> <li>2.5. <u>If Y/PY/NI to 2.4</u>: Were these deviations from intended intervention balanced between groups?</li> <li>2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?</li> <li>2.7 <u>If N/PN/NI to 2.6</u>: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?</li> <li>Risk-of-bias judgement</li> <li>Optional: What is the predicted direction of bias due to deviations from intended interventions?</li> </ul>		Y <u>PY</u> <u>Y</u> <u>Y</u> PY Some concerns Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A

2.2. Were carers and people delivering the interventions aware of participants'		N/A
assigned intervention during the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol	N/A	N/A
interventions balanced across intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that	N/A	N/A
could have affected the outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention	N/A	Υ
regimen that could have affected participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis	N/A	N/A
used to estimate the effect of adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from	N/A	N/A
intended interventions?		

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants		<u>Y</u>
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by	N/A	N/A
missing outcome data?		
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true	N/A	N/A
value?		
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended		N/A
on its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome		NA
data?		

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 <u>If N/PN/NI to 4.1 and 4.2</u> : Were outcome assessors aware of the intervention received by study participants?		<u>PN</u>
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		N/A
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a		<u>PY</u>
pre-specified analysis plan that was finalized before unblinded outcome		
data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the		
basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions,		<u>N</u>
time points) within the outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

# Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall	NA
predicted direction of bias for	
this outcome?	

Study c	letails			
Refere	ence	Buszman PE, Buszman PP, Bar Comparison With Surgical Rev	asiewicz-Szkróbka I, N ascularization. JACC C	1ilewski KP, Żurakowski A, Orlik B, et al. Le ardiovasc Interv. 2016 Feb;9(4):318–27.
Study c X D	<b>lesign</b> Individua Cluster-r Individua	ally-randomized parallel-group randomized parallel-group trial ally randomized cross-over (or o	trial other matched) trial	
<b>For the</b> Experi	<b>purposes</b> imental:	s of this assessment, the interve PCI	entions being compare Comparator: CABG	ed are defined as
Specif	y which o	outcome is being assessed for ri	sk of bias	Non-cardiac mortality
<b>Specif</b> altern = 1.52 paragi	<b>y the nun</b> ative anal (95% CI ( raph) that	nerical result being assessed. In lyses being presented, specify t 0.83 to 2.77) and/or a reference t uniquely defines the result bei	case of multiple he numeric result (e.g e (e.g. to a table, figure ng assessed.	RR e or
Is the r ✓	eview tea to assess to assess	<b>m's aim for this result?</b> s the effect of <i>assignment to int</i> s the effect of <i>adhering to inter</i>	<i>tervention</i> (the 'intenti vention (the 'per-proto	on-to-treat' effect) ocol' effect)
<b>If the a</b> that sh	<b>im is to a</b> s ould be a	ssess the effect of <i>adhering to i</i> ddressed (at least one must be	<b>ntervention</b> , select the checked):	deviations from intended intervention
	occurren failures ir non-adhe	ce of non-protocol interventior n implementing the interventio erence to their assigned interve	ns n that could have affeo ntion by trial participa	cted the outcome nts
Which	of the foll	lowing sources were <u>obtained</u> t	o help inform the risk-	of-bias assessment? (tick as many as
✓ □ □ □ □ □ □ □ □	Journal a Trial prot Statistica Non-com Company "Grey lite Conferen Regulato Research Grant da Personal Personal	rticle(s) with results of the trial cocol I analysis plan (SAP) mercial trial registry record (e. rowned trial registry record (e. erature" (e.g. unpublished thesi ace abstract(s) about the trial ry document (e.g. Clinical Study ethics application tabase summary (e.g. NIH RePC communication with trialist communication with the spons	g. ClinicalTrials.gov rec g. GSK Clinical Study R s) v Report, Drug Approva DRTER or Research Cou or	ord) egister record) al Package) incils UK Gateway to Research)

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Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising from the randomization	n process
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Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		<u>Y</u>
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during		Υ
the trial?		
2.2. Were carers and people delivering the interventions aware of		Y
participants' assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the		Υ
intended intervention that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the		<u>PY</u>
outcome?		
2.5. If Y/PY/NI to 2.4: Were these deviations from intended		<u>Y</u>
intervention balanced between groups?		
2.6 Was an appropriate analysis used to estimate the effect of		<u>Y</u>
assignment to intervention?		
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact		PY
(on the result) of the failure to analyse participants in the group to		
which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias due to deviations		Unpredictable
from intended interventions?		
<ul> <li>participants' assigned intervention during the trial?</li> <li>2.3. <u>If Y/PY/NI to 2.1 or 2.2</u>: Were there deviations from the intended intervention that arose because of the trial context?</li> <li>2.4 <u>If Y/PY to 2.3</u>: Were these deviations likely to have affected the outcome?</li> <li>2.5. <u>If Y/PY/NI to 2.4</u>: Were these deviations from intended intervention balanced between groups?</li> <li>2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?</li> <li>2.7 <u>If N/PN/NI to 2.6</u>: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?</li> <li>Risk-of-bias judgement</li> <li>Optional: What is the predicted direction of bias due to deviations from intended interventions?</li> </ul>		Y <u>PY</u> <u>Y</u> <u>Y</u> PY Some concerns Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A

2.2. Were carers and people delivering the interventions aware of participants'		N/A
assigned intervention during the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol	N/A	N/A
interventions balanced across intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that	N/A	N/A
could have affected the outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention	N/A	Υ
regimen that could have affected participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis		N/A
used to estimate the effect of adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from	N/A	N/A
intended interventions?		

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants		<u>Y</u>
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by	N/A	N/A
missing outcome data?		
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true	N/A	N/A
value?		
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended		N/A
on its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome		NA
data?		

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 <u>If N/PN/NI to 4.1 and 4.2</u> : Were outcome assessors aware of the intervention received by study participants?		<u>PN</u>
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		N/A
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a		<u>PY</u>
pre-specified analysis plan that was finalized before unblinded outcome		
data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the		
basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions,		<u>N</u>
time points) within the outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

# Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall	NA
predicted direction of bias for	
this outcome?	

