

Stent thrombosis and adverse cardiovascular outcomes observed between six months and five years with sirolimus-eluting stents and other drug-eluting stents in patients with Type 2 diabetes mellitus complicated by coronary artery disease

A systematic review and meta-analysis

Pravesh Kumar Bundhun (MD)^a, M. Zafooruddin Sani Soogund (MBBS)^b, Manish Pursun (MBBS)^b, Meng-Hua Chen (PhD)^{a,*}

Abstract

This study aimed to compare 6 months to 5 years stent thrombosis (ST) and adverse cardiovascular outcomes associated with sirolimus-eluting stents (SES) and other drug-eluting stents (DES) in patients with type 2 diabetes mellitus (T2DM).

Electronic databases were searched for studies comparing SES with other DES in patients with T2DM. Total ST, definite ST, probable ST, and other adverse cardiovascular outcomes reported between 6 months and 5 years were considered as the clinical end points in this study. Odds ratios (ORs) with 95% confidence intervals (Cls) were calculated for categorical variables and the pooled analyses were performed with RevMan 5.3 software.

Twenty-nine studies involving a total number of 25,729 patients with diabetes were included in this meta-analysis. SES were not associated with significantly higher total, definite, and probable STs with OR: 0.95, 95% CI: 0.77-1.17, P=0.62; OR: 0.94, 95% CI: 0.65–1.37, P=0.76; and OR: 1.05, 95% CI: 0.77-1.45, P=0.74, respectively. SES were also noninferior to the other non-sirolimus eluting drug eluting stents (non-SE DES) in terms of all-cause mortality, cardiac death, myocardial infarction, and stroke with OR: 0.92, 95% CI: 0.82–1.03, P=0.16; OR: 1.09, 95% CI: 0.88–1.35, P=0.44; OR: 0.92, 95% CI: 0.80–1.06, P=0.26; and OR: 0.79, 95% CI: 0.49–1.28, P=0.43, respectively. Target vessel revascularization, target lesion revascularization, and major adverse cardiac events were also similarly reported between SES and non-SE DES with OR: 1.04, 95% CI: 0.83–1.31, P=0.72; OR: 1.25, 95% CI: 0.95–1.64, P=0.11; and OR: 1.06, 95% CI: 0.90–1.25, P=0.49, respectively.

During this particular follow-up period, SES were not associated with any increase in ST among these patients with T2DM. Mortality and other adverse cardiovascular outcomes were also not significantly different between these 2 groups. Hence, SES should be considered neither superior nor inferior to other DES. They are expected to be equally effective and safe to use in patients with T2DM.

Abbreviations: DES = drug-eluting stent, EES = everolimus-eluting stent, PES = paclitaxel-eluting stent, SES = sirolimus-eluting stent, T2DM = type 2 diabetes mellitus, ZES = zotarolimus-eluting stent.

Keywords: adverse cardiovascular outcomes, coronary artery diseases, drug-eluting stents, sirolimus-eluting stents, stent thrombosis, type 2 diabetes mellitus

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^a Institute of Cardiovascular Diseases, the First Affiliated Hospital, ^b Guangxi Medical University, Nanning, Guangxi, PR China.

^{*} Correspondence: Meng-Hua Chen, Institute of Cardiovascular Diseases, the First Affiliated Hospital, Guangxi Medical University, Nanning, Guangxi, 530027, PR China (e-mail: xyicucmh@sina.com).

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1. Introduction

Percutaneous coronary intervention with drug-eluting stents (DES) is becoming more demanding year by year, especially among patients with diabetes with coronary artery diseases.^[1] Even if the revascularization rate has significantly decreased in patients with diabetes treated by DES,^[2] stent thrombosis (ST) is still a major concern in these patients.^[3] Recently, controversies were observed when different types of individual DES were compared. In patients with type 2 diabetes mellitus (T2DM), several studies showed sirolimus-eluting stents (SES) to be more effective compared to paclitaxel-eluting stents (PES).^[4] However, other studies showed SES and PES to be comparable.^[5] When SES were compared to everolimus-eluting stents (EES), EES were associated with better outcomes in patients with T2DM.^[6] However, in other studies EES were noninferior to SES.^[7] It is believed that different follow-up periods reported in several

cohorts could indirectly have contributed to these controversies. Therefore, this study aimed to compare 6 months to 5 years ST and other adverse cardiovascular outcomes associated with SES and other DES, referred in this study as "non-SE DES," using a larger number of patients with diabetes.