Study c	Study details					
Refere	ence	Kapur A, Hall RJ, Malik IS, Qureshi AC, Butts J Intervention With Coronary Artery Bypass Gr	de Belder M, et afting in Diabetic	al. Randomized Comparison of F Patients. J Am Coll Cardiol. 2010		
Study o X	<b>lesign</b> Individua Cluster-r Individua	ally-randomized parallel-group trial andomized parallel-group trial ally randomized cross-over (or other matched)	trial			
<b>For the</b> Experi	<b>purposes</b> imental:	PCI Comparator:	ompared are defi CABG	ined as		
Specif	y which o	utcome is being assessed for risk of bias	No	n-cardiac mortality		
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.Manuscript results						
Is the r ✓	eview tea to assess to assess	<b>m's aim for this result?</b> The effect of <i>assignment to intervention</i> (the sthe effect of <i>adhering to intervention</i> (the 'pe	'intention-to-trea r-protocol' effec	ať effect) t)		
If the a that sh	<b>im is to a</b> s ould be a	<b>ssess the effect of <i>adhering to intervention</i></b> , se ddressed (at least one must be checked):	ect the deviatior	ns from intended intervention		
	occurren failures ir non-adhe	ce of non-protocol interventions n implementing the intervention that could ha erence to their assigned intervention by trial p	ve affected the o articipants	utcome		
Which	of the foll	owing sources were <u>obtained</u> to help inform t	he risk-of-bias as	sessment? (tick as many as		
<pre>&gt;&gt;</pre>	Journal a Trial prot Statistica Non-com Company "Grey lite Conferen Regulato Research Grant dar Personal	rticle(s) with results of the trial ocol I analysis plan (SAP) mercial trial registry record (e.g. ClinicalTrials. r-owned trial registry record (e.g. GSK Clinical S erature" (e.g. unpublished thesis) ce abstract(s) about the trial ry document (e.g. Clinical Study Report, Drug ethics application cabase summary (e.g. NIH RePORTER or Resea communication with trialist communication with the sponsor	gov record) Study Register rec Approval Package Tch Councils UK C	cord) e) Gateway to Research)		

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising from the randomization	n process
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Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		<u>Y</u>
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during		Υ
the trial?		
2.2. Were carers and people delivering the interventions aware of		Y
participants' assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the		Υ
intended intervention that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the		<u>PY</u>
outcome?		
2.5. If Y/PY/NI to 2.4: Were these deviations from intended		<u>Y</u>
intervention balanced between groups?		
2.6 Was an appropriate analysis used to estimate the effect of		<u>Y</u>
assignment to intervention?		
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact		PY
(on the result) of the failure to analyse participants in the group to		
which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias due to deviations		Unpredictable
from intended interventions?		
<ul> <li>participants' assigned intervention during the trial?</li> <li>2.3. <u>If Y/PY/NI to 2.1 or 2.2</u>: Were there deviations from the intended intervention that arose because of the trial context?</li> <li>2.4 <u>If Y/PY to 2.3</u>: Were these deviations likely to have affected the outcome?</li> <li>2.5. <u>If Y/PY/NI to 2.4</u>: Were these deviations from intended intervention balanced between groups?</li> <li>2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?</li> <li>2.7 <u>If N/PN/NI to 2.6</u>: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?</li> <li>Risk-of-bias judgement</li> <li>Optional: What is the predicted direction of bias due to deviations from intended interventions?</li> </ul>		Y <u>PY</u> <u>Y</u> <u>Y</u> PY Some concerns Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A

2.2. Were carers and people delivering the interventions aware of participants'		N/A
assigned intervention during the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol	N/A	N/A
interventions balanced across intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that	N/A	N/A
could have affected the outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention	N/A	Υ
regimen that could have affected participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis	N/A	N/A
used to estimate the effect of adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from	N/A	N/A
intended interventions?		

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants		<u>Y</u>
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by	N/A	N/A
missing outcome data?		
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true	N/A	N/A
value?		
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended		N/A
on its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome		NA
data?		
Signalling questions	Comments	Response options
--	----------	---------------------
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 <u>If N/PN/NI to 4.1 and 4.2</u> : Were outcome assessors aware of the intervention received by study participants?		<u>PN</u>
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		N/A
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a		<u>PY</u>
pre-specified analysis plan that was finalized before unblinded outcome		
data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the		
basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions,		<u>N</u>
time points) within the outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Risk-of-bias judgement	Low
Optional: What is the overall	NA
predicted direction of bias for	
this outcome?	

Study d	letails			
Refere	ence	Blazek S, Holzhey D, Jungert C, I Invasive Bypass Surgery for Ster Jan;6(1):20–6.	Borger MA, Fuernau G, Des nosis of the Left Anterior D	sch S, et al. Comparison of Bare-Met escending Coronary Artery. JACC Ca
Study d X	l <b>esign</b> Individua Cluster-r Individua	ally-randomized parallel-group tr andomized parallel-group trial ally randomized cross-over (or ot	ial ther matched) trial	
<b>For the</b> Experi	<b>purposes</b> mental:	s of this assessment, the interver	ntions being compared are Comparator: CABG	defined as
Specif	y which o	utcome is being assessed for risk	< of bias	Non-cardiac mortality
<b>Specif</b> altern = 1.52 paragi	<b>y the nun</b> ative anal (95% CI ( raph) that	nerical result being assessed. In or yses being presented, specify the 0.83 to 2.77) and/or a reference cuniquely defines the result bein	case of multiple e numeric result (e.g. RR (e.g. to a table, figure or ng assessed.	Manuscript results
<ul> <li>Is the review team's aim for this result?</li> <li>✓ to assess the effect of assignment to intervention (the 'intention-to-treat' effect)</li> <li>□ to assess the effect of adhering to intervention (the 'per-protocol' effect)</li> </ul>				
If the a that sho D D	<b>im is to as</b> ould be a occurren failures ir non-adhe	asess the effect of adhering to interded defined to a set of definition of the set of th	<i>tervention,</i> select the devia hecked): that could have affected th tion by trial participants	ations from intended intervention he outcome
Which	of the foll	owing sources were <u>obtained</u> to	help inform the risk-of-bia	as assessment? (tick as many as
	Journal a Trial prot Statistica Non-com Company "Grey lite Conferen Regulato Research Grant dat Personal Personal	rticle(s) with results of the trial ocol I analysis plan (SAP) mercial trial registry record (e.g. -owned trial registry record (e.g erature" (e.g. unpublished thesis) ce abstract(s) about the trial ry document (e.g. Clinical Study F ethics application tabase summary (e.g. NIH RePOF communication with trialist communication with the sponso	ClinicalTrials.gov record) . GSK Clinical Study Registe ) Report, Drug Approval Pacl RTER or Research Councils r	er record) kage) UK Gateway to Research)

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Domain I. RISK OF DIAS AFISING FOULT LIFE FAILUOHIZATION PLOCES:	Domain 1	1: Risk	of bias	arising	from	the	randomization	process
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Signalling questions	Comments	Response
		options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled		<u>Y</u>
and assigned to interventions?		
1.3 Did baseline differences between intervention groups suggest a problem		<u>N</u>
with the randomization process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the		Unpredictable
randomization process?		

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during		Y
the trial?		
2.2. Were carers and people delivering the interventions aware of		Y
participants' assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the		Y
intended intervention that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the		<u>PY</u>
outcome?		
2.5. If Y/PY/NI to 2.4: Were these deviations from intended		<u>Y</u>
intervention balanced between groups?		
2.6 Was an appropriate analysis used to estimate the effect of		<u>Y</u>
assignment to intervention?		
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact		PY
(on the result) of the failure to analyse participants in the group to		
which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias due to deviations		Unpredictable
from intended interventions?		

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of adhering to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A

2.2. Were carers and people delivering the interventions aware of participants'		N/A
assigned intervention during the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol	N/A	N/A
interventions balanced across intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that	N/A	N/A
could have affected the outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention	N/A	Υ
regimen that could have affected participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis	N/A	N/A
used to estimate the effect of adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from	N/A	N/A
intended interventions?		, / (

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants		<u>Y</u>
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by	N/A	N/A
missing outcome data?		
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true	N/A	N/A
value?		
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended		N/A
on its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome		NA
data?		

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 <u>If N/PN/NI to 4.1 and 4.2</u> : Were outcome assessors aware of the intervention received by study participants?		<u>PN</u>
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		N/A
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a		<u>PY</u>
pre-specified analysis plan that was finalized before unblinded outcome		
data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the		
basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions,		<u>N</u>
time points) within the outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Risk-of-bias judgement	Low
Optional: What is the overall	NA
predicted direction of bias for	
this outcome?	

Study o	letails					
Refere	ence	Drenth DJ, Veeger NJGM, Middel B, Zijlstra F, Boonstra PW. Comparison of late (four years) fu between percutaneous transluminal angioplasty intervention and off-pump left internal mam for isolated high-grade narrowing of the proximal left anterior descending coronary artery. Ar Dec;94(11):1414–7.				
Study of X	<b>lesign</b> Individua Cluster-r Individua	ally-randomized parallel-group randomized parallel-group trial ally randomized cross-over (or o	trial other matched) trial			
<b>For the</b> Exper	<b>purposes</b> imental:	s of this assessment, the interventer of the interventer of the second sec	entions being compared are Comparator: CABG	defined as		
Specif	y which o	outcome is being assessed for ri	sk of bias	Non-cardiac mortality		
<b>Specif</b> altern = 1.52 parag	<b>y the nun</b> ative anal (95% CI ( raph) that	nerical result being assessed. In lyses being presented, specify t D.83 to 2.77) and/or a reference t uniquely defines the result be	case of multiple he numeric result (e.g. RR e (e.g. to a table, figure or ing assessed.	Manuscript results		
Is the r ✓	eview tea to assess to assess	m's aim for this result…? s the effect of <i>assignment to in</i> s the effect of <i>adhering to inter</i>	<i>tervention</i> (the 'intention-to vention (the 'per-protocol' e	effect)		
<b>If the a</b> that sh □ □	<b>im is to as</b> ould be ac occurren failures ir non-adhe	ssess the effect of adhering to i ddressed (at least one must be ce of non-protocol intervention n implementing the interventio erence to their assigned interve	ntervention, select the devia checked): ns n that could have affected t ention by trial participants	ations from intended intervention he outcome		
Which	of the foll	lowing sources were <u>obtained</u> t	o help inform the risk-of-bia	as assessment? (tick as many as		
<pre>&gt;&gt;priy/ </pre>	Journal a Trial prot Statistica Non-com Company "Grey lite Conferen Regulato Research Grant dat Personal Personal	rticle(s) with results of the trial cocol I analysis plan (SAP) mercial trial registry record (e., -owned trial registry record (e. erature" (e.g. unpublished thesi ace abstract(s) about the trial ry document (e.g. Clinical Study ethics application tabase summary (e.g. NIH RePC communication with trialist communication with the spons	g. ClinicalTrials.gov record) g. GSK Clinical Study Registe s) v Report, Drug Approval Pac DRTER or Research Councils	er record) kage) UK Gateway to Research)		

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Domain 1: Risk of bias arising from the randomization	n process
---	-----------

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		<u>Y</u>
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during		Υ
the trial?		
2.2. Were carers and people delivering the interventions aware of		Y
participants' assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the		Υ
intended intervention that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the		<u>PY</u>
outcome?		
2.5. If Y/PY/NI to 2.4: Were these deviations from intended		<u>Y</u>
intervention balanced between groups?		
2.6 Was an appropriate analysis used to estimate the effect of		<u>Y</u>
assignment to intervention?		
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact		PY
(on the result) of the failure to analyse participants in the group to		
which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias due to deviations		Unpredictable
from intended interventions?		
<ul> <li>participants' assigned intervention during the trial?</li> <li>2.3. <u>If Y/PY/NI to 2.1 or 2.2</u>: Were there deviations from the intended intervention that arose because of the trial context?</li> <li>2.4 <u>If Y/PY to 2.3</u>: Were these deviations likely to have affected the outcome?</li> <li>2.5. <u>If Y/PY/NI to 2.4</u>: Were these deviations from intended intervention balanced between groups?</li> <li>2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?</li> <li>2.7 <u>If N/PN/NI to 2.6</u>: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?</li> <li>Risk-of-bias judgement</li> <li>Optional: What is the predicted direction of bias due to deviations from intended interventions?</li> </ul>		Y <u>PY</u> <u>Y</u> <u>Y</u> PY Some concerns Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A

2.2. Were carers and people delivering the interventions aware of participants'		N/A
assigned intervention during the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol	N/A	N/A
interventions balanced across intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that	N/A	N/A
could have affected the outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention	N/A	Υ
regimen that could have affected participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis	N/A	N/A
used to estimate the effect of adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from	N/A	N/A
intended interventions?		

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants		<u>Y</u>
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by	N/A	N/A
missing outcome data?		
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true	N/A	N/A
value?		
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended		N/A
on its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome		NA
data?		