2. Methods

2.1. Data sources and search strategies

PubMed, Medline, EMBASE, and the Cochrane library were searched for randomized controlled trials and observational studies comparing SES with other DES in patients with diabetes by tying the words or phrase "sirolimus eluting stents and drug eluting stents and diabetes mellitus." The word "drug eluting stents" was later replaced by the specific names of other DES such as "paclitaxel eluting stents, everolimus eluting stents and zotarolimus eluting stents." To further enhance this search, abbreviations of the above-mentioned words such as "SES, DES, PES, EES, ZES" were also used. Reference lists of most suitable articles were also checked for relevant studies. This search was restricted only to articles published in English.

2.2. Inclusion and exclusion criteria

Studies were included if:

- (a) They were randomized controlled trials or observational studies.
- (b) They compared SES with non-SE DES in patients with T2DM.
- (c) They reported ST and/or other adverse cardiovascular outcomes observed between SES and non-SE DES.
- (d) They had a follow-up period between 6 months and 5 years.

Studies were excluded if:

- (a) They were meta-analyses, case studies, or letters to editors.
- (b) They did not compare SES with non-SE DES in patients with T2DM.
- (c) They did not report ST and/or other adverse cardiovascular outcomes observed between SES and other DES.
- (d) They had a follow-up period of <6 months.
- (e) They were associated with the same trial or they were duplicates.

2.3. Outcomes and follow-ups

This study assessed 6 months to 5 years ST and other cardiovascular outcomes in patients with diabetes treated by SES and non-SE DES. The end points analyzed in this study included: (a) ST that was defined according to the Academic Research

Consortium^[8] and involved:

- (i) Total ST
- (ii) Definite ST
- (iii) Probable ST
- (b) All-cause mortality
- (c) Cardiac mortality
- (d) Myocardial infarction (MI)
- (e) Target vessel revascularization (TVR)
- (f) Target lesion revascularization (TLR)
- (g) Stroke

Major adverse cardiac events (MACEs) that consisted of death, MI, and revascularization (composite end point, which consisted of death, MI, and ST, was reported in only 1 study and was therefore considered in the same category as MACEs)

Table 1

Reported outcomes and follow-up periods.

Studies	Reported outcomes	Follow-up periods
Billinger2008	Death, cardiac death, MI, TLR, TVR, ST, MACEs	2 y
Briguori2011	Death, MI, TLR, TVR, MACEs, ST	3 y
Buch2008	Death, MI, TLR, TVR, MACEs, ST	1 y
Chong2010	MACEs, MI, TVR, ST, death	1.5 y
Costa2015	MACEs, cardiac death, MI, TLR, ST	1 y
Desch2011	Death, cardiac death, MI, ST, TLR, TVR	9 mo
Franzone2015	Death, cardiac death, MI, TVR, TLR, ST, stroke	1 y
Jesen2012	Death, cardiac death, MI, TLR, TVR, ST,	18 mo
	composite end points	
Kedhi2012	Death, ST	1 y
Kim2008	Death, cardiac death, TVR, ST, MACEs	З у
Kim2011	Death, cardiac death, MI, TLR, TVR, MACEs, ST	1 y
Kuchulakanti2006	Death, MI, TVR, TLR, MACEs, ST	6 mo
Kufner2014	TLR, ST, MACEs	1 y
Lee2011	Death, cardiac death, MI, TLR, TVR, MACEs, ST	4 y
Maeng2009	Death, cardiac death, MI, ST, TLR, MACEs	8 mo
Maeng2015	MACEs, death, cardiac death, MI, ST, TLR, TVR	4 y
Nakamura2016	Death, cardiac death, MACEs, MI, stroke, TLR, TVR, ST	Зу
Olesen2014	Death, cardiac death, MACEs, ST, TLR, TVR, MI	5 y
Simek2013	Death, cardiac death, MI, ST, TVR, TLR	3 ý
Stankovic2006	Death, MI, MACEs, TVR, TLR	9 mo
Wolf2010	Death, MI, ST	2 y
Chiu2009	MI, death	3 ý
Daemen2007	Death, TVR, MACEs	2 y
Jang2013	Death, cardiac death, MI, TLR, TVR, MACEs, ST	2 y
Sato2012	TLR, MACEs	8 mo
Balducelli2010	Death, MI, MACEs, TVR, ST	2у
Buja2012	MACEs, death, MI, TLR	5 y
Jeong2013	MACEs, death, MI, TVR, cardiac death, stroke, TLR	2 y
Kim m2008	Death, MI, TVR, TLR	6 mo

 $\label{eq:MACE} MACE = major adverse cardiac event, MI = myocardial infarction, ST = stent thrombosis, TLR = target lesion revascularization, TVR = target vessel revascularization.$

Patients were followed for a period ranging from 6 months to 5 years. However, ST was also analyzed during a follow-up period ranging from 6 months to 2 years and a follow-up period of >2 years. The outcomes reported in each study along with their follow-up periods have been summarized in Table 1.

According to Table 1, ST was reported in >20 studies, whereas all-cause mortality was reported in 26 studies. When ST was further subdivided, definite ST was reported in 12 studies, whereas only 9 studies reported probable ST. MI was reported in 25 studies and MACEs were reported in 24 studies. TVR and TLR were reported in 22 studies each and stroke was reported in only 3 studies.

2.4. Data extraction and review

Three authors (PKB, MZSS, and MP) independently reviewed the studies that were selected for this meta-analysis and then assessed whether these articles were fully eligible. The type of study reported, data concerning the total number of patients with T2DM treated by SES and the other DES, respectively, the different types of DES involved, data concerning the baseline features of the patients included, the reported outcomes, as well as the corresponding follow-up periods were carefully extracted. This was not an easy task for the authors; therefore, any disagreement or confusion about including certain studies or data was carefully discussed in order to finally reach a decision. However, if a final decision could not be reached, the fourth

2.5. Statistical analysis

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses were considered in this study.^[10] Assessment of heterogeneity during the subgroup analysis was performed using the following:

- a. Cochrane Q-statistic test, whereby a "*P* value" ≤ 0.05 was considered statistically significant and a "*P* value" > 0.05 was considered statistically insignificant
- b. Cochrane I²-statistic test, whereby an I² value of 0% indicated no heterogeneity, and an increased heterogeneity was represented by a larger value (an I² value of <25% indicated a low heterogeneity, an I² value ranging from 25% to 50% represented a moderate heterogeneity, and an I² value of >50% indicated a higher heterogeneity)

If I^2 was \leq 50%, a fixed effect model was used during the statistical analysis. However, if I^2 was >50%, a random effect model was used.

Funnel plots were assessed for publication bias. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for categorical variables. The pooled analyses were performed with RevMan 5.3 software.

Ethical approval was not necessary for this type of study that involved data obtained from randomized trials and observational cohorts.