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 <u>If N/PN/NI to 4.1 and 4.2</u> : Were outcome assessors aware of the intervention received by study participants?		<u>PN</u>
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		N/A
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a		<u>PY</u>
pre-specified analysis plan that was finalized before unblinded outcome		
data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the		
basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions,		<u>N</u>
time points) within the outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Risk-of-bias judgement	Low
Optional: What is the overall	NA
predicted direction of bias for	
this outcome?	

Study details						
Refere	ence	Hong SJ, Lim D-S, Seo HS, Kim Y-H, Shim WJ, Park CG, et al. Percutaneous coronary interventic implantation vs. minimally invasive direct coronary artery bypass (MIDCAB) in patients with le coronary artery stenosis. Catheter Cardiovasc Interv. 2005 Jan;64(1):75–81.				
Study o X	<b>lesign</b> Individua Cluster-r Individua	ally-randomized parallel-group randomized parallel-group trial ally randomized cross-over (or c	trial other matched) trial			
<b>For the</b> Exper	<b>purposes</b> imental: [	<b>s of this assessment, the interve</b> PCI	entions being compared are Comparator: CABG	defined as		
Specif	y which o	utcome is being assessed for ris	sk of bias	Non-cardiac mortality		
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.Manuscript results						
Is the r ✓	eview tea to assess to assess	<b>m's aim for this result…?</b> s the effect of <i>assignment to int</i> s the effect of <i>adhering to inter</i>	<i>tervention</i> (the 'intention-to vention (the 'per-protocol' e	-treat' effect) effect)		
<ul> <li>If the aim is to assess the effect of adhering to intervention, select the deviations from intended intervention that should be addressed (at least one must be checked):         <ul> <li>occurrence of non-protocol interventions</li> <li>failures in implementing the intervention that could have affected the outcome</li> <li>non-adherence to their assigned intervention by trial participants</li> </ul> </li> </ul>						
Which	of the foll	owing sources were <u>obtained</u> t	o help inform the risk-of-bia	as assessment? (tick as many as		
<ul> <li>Journal article(s) with results of the trial</li> <li>Trial protocol</li> <li>Statistical analysis plan (SAP)</li> <li>Non-commercial trial registry record (e.g. ClinicalTrials.gov record)</li> <li>Company-owned trial registry record (e.g. GSK Clinical Study Register record)</li> <li>"Grey literature" (e.g. unpublished thesis)</li> <li>Conference abstract(s) about the trial</li> <li>Regulatory document (e.g. Clinical Study Report, Drug Approval Package)</li> <li>Research ethics application</li> <li>Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)</li> <li>Personal communication with the sponsor</li> </ul>						

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Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising from the randomization	n process
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Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		<u>Y</u>
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during		Υ
the trial?		
2.2. Were carers and people delivering the interventions aware of		Y
participants' assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the		Υ
intended intervention that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the		<u>PY</u>
outcome?		
2.5. If Y/PY/NI to 2.4: Were these deviations from intended		<u>Y</u>
intervention balanced between groups?		
2.6 Was an appropriate analysis used to estimate the effect of		<u>Y</u>
assignment to intervention?		
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact		PY
(on the result) of the failure to analyse participants in the group to		
which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias due to deviations		Unpredictable
from intended interventions?		
<ul> <li>participants' assigned intervention during the trial?</li> <li>2.3. <u>If Y/PY/NI to 2.1 or 2.2</u>: Were there deviations from the intended intervention that arose because of the trial context?</li> <li>2.4 <u>If Y/PY to 2.3</u>: Were these deviations likely to have affected the outcome?</li> <li>2.5. <u>If Y/PY/NI to 2.4</u>: Were these deviations from intended intervention balanced between groups?</li> <li>2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?</li> <li>2.7 <u>If N/PN/NI to 2.6</u>: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?</li> <li>Risk-of-bias judgement</li> <li>Optional: What is the predicted direction of bias due to deviations from intended interventions?</li> </ul>		Y <u>PY</u> <u>Y</u> <u>Y</u> PY Some concerns Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A

2.2. Were carers and people delivering the interventions aware of participants'		N/A
assigned intervention during the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol	N/A	N/A
interventions balanced across intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that	N/A	N/A
could have affected the outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention	N/A	Υ
regimen that could have affected participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis	N/A	N/A
used to estimate the effect of adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from	N/A	N/A
intended interventions?		

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants		<u>Y</u>
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by	N/A	N/A
missing outcome data?		
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true	N/A	N/A
value?		
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended		N/A
on its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome		NA
data?		

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 <u>If N/PN/NI to 4.1 and 4.2</u> : Were outcome assessors aware of the intervention received by study participants?		<u>PN</u>
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		N/A
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a		<u>PY</u>
pre-specified analysis plan that was finalized before unblinded outcome		
data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the		
basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions,		<u>N</u>
time points) within the outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Risk-of-bias judgement	Low
Optional: What is the overall	NA
predicted direction of bias for	
this outcome?	

Study details			
Reference	Kim JW, Lim DS, Sun K, Shim WJ, Rho YM. Stenting or MIDCAB using ministernotomy for revas anterior descending artery? Int J Cardiol. 2005 Mar;99(3):437–41.		
Study design X Indiv Clus <sup>a</sup> Indiv	idually-randomized parallel-group trial er-randomized parallel-group trial idually randomized cross-over (or other matched) trial		
For the purp Experiment	oses of this assessment, the interventions being compared are defined as al: PCI Comparator: CABG		
Specify whi	ch outcome is being assessed for risk of bias Non-cardiac mortality		
<b>Specify the</b> alternative = 1.52 (95% paragraph)	numerical result being assessed. In case of multiple analyses being presented, specify the numeric result (e.g. RR CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or that uniquely defines the result being assessed.Manuscript results		
<ul> <li>Is the review team's aim for this result?</li> <li>✓ to assess the effect of assignment to intervention (the 'intention-to-treat' effect)</li> <li>□ to assess the effect of adhering to intervention (the 'per-protocol' effect)</li> </ul>			
that should b	to assess the effect of <i>adhering to intervention</i> , select the deviations from intended intervention be addressed (at least one must be checked):		
□ occui □ failur □ non-a	rence of non-protocol interventions es in implementing the intervention that could have affected the outcome adherence to their assigned intervention by trial participants		
Which of the	following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as		
<ul> <li>✓ Jourr</li> <li>□ Trial</li> <li>□ Statis</li> <li>□ Non-</li> <li>□ Comp</li> <li>□ Confe</li> <li>□ Confe</li> <li>□ Regu</li> <li>□ Resea</li> <li>□ Gran</li> <li>□ Perso</li> <li>□ Perso</li> </ul>	al article(s) with results of the trial protocol tical analysis plan (SAP) commercial trial registry record (e.g. ClinicalTrials.gov record) pany-owned trial registry record (e.g. GSK Clinical Study Register record) v literature" (e.g. unpublished thesis) erence abstract(s) about the trial latory document (e.g. Clinical Study Report, Drug Approval Package) arch ethics application t database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research) onal communication with trialist		