3. Results

3.1. Search results

A total number of 577 articles were obtained from PubMed, Medline, EMBASE, the Cochrane library, and the reference lists of suitable articles. A total of 496 articles were eliminated after a careful assessment of the titles and abstracts because they were not related to the topic of this research. Another 41 articles were

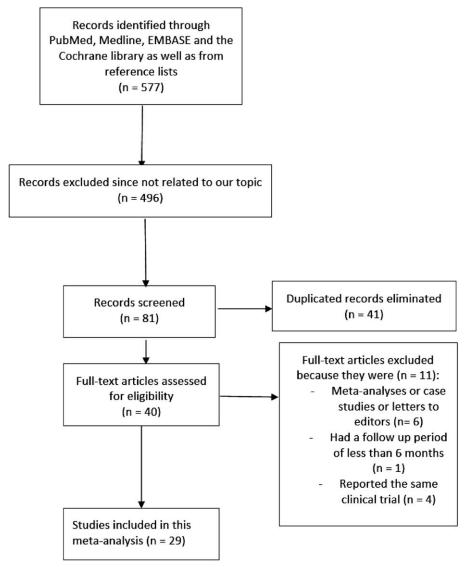




Table 2 General features of the studies included.

Studies	Type of study	Type of DES	Total number of patients with SES, n	Total number of patients with other DES, n
Billinger2008 ^[11]	RCT	PES	108	93
Briguori2011 ^[12]	Observational	PES, EES	76	150
Buch2008 ^[13]	Observational	PES	405	189
Chong2010 ^[14]	Observational	PES, ZES	79	209
Costa2015 ^[15]	Observational	EES	380	413
Desch2011 ^[16]	RCT	PES	118	114
Franzone2015 ^[17]	RCT	EES	257	229
Jesen2012 ^[18]	BCT	EES	196	194
Kedhi2012 ^[19]	Observational	EES, PES	1,370	6,764
Kim2008 ^[20]	Observational	PES	428	206
Kim2011 ^[21]	RCT	EES	151	149
Kuchulakanti2006 ^[22]	Observational	PES	630	221
Kufner2014 ^[23]	RCT	PES	86	76
Lee2011 ^[24]	RCT	PES	200	200
Maeng2009 ^[25]	RCT	PES	76	77
Maeng2015 ^[26]	RCT	EES	105	108
Nakamura2016 ^[27]	RCT	PES	846	859
Olesen2014 ^[28]	RCT	ZES	168	169
Simek2013 ^[29]	Observational	EES, PES	612	1,351
Stankovic2006 ^[30]	Observational	PES	147	113
Wolf2010 ^[31]	Observational	PES	677	328
Chiu2009 ^[32]	Observational	PES	835	835
Daemen2007 ^[33]	Observational	PES	206	250
Jang2013 ^[34]	RCT	ZES, PES	247	513
Sato2012 ^[35]	Observational	PES	129	54
Balducelli2010 ^[36]	Observational	PES	606	339
Buja2012 ^[37]	Observational	PES	780	637
Jeong2013 ^[38]	Observational	PES, EES, ZES	516	285
Kim m2008 ^[39]	Observational	PES	85	84
Total, n			10,520	15,209

DES = drug-eluting stent, EES = everolimus-eluting stent, PES = paclitaxel-eluting stent, RCT = randomized controlled trial, SES = sirolimus-eluting stent, ZES = zotarolimus-eluting stent.

eliminated because they were duplicates. Forty full-text articles were assessed for eligibility. Eleven articles were further eliminated because 2 articles were meta-analyses, 4 articles were case studies or letters addressed to editors, 1 study reported a follow-up period of <6 months, and 4 studies were associated with the same trials. Finally, 29 articles were selected and included in this meta-analysis. Fig. 1 represents the flow diagram for the study selection.

3.2. General features of the studies included

Twenty-nine studies (12 trials and 17 observational studies) involving a total number of 25,729 patients with T2DM (10,520 patients were treated by SES and 15,209 patients were treated by non-SS DES) were included in this meta-analysis. SES were compared with PES, EES, and zotarolimus-eluting stents (ZES). Twenty-three studies compared SES with PES. Nine studies compared SES with EES, whereas only 4 studies compared SES with ZES in these patients with T2DM. Study Kedhi2012 involved the largest number of patients treated by SES and non-SS DES. The general features of the studies included in this meta-analysis have been summarized in Table 2.

3.3. Baseline features of the studies included

The baseline characteristics of the studies included in this metaanalysis have been summarized in Table 3.

Studies not included in Table 3 did not report any baseline feature in their original manuscript and were therefore ignored.