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising from the randomization	n process
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Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		<u>Y</u>
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during		Υ
the trial?		
2.2. Were carers and people delivering the interventions aware of		Y
participants' assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the		Υ
intended intervention that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the		<u>PY</u>
outcome?		
2.5. If Y/PY/NI to 2.4: Were these deviations from intended		<u>Y</u>
intervention balanced between groups?		
2.6 Was an appropriate analysis used to estimate the effect of		<u>Y</u>
assignment to intervention?		
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact		PY
(on the result) of the failure to analyse participants in the group to		
which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias due to deviations		Unpredictable
from intended interventions?		
<ul> <li>participants' assigned intervention during the trial?</li> <li>2.3. <u>If Y/PY/NI to 2.1 or 2.2</u>: Were there deviations from the intended intervention that arose because of the trial context?</li> <li>2.4 <u>If Y/PY to 2.3</u>: Were these deviations likely to have affected the outcome?</li> <li>2.5. <u>If Y/PY/NI to 2.4</u>: Were these deviations from intended intervention balanced between groups?</li> <li>2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?</li> <li>2.7 <u>If N/PN/NI to 2.6</u>: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?</li> <li>Risk-of-bias judgement</li> <li>Optional: What is the predicted direction of bias due to deviations from intended interventions?</li> </ul>		Y <u>PY</u> <u>Y</u> <u>Y</u> PY Some concerns Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A

2.2. Were carers and people delivering the interventions aware of participants'		N/A
assigned intervention during the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol	N/A	N/A
interventions balanced across intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that	N/A	N/A
could have affected the outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention	N/A	Υ
regimen that could have affected participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis	N/A	N/A
used to estimate the effect of adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from	N/A	N/A
intended interventions?		

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants		<u>Y</u>
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by	N/A	N/A
missing outcome data?		
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true	N/A	N/A
value?		
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended		N/A
on its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome		NA
data?		

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 <u>If N/PN/NI to 4.1 and 4.2</u> : Were outcome assessors aware of the intervention received by study participants?		<u>PN</u>
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		N/A
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a		<u>PY</u>
pre-specified analysis plan that was finalized before unblinded outcome		
data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the		
basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions,		<u>N</u>
time points) within the outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Risk-of-bias judgement	Low
Optional: What is the overall	NA
predicted direction of bias for	
this outcome?	

Study de	etails			
Referer	nce	Ahn J-M, Roh J-H, Kim Y-H, Par Main Coronary Artery Disease 206.	rk D-W, Yun S-C, Lee PH, et a : 5-Year Outcomes of the PF	al. Randomized Trial of Stents Versus RECOMBAT Study. J Am Coll Cardiol.
Study de X	<b>esign</b> Individua Cluster-r Individua	ally-randomized parallel-group randomized parallel-group trial ally randomized cross-over (or c	trial other matched) trial	
<b>For the p</b> Experin	purposes nental: [	<b>s of this assessment, the interve</b> PCI	entions being compared are Comparator: CABG	defined as
Specify	which o	utcome is being assessed for ris	sk of bias	Non-cardiac mortality
<b>Specify</b> alterna = 1.52 ( paragra	tive anal tive anal (95% CI ( aph) that	nerical result being assessed. In lyses being presented, specify th 0.83 to 2.77) and/or a reference c uniquely defines the result bei	case of multiple he numeric result (e.g. RR e (e.g. to a table, figure or ing assessed.	Manuscript results
ls the re √	<b>view tea</b> to assess to assess	<b>m's aim for this result?</b> s the effect of <i>assignment to int</i> s the effect of <i>adhering to inter</i>	<i>tervention</i> (the 'intention-to vention (the 'per-protocol' e	effect)
If the air that sho c f f r	m is to as uld be ad occurren ailures ir non-adhe	ssess the effect of adhering to in ddressed (at least one must be ce of non-protocol intervention n implementing the intervention erence to their assigned interve	<i>ntervention</i> , select the devia checked): ns n that could have affected t ntion by trial participants	ations from intended intervention he outcome
Which o apply)	f the foll	owing sources were <u>obtained</u> t	o help inform the risk-of-bia	as assessment? (tick as many as
<ul> <li>J</li> <li>T</li> <li>S</li> <li>M</li> <li>C</li> <li>M</li> <li>C</li> <li>M</li> <li>C</li> <li>M</li> <li>C</li> <li>M</li> <li>C</li> <li>M</li> <li>M&lt;</li></ul>	ournal a Frial prot Statistica Non-com Company (Grey lite Conferen Regulato Research Grant dat Personal Personal	rucie(s) with results of the trial socol I analysis plan (SAP) mercial trial registry record (e.g rowned trial registry record (e.g rature" (e.g. unpublished thesis ace abstract(s) about the trial ry document (e.g. Clinical Study ethics application tabase summary (e.g. NIH RePC communication with trialist communication with the spons	g. ClinicalTrials.gov record) g. GSK Clinical Study Registe s) v Report, Drug Approval Pac DRTER or Research Councils or	er record) kage) UK Gateway to Research)

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Domain I. RISK OF DIAS AFISING FOULT LIFE FAILUOHIZATION PLOCES:	Domain 1	1: Risk	of bias	arising	from	the	randomization	process
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Signalling questions	Comments	Response
		options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled		<u>Y</u>
and assigned to interventions?		
1.3 Did baseline differences between intervention groups suggest a problem		<u>N</u>
with the randomization process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the		Unpredictable
randomization process?		

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during		Y
the trial?		
2.2. Were carers and people delivering the interventions aware of		Y
participants' assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the		Y
intended intervention that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the		<u>PY</u>
outcome?		
2.5. If Y/PY/NI to 2.4: Were these deviations from intended		<u>Y</u>
intervention balanced between groups?		
2.6 Was an appropriate analysis used to estimate the effect of		<u>Y</u>
assignment to intervention?		
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact		PY
(on the result) of the failure to analyse participants in the group to		
which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias due to deviations		Unpredictable
from intended interventions?		