A mean age ranging from 57.4 to 72.7 years was reported among the patients. More details concerning the percentage of males in each study and groups, patients with hypertension, dyslipidemia, and the percentage of patients who smoke have all been listed in Table 3. According to Table 3, there was no significant difference in the baseline features among patients treated by SES and patients treated by non-SE DES.

Table 4 lists the percentage of patients on insulin therapy.

Studies not included in Table 4 did not report the number of patients on insulin therapy and they have therefore been ignored.

According to Table 4, study Buch2008 involved 100% of patients with insulin-treated T2DM in the SES and non-SE DES groups, whereas study Kedhi2012 reported 45% of patients in the SES group who were on insulin therapy and 42% patients in the non-SE DES group treated by insulin therapy. Details involving insulin treatment have been given in Table 4.

3.4. Stent thrombosis associated with SES and non-SE DES

Table 5 summarizes the results of this meta-analysis.

Between 6 months and 5 years, SES were not associated with significantly higher total, definite, and probable STs with OR: 0.95, 95% CI: 0.77–1.17, P=0.62; OR: 0.94, 95% CI: 0.65–1.37, P=0.76; and OR: 1.05, 95% CI: 0.77–1.45, P=0.74, respectively, compared to non-SE DES. SES were non-inferior to non-SE DES in these patients with T2DM. Results comparing 6 months to 5 years ST have been represented in Fig. 2.

Table 3

Baseline features of the studies included in this meta-analysis.

Studies			SES/DES		
	Mean age, y	Males, %	HT, %	Ds, %	Cs, %
Billinger2008	57.4/63.4	69.4/72.0	79.6/81.7	65.7/55.9	23.2/17.2
Briguori2011	64.0/64.5	57.0/57.5	72.5/75.3	61.8/62.0	17.0/19.0
Buch2008	63.8/62.5	49.7/51.9	91.8/90.0	90.4/81.7	17.0/13.0
Chong2010	60.0/59.7	68.4/68.9	75.9/75.4	82.3/76.5	26.6/26.7
Costa2015	62.1/61.7	80.5/69.8	85.4/87.7	69.8/68.1	5.70/4.80
Desch2011	67.0/67.3	69.0/68.0	98.0/97.0	_	23.0/27.0
Franzone2015	68.6/67.1	77.0/75.5	86.0/82.5	73.5/75.1	21.8/23.1
Jesen2012	63.3/63.9	73.5/75.3	75.8/78.0	82.5/88.0	27.7/24.3
Kedhi2012	65.9/67.1	68.0/70.0	77.7/80.9	78.8/77.4	61.0/61.3
Kim2008	62.3/64.7	59.8/64.6	68.5/68.0	37.4/35.0	26.4/31.6
Kim2011	63.5/63.2	65.6/52.3	72.8/68.5	35.1/41.6	27.2/20.8
Kuchulakanti2006	64.3/65.8	57.0/64.0	89.0/89.0	90.0/87.0	16.0/16.0
Lee2011	61.1/60.7	61.0/55.0	57.0/62.0	27.5/31.5	27.0/28.5
Maeng2009	66.0/65.0	84.0/74.0	63.0/75.0	86.0/91.0	38.0/23.0
Maeng2015	62.5/63.0	_	71.4/76.8	82.7/91.0	23.7/22.7
Nakamura2016	69.0/68.7	71.3/73.6	78.0/82.7	67.7/68.9	18.9/20.7
Simek2013	64.1/65.6	70.4/68.7	74.7/68.6	62.9/66.8	39.9/28.2
Stankovic2006	65.0/63.0	84.4/82.3	71.4/70.8	67.3/63.7	53.7/47.8
Wolf2010	63.0/64.3	61.9/61.3	86.9/93.3	84.7/90.6	31.6/31.0
Chiu2009	62.2/63.2	68.3/68.5	36.4/36.8	_	_
Daemen2007	62.0/63.8	66.0/67.0	69.0/70.0	70.0/83.0	20.0/19.0
Jang2013	63.2/62.7	59.9/61.4	71.3/72.7	48.2/48.7	23.9/25.3
Sato2012	67.3/68.8	72.1/70.4	62.0/63.0	60.5/61.1	27.9/24.0
Balducelli2010	67.0/65.9	68.0/72.9	70.3/68.1	47.9/61.1	28.4/29.2
Buja2012	72.7/72.5	66.7/65.6	83.3/86.0	67.3/66.0	16.4/17.6
Jeong2013	66.8/66.8	62.0/62.0	72.0/72.0	_	42.4/42.4
Kim m2008	62.9/61.5	71.8/76.2	63.5/72.8	30.6/31.0	20.0/26.2