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of adhering to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A

2.2. Were carers and people delivering the interventions aware of participants'		N/A
assigned intervention during the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol	N/A	N/A
interventions balanced across intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that	N/A	N/A
could have affected the outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention	N/A	Υ
regimen that could have affected participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis	N/A	N/A
used to estimate the effect of adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from	N/A	N/A
intended interventions?		, / (

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants		<u>Y</u>
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by	N/A	N/A
missing outcome data?		
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true	N/A	N/A
value?		
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended		N/A
on its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome		NA
data?		

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 <u>If N/PN/NI to 4.1 and 4.2</u> : Were outcome assessors aware of the intervention received by study participants?		<u>PN</u>
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		N/A
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a		<u>PY</u>
pre-specified analysis plan that was finalized before unblinded outcome		
data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the		
basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions,		<u>N</u>
time points) within the outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Risk-of-bias judgement	Low
Optional: What is the overall	NA
predicted direction of bias for	
this outcome?	

Study d	etails			
Refere	nce	Pohl T, Giehrl W, Reichart B, Ku percutaneous intervention and Cardiovasc Interv. 2004 Jul;62(3	ipatt C, Raake P, Paul S, et a bypass surgery: Results of 3):323–30.	al. Retroinfusion-supported stenting the prospective randomized myopr
Study d X □	<b>esign</b> Individua Cluster-r Individua	ally-randomized parallel-group tr andomized parallel-group trial ally randomized cross-over (or ot	rial ther matched) trial	
<b>For the</b> Experi	<b>purposes</b> mental:	s of this assessment, the interver	ntions being compared are Comparator: CABG	defined as
Specify	y which o	utcome is being assessed for risl	k of bias	Non-cardiac mortality
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.Manuscript results				Manuscript results
ls the re ✓	eview tea to assess to assess	<b>m's aim for this result?</b> The effect of <i>assignment to inte</i> The effect of <i>adhering to interve</i>	ervention (the 'intention-to ention (the 'per-protocol' e	-treat' effect) effect)
If the ai that sho D D	<b>m is to as</b> ould be ac occurren failures ir non-adhe	ssess the effect of adhering to in ddressed (at least one must be c ce of non-protocol interventions n implementing the intervention erence to their assigned interven	t <b>ervention</b> , select the devia hecked): that could have affected the ntion by trial participants	ations from intended intervention he outcome
Which o	of the foll	owing sources were <u>obtained</u> to	help inform the risk-of-bia	as assessment? (tick as many as
	Journal a Trial prot Statistica Non-com Company "Grey lite Conferen Regulato Research Grant da Personal Personal	rticle(s) with results of the trial ocol I analysis plan (SAP) mercial trial registry record (e.g. -owned trial registry record (e.g erature" (e.g. unpublished thesis ce abstract(s) about the trial ry document (e.g. Clinical Study ethics application tabase summary (e.g. NIH RePOF communication with trialist communication with the sponso	. ClinicalTrials.gov record) g. GSK Clinical Study Registe ) Report, Drug Approval Pacl RTER or Research Councils or	er record) kage) UK Gateway to Research)

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Domain 1: Risk of bias arising from the randomization	n process
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Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		<u>Y</u>
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during		Υ
the trial?		
2.2. Were carers and people delivering the interventions aware of		Y
participants' assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the		Υ
intended intervention that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the		<u>PY</u>
outcome?		
2.5. If Y/PY/NI to 2.4: Were these deviations from intended		<u>Y</u>
intervention balanced between groups?		
2.6 Was an appropriate analysis used to estimate the effect of		<u>Y</u>
assignment to intervention?		
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact		PY
(on the result) of the failure to analyse participants in the group to		
which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias due to deviations		Unpredictable
from intended interventions?		
<ul> <li>participants' assigned intervention during the trial?</li> <li>2.3. <u>If Y/PY/NI to 2.1 or 2.2</u>: Were there deviations from the intended intervention that arose because of the trial context?</li> <li>2.4 <u>If Y/PY to 2.3</u>: Were these deviations likely to have affected the outcome?</li> <li>2.5. <u>If Y/PY/NI to 2.4</u>: Were these deviations from intended intervention balanced between groups?</li> <li>2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?</li> <li>2.7 <u>If N/PN/NI to 2.6</u>: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?</li> <li>Risk-of-bias judgement</li> <li>Optional: What is the predicted direction of bias due to deviations from intended interventions?</li> </ul>		Y <u>PY</u> <u>Y</u> <u>Y</u> PY Some concerns Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A

2.2. Were carers and people delivering the interventions aware of participants'		N/A
assigned intervention during the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol	N/A	N/A
interventions balanced across intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that	N/A	N/A
could have affected the outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention	N/A	Υ
regimen that could have affected participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis	N/A	N/A
used to estimate the effect of adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from	N/A	N/A
intended interventions?		

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants		<u>Y</u>
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by	N/A	N/A
missing outcome data?		
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true	N/A	N/A
value?		
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended		N/A
on its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome		NA
data?		

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 <u>If N/PN/NI to 4.1 and 4.2</u> : Were outcome assessors aware of the intervention received by study participants?		<u>PN</u>
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		N/A
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a		<u>PY</u>
pre-specified analysis plan that was finalized before unblinded outcome		
data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the		
basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions,		<u>N</u>
time points) within the outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Risk-of-bias judgement	Low
Optional: What is the overall	NA
predicted direction of bias for	
this outcome?	