Cs = current smoker, DES = drug-eluting stent, Ds = dyslipidemia, HT = hypertension, SES = sirolimus-eluting stent.

Six months to 2 years ST and ST >2-year follow-up were also analyzed.

From 6 months to 2 years, total ST was noninferior between these 2 groups with OR: 1.04, 95% CI: 0.76–1.42, P=0.81. Definite and probable STs were also similarly reported with OR: 1.51, 95% CI: 0.82–2.78, P=0.19 and OR: 1.55, 95% CI: 0.84–2.85, P=0.16, respectively, in these patients with T2DM. These results have been represented in Fig. 3.

Detients from the	Dellente from
Patients on insulin therapy.	
Table 4	

Studies	Patients from the	Patients from the other DES group, %		
Studies	SES group, %	other DES group, %		
Briguori2011	30.0	25.0		
Buch2008	100	100		
Desch2011	45.0	42.0		
Franzone2015	34.6	31.0		
Kedhi2012	49.5	49.8		
Kim2008	8.90	9.70		
Kim2011	12.6	18.1		
Lee2011	16.0	16.5		
Maeng2009	41.0	38.0		
Simek2013	24.0	24.5		
Stankovic2006	29.3	34.5		
Wolf2010	33.4	29.6		
Daemen2007	31.0	28.0		
Balducelli2010	31.2	26.3		
Buja2012	31.0	35.8		
Kim m2008	18.8	13.1		

After 2 years, total, definite, and probable STs were not significantly different in these patients with diabetes with OR: 0.88, 95% CI: 0.67–1.16, P=0.31; OR: 0.69, 95% CI: 0.42–1.12, P=0.13; and OR: 0.90, 95% CI: 0.62–1.32, P=0.59, respectively. These results have been illustrated in Fig. 4.

Outcomes analyzed	Number of studies involved	OR with 95% Cl	Р	I², %
6 mo to 5 y				
All-cause mortality	26	0.92 (0.82-1.03)	0.16	0
Cardiac death	15	1.09 (0.88-1.35)	0.44	17
MI	25	0.92 (0.80-1.06)	0.26	27
Stroke	3	0.79 (0.49-1.28)	0.34	0
MACEs	24	1.06 (0.90-1.25)	0.49	62
TLR	22	1.25 (0.95-1.64)	0.11	68
TVR	22	1.04 (0.83–1.31)	0.72	66
Total ST	21	0.95 (0.77-1.17)	0.62	5
Definite ST	12	0.94 (0.65–1.37)	0.76	48
Probable ST	9	1.05 (0.77-1.45)	0.74	15
6 mo to 2 y				
Total ST	14	1.04 (0.76-1.42)	0.81	11
Definite ST	7	1.51 (0.82–2.78)	0.19	50
Probable ST	5	1.55 (0.84–2.85)	0.16	45
More than 2 y				
Total ST	7	0.88 (0.67-1.16)	0.38	8
Definite ST	5	0.69 (0.42-1.12)	0.13	35
Probable ST	4	0.90 (0.62-1.32)	0.59	0

CI = confidence interval, MACE = major adverse cardiac event, MI = myocardial infarction, OR = odds ratio, ST = stent thrombosis, TLR = target lesion revascularization, TVR = target vessel revascularization.

DES = drug-eluting stent, SES = sirolimus-eluting stent.

24	non-SE		SES		M-1-1-6	Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I M-H, Fixed, 95% Cl
.2.1 Total stent thror			-		4 001	4 00 10 00 5 100	
Balducelli2010	7	339	7	606	1.6%	1.80 [0.63, 5.19]	
Briguori2011	3	75	1	76	0.3%	3.13 [0.32, 30.74]	
3uch2008	2	131	6	301	1.1%	0.76 [0.15, 3.83]	
Chong2008	3	209	1	79	0.5%	1.14 [0.12, 11.08]	
Costa2015	14	413	2	380	0.6%	6.63 [1.50, 29.37]	
Desch2011	3	114	4	118	1.2%	0.77 [0.17, 3.52]	
Franzone2015	11	229	17	257	4.8%	0.71 [0.33, 1.55]	
lang2013	8	513	0	247	0.2%	8.32 [0.48, 144.79]	
lesen2012	5	194	8	196	2.5%	0.62 [0.20, 1.94]	
Kedhi2012	61	6764	18	1370	9.4%	0.68 [0.40, 1.16]	
Kim2008	17	206	26	428	4.9%	1.39 [0.74, 2.63]	
Kim2011	1	149	1	151	0.3%	1.01 [0.06, 16.35]	
Kuchulakanti2006	0	221	2	630	0.4%	0.57 [0.03, 11.87]	
(ufner2014	1	76	1	86	0.3%	1.13 [0.07, 18.44]	
.ee2011	3	200	8	200	2.5%	0.37 [0.10, 1.40]	
laeng2009	2	77	0	76	0.2%	5.07 [0.24, 107.29]	
laeng2015	5	108	3	105	0.9%	1.65 [0.38, 7.09]	— <u> </u>
lakamura2016	3	179	2	159	0.7%	1.34 [0.22, 8.11]	
Dlesen2014	1	169	2	168	0.6%	0.49 [0.04, 5.50]	
Simek2013	105	1351	60	612	24.2%	0.78 [0.56, 1.08]	-=+
Volf2010	4	328	9	677	1.8%	0.92 [0.28, 3.00]	
ubtotal (95% CI)		12045		6922	59.0%	0.95 [0.77, 1.17]	+
otal events	259		178				
leterogeneity: Chi ² = 2 est for overall effect: 2				= 5%			
.2.2 Definite stent th	rombosis	5					
Chong2008	7	209	3	79	1.3%	0.88 [0.22, 3.48]	
Costa2015	14	413	2	380	0.6%	6.63 [1.50, 29.37]	
ranzone2015	1	229	5	257	1.5%	0.22 [0.03, 1.91]	
ang2013	6	513	0	247	0.2%	6.34 [0.36, 112.99]	
esen2012	0	194	4	196	1.4%	0.11 [0.01, 2.06]	· · · · · · · · · · · · · · · · · · ·
(im2008	4	206	3	428	0.6%	2.81 [0.62, 12.65]	
Kufner2014	4	76	1	420	0.0%	1.13 [0.07, 18.44]	
	2	70	0	76	0.3 %		
Maeng2009	2	108	2	105	0.2%	5.07 [0.24, 107.29]	•
Maeng2015						0.19 [0.01, 4.02]	·
Vakamura2016	3	179	1	159	0.3%	2.69 [0.28, 26.16]	
Dlesen2014	1	169	2	168	0.6%	0.49 [0.04, 5.50]	
Simek2013	28	1351	23	612	9.8%	0.54 [0.31, 0.95]	
Subtotal (95% CI)		3724		2793	17.7%	0.94 [0.65, 1.37]	
otal events	67		46				
leterogeneity: Chi ² = 2 fest for overall effect: 2				= 48%			
.2.3 Probable stent t	hrombos	is					
Chong2008	7	209	3	79	1.3%	0.88 [0.22, 3.48]	
Costa2015	14	413	2	380	0.6%	6.63 [1.50, 29.37]	
ranzone2015	6	229	6	257	1.7%	1.13 [0.36, 3.54]	
ang2013	2	513	0 0	247	0.2%	2.42 [0.12, 50.58]	
esen2012	2	194	5	196	1.6%	0.40 [0.08, 2.08]	
(im2008	3	206	9	428	1.8%	0.69 [0.18, 2.57]	
Maeng2015	1	108	9	420	0.2%	2.94 [0.12, 73.09]	
lakamura2016	0	179	1	159	0.2%	0.29 [0.01, 7.28]	
imek2013	76			612			_ _
Subtotal (95% CI)	10	1351 3402	37	2463	15.2% 23.2%	0.93 [0.62, 1.39] 1.05 [0.77, 1.45]	
		J402	~~~	2403	∠J. ∠70	1.00 [0.77, 1.40]	Ţ
otal events leterogeneity: Chi² = 9 est for overall effect: 2				5%			
		40474		40470	400.00/	0.07 [0.00.4.4.1]	
fotal (95% CI)		19171		12178	100.0%	0.97 [0.83, 1.14]	T
	437		287				
otal events leterogeneity: Chi² = 5 est for overall effect: 2	51.86, df =		0.12); I ² :	= 21%			0.01 0.1 1 10 10