Study o	letails			
Refere	ence	Thiele H, Neumann-Schniedev Minimally Invasive Direct Corc Anterior Descending Coronary	vind P, Jacobs S, Boud onary Artery Bypass Su Artery Stenosis. J Am	riot E, Walther T, Mohr F-W, et al. Randor rgery Versus Sirolimus-Eluting Stenting in Coll Cardiol. 2009 Jun;53(25):2324–31.
Study o X	<b>lesign</b> Individua Cluster-r Individua	ally-randomized parallel-group randomized parallel-group trial ally randomized cross-over (or o	trial other matched) trial	
For the Exper	<b>purpose</b> imental:	s of this assessment, the interve PCI	entions being compare Comparator: CABG	ed are defined as
Specif	y which o	outcome is being assessed for ri	sk of bias	Non-cardiac mortality
<b>Specif</b> altern = 1.52 parag	<b>y the nun</b> ative anal (95% CI ( raph) that	nerical result being assessed. In lyses being presented, specify t 0.83 to 2.77) and/or a reference t uniquely defines the result bei	case of multiple he numeric result (e.g e (e.g. to a table, figur ng assessed.	Manuscript results RR e or
Is the r ✓	eview tea to assess to assess	m's aim for this result…? s the effect of <i>assignment to int</i> s the effect of <i>adhering to inter</i>	<i>tervention</i> (the 'intent vention (the 'per-prote	on-to-treat' effect) ocol' effect)
If the a that sh □ □	<b>im is to a</b> s ould be a occurren failures ir non-adhe	ssess the effect of adhering to in ddressed (at least one must be ce of non-protocol intervention n implementing the interventio erence to their assigned interve	ntervention, select the checked): is n that could have affe ntion by trial participa	e deviations from intended intervention cted the outcome ints
Which	of the foll	lowing sources were <u>obtained</u> t	o help inform the risk	of-bias assessment? (tick as many as
<ul> <li>✓</li> <li>□</li> <li>□</li></ul>	Journal a Trial prot Statistica Non-com Company "Grey lite Conferen Regulato Research Grant da Personal Personal	rticle(s) with results of the trial cocol I analysis plan (SAP) mercial trial registry record (e. rowned trial registry record (e. erature" (e.g. unpublished thesi nce abstract(s) about the trial ry document (e.g. Clinical Study ethics application tabase summary (e.g. NIH RePC communication with trialist communication with the spons	g. ClinicalTrials.gov red g. GSK Clinical Study R s) r Report, Drug Approv DRTER or Research Cou or	ord) egister record) al Package) uncils UK Gateway to Research)

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Domain 1: Risk of bias arising from the randomization	n process
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Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		<u>Y</u>
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during		Υ
the trial?		
2.2. Were carers and people delivering the interventions aware of		Y
participants' assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the		Υ
intended intervention that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the		<u>PY</u>
outcome?		
2.5. If Y/PY/NI to 2.4: Were these deviations from intended		<u>Y</u>
intervention balanced between groups?		
2.6 Was an appropriate analysis used to estimate the effect of		<u>Y</u>
assignment to intervention?		
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact		PY
(on the result) of the failure to analyse participants in the group to		
which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias due to deviations		Unpredictable
from intended interventions?		
<ul> <li>participants' assigned intervention during the trial?</li> <li>2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?</li> <li>2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?</li> <li>2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?</li> <li>2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?</li> <li>2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?</li> <li>Risk-of-bias judgement</li> <li>Optional: What is the predicted direction of bias due to deviations from intended interventions?</li> </ul>		Y <u>PY</u> <u>Y</u> <u>Y</u> PY Some concerns Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A

2.2. Were carers and people delivering the interventions aware of participants'		N/A
assigned intervention during the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol	N/A	N/A
interventions balanced across intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that	N/A	N/A
could have affected the outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention	N/A	Υ
regimen that could have affected participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis	N/A	N/A
used to estimate the effect of adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from	N/A	N/A
intended interventions?		

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants		<u>Y</u>
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by	N/A	N/A
missing outcome data?		
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true	N/A	N/A
value?		
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended		N/A
on its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome		NA
data?		

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 <u>If N/PN/NI to 4.1 and 4.2</u> : Were outcome assessors aware of the intervention received by study participants?		<u>PN</u>
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		N/A
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a		<u>PY</u>
pre-specified analysis plan that was finalized before unblinded outcome		
data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the		
basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions,		<u>N</u>
time points) within the outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Risk-of-bias judgement	Low
Optional: What is the overall	NA
predicted direction of bias for	
this outcome?	

Study o	details					
Refer	ence	Goy J-J, Kaufmann U, Hurni M, Cook S, Versaci F, Ruchat P, et al. 10-year follow-up of a prospe comparing bare-metal stenting with internal mammary artery grafting for proximal, isolated c coronary artery stenosis the SIMA (Stenting versus Internal Mammary Artery grafting) trial. J A 2;52(10):815–7.				
Study o X	<b>lesign</b> Individua Cluster-r Individua	ally-randomized parallel-group t andomized parallel-group trial ally randomized cross-over (or o	rial ther matched) trial			
<b>For the</b> Exper	<b>purposes</b> imental:	s of this assessment, the interver PCI	ntions being compared are Comparator: CABG	defined as		
Specif	y which o	utcome is being assessed for ris	k of bias	Non-cardiac mortality		
<b>Specif</b> altern = 1.52 parag	<b>fy the nun</b> ative anal 2 (95% CI ( raph) that	nerical result being assessed. In orgenerical result being assessed, in orgen being presented, specify the D.83 to 2.77) and/or a reference the uniquely defines the result beir	case of multiple ne numeric result (e.g. RR (e.g. to a table, figure or ng assessed.	Manuscript results		
Is the r ✓	eview tea to assess to assess	<b>m's aim for this result?</b> The effect of <i>assignment to inte</i> The effect of <i>adhering to interv</i>	ervention (the 'intention-to rention (the 'per-protocol' e	-treat' effect) effect)		
If the a that sh □ □	im is to as ould be a occurren failures ir non-adhe	<b>Seess the effect of adhering to in</b> ddressed (at least one must be o ce of non-protocol interventions in implementing the intervention erence to their assigned interver	n <b>tervention</b> , select the devia checked): s I that could have affected th ntion by trial participants	ations from intended intervention he outcome		
Which	of the foll	owing sources were <u>obtained</u> to	help inform the risk-of-bia	as assessment? (tick as many as		
	Journal a Trial prot Statistica Non-com Company "Grey lite Conferen Regulato Research Grant dat Personal Personal	rticle(s) with results of the trial ocol I analysis plan (SAP) mercial trial registry record (e.g r-owned trial registry record (e.g erature" (e.g. unpublished thesis ce abstract(s) about the trial ry document (e.g. Clinical Study ethics application tabase summary (e.g. NIH RePOI communication with trialist communication with the sponso	. ClinicalTrials.gov record) g. GSK Clinical Study Registe ) Report, Drug Approval Pacl RTER or Research Councils pr	er record) kage) UK Gateway to Research)		

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Domain 1: Risk of bias arising from the randomization	n process
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Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		<u>Y</u>
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during		Υ
the trial?		
2.2. Were carers and people delivering the interventions aware of		Y
participants' assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the		Υ
intended intervention that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the		<u>PY</u>
outcome?		
2.5. If Y/PY/NI to 2.4: Were these deviations from intended		<u>Y</u>
intervention balanced between groups?		
2.6 Was an appropriate analysis used to estimate the effect of		<u>Y</u>
assignment to intervention?		
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact		PY
(on the result) of the failure to analyse participants in the group to		
which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias due to deviations		Unpredictable
from intended interventions?		
<ul> <li>participants' assigned intervention during the trial?</li> <li>2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?</li> <li>2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?</li> <li>2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?</li> <li>2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?</li> <li>2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?</li> <li>Risk-of-bias judgement</li> <li>Optional: What is the predicted direction of bias due to deviations from intended interventions?</li> </ul>		Y <u>PY</u> <u>Y</u> <u>Y</u> PY Some concerns Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A

2.2. Were carers and people delivering the interventions aware of participants'		N/A
assigned intervention during the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol	N/A	N/A
interventions balanced across intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that	N/A	N/A
could have affected the outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention	N/A	Υ
regimen that could have affected participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis	N/A	N/A
used to estimate the effect of adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Optional: What is the predicted direction of bias due to deviations from	N/A	N/A
intended interventions?		

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants		<u>Y</u>
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by	N/A	N/A
missing outcome data?		
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true	N/A	N/A
value?		
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended		N/A
on its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome		NA
data?		

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 <u>If N/PN/NI to 4.1 and 4.2</u> : Were outcome assessors aware of the intervention received by study participants?		<u>PN</u>
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		N/A
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a		<u>PY</u>
pre-specified analysis plan that was finalized before unblinded outcome		
data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the		
basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions,		<u>N</u>
time points) within the outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

Risk-of-bias judgement	Low
Optional: What is the overall	NA
predicted direction of bias for	
this outcome?	

Study details				
Refere	ence	Eefting F, Nathoe H, van Dijk E Pump Bypass Surgery in Patier	D, Jansen E, Lahpor J, Stella nts Referred for Angioplast	P, et al. Randomized Comparison Bet y. Circulation. 2003 Dec 9;108(23):28
Study c X D	<b>lesign</b> Individua Cluster-r Individua	ally-randomized parallel-group randomized parallel-group trial ally randomized cross-over (or o	trial other matched) trial	
<b>For the</b> Experi	<b>purposes</b> imental:	s of this assessment, the interve PCI	entions being compared an Comparator: CABG	e defined as
Specif	y which o	utcome is being assessed for ri	sk of bias	Non-cardiac mortality
<b>Specif</b> altern = 1.52 parage	<b>y the nun</b> ative anal (95% CI ( raph) that	nerical result being assessed. In lyses being presented, specify t D.83 to 2.77) and/or a reference t uniquely defines the result bei	case of multiple he numeric result (e.g. RR e (e.g. to a table, figure or ing assessed.	Manuscript results
Is the r ✓	eview tea to assess to assess	m's aim for this result? s the effect of <i>assignment to int</i> s the effect of <i>adhering to inter</i>	<i>tervention</i> (the 'intention-t vention (the 'per-protocol'	o-treat' effect) effect)
If the a that sh	im is to as ould be a occurren failures ir non-adhe	ssess the effect of adhering to in ddressed (at least one must be ce of non-protocol intervention n implementing the interventio erence to their assigned interve	<i>ntervention,</i> select the dev checked): ns n that could have affected ention by trial participants	iations from intended intervention the outcome
Which apply) ✓ □	<b>of the foll</b> Journal a Trial prot Statistica	lowing sources were <u>obtained</u> t rticle(s) with results of the trial cocol I analysis plan (SAP)	o help inform the risk-of-b	ias assessment? (tick as many as
	Non-com Company "Grey lite Conferen Regulato	mercial trial registry record (e. y-owned trial registry record (e. erature" (e.g. unpublished thesi nce abstract(s) about the trial ry document (e.g. Clinical Study	g. ClinicalTrials.gov record) g. GSK Clinical Study Regist s) / Report, Drug Approval Pa	cer record) ckage)
	Research Grant da Personal Personal	ethics application tabase summary (e.g. NIH RePC communication with trialist communication with the spons	ORTER or Research Councils	s UK Gateway to Research)

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain I. RISK OF DIAS AFISING FOULT LIFE FAILUOHIZATION PLOCES:	Domain 1	L: Risk	of bias	arising	from	the	randomization	process
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Signalling questions	Comments	Response
		options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled		<u>Y</u>
and assigned to interventions?		
1.3 Did baseline differences between intervention groups suggest a problem		<u>N</u>
with the randomization process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the		Unpredictable
randomization process?		

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during		Y
the trial?		
2.2. Were carers and people delivering the interventions aware of		Y
participants' assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the		Y
intended intervention that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the		<u>PY</u>
outcome?		
2.5. If Y/PY/NI to 2.4: Were these deviations from intended		<u>Y</u>
intervention balanced between groups?		
2.6 Was an appropriate analysis used to estimate the effect of		<u>Y</u>
assignment to intervention?		
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact		PY
(on the result) of the failure to analyse participants in the group to		
which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias due to deviations		Unpredictable
from intended interventions?		

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of adhering to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	N/A	N/A

2.2. Were carers and people delivering the interventions aware of participants'		N/A
assigned intervention during the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol	N/A	N/A
interventions balanced across intervention groups?		
2.4. [If applicable:] Were there failures in implementing the intervention that	N/A	N/A
could have affected the outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention	N/A	Y
regimen that could have affected participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis	N/A	N/A
used to estimate the effect of adhering to the intervention?		
Risk-of-bias judgement	N/A	N/A
Ontional: What is the predicted direction of bias due to deviations from	Ν/Δ	Ν/Δ
intended interventions?		

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants		<u>Y</u>
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by	N/A	N/A
missing outcome data?		
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true	N/A	N/A
value?		
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended		N/A
on its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to missing outcome		NA
data?		
Signalling questions	Comments	Response options
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4.1 Was the method of measuring the outcome inappropriate?		<u>N</u>
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		<u>N</u>
4.3 <u>If N/PN/NI to 4.1 and 4.2</u> : Were outcome assessors aware of the intervention received by study participants?		<u>PN</u>
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		N/A
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		N/A
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias in measurement of the outcome?		NA

## Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a		<u>PY</u>
pre-specified analysis plan that was finalized before unblinded outcome		
data were available for analysis?		
Is the numerical result being assessed likely to have been selected, on the		
basis of the results, from		
5.2 multiple eligible outcome measurements (e.g. scales, definitions,		<u>N</u>
time points) within the outcome domain?		
5.3 multiple eligible analyses of the data?		<u>N</u>
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias due to selection of the reported result?		NA

## Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall	NA
predicted direction of bias for	
this outcome?	

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