Figure 2. Comparing stent thrombosis between SES and non-SE DES during a follow-up period ranging from 6 months to 5 years. CI = confidence interval, DES = drug-eluting stent, df = degree of freedom, SES = sirolimus-eluting stent.

3.5. Adverse cardiovascular outcomes associated with SES and non-SE DES

Six months to 5 years adverse cardiovascular outcomes associated with SES and non-SE DES were also compared in these patients with T2DM. SES were noninferior to the other

non-SE DES in terms of all-cause mortality, cardiac death, MI, and stroke with OR: 0.92, 95% CI: 0.82–1.03, P=0.16; OR: 1.09, 95% CI: 0.88–1.35, P=0.44; OR: 0.92, 95% CI: 0.80–1.06, P=0.26; and OR: 0.79, 95% CI: 0.49–1.28, P=0.43, respectively. These results have been shown in Fig. 5.

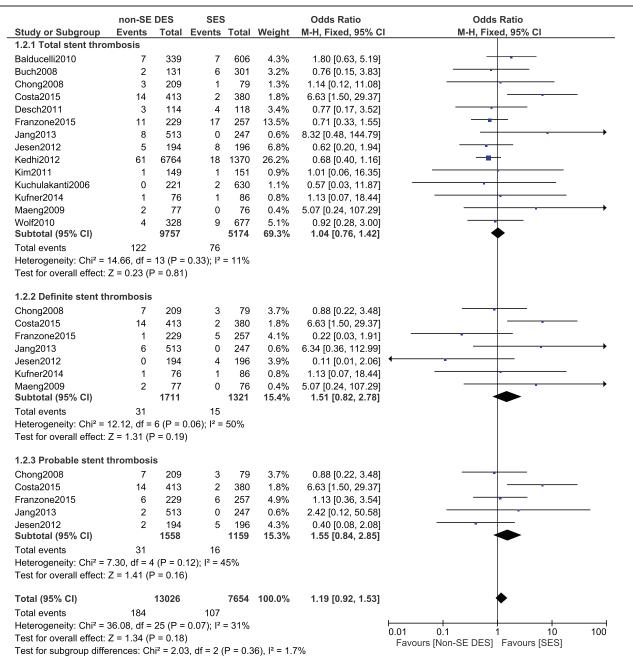


Figure 3. Comparing stent thrombosis between SES and non-SE DES during a follow-up period ranging from 6 months to 2 years. CI = confidence interval, DES = drug-eluting stent, df = degree of freedom, SES = sirolimus-eluting stent.

TVR, TLR, and MACEs were also similarly reported with SES and non-SS DES, with OR: 1.04, 95% CI: 0.83–1.31, P=0.72; OR: 1.25, 95% CI: 0.95–1.64, P=0.11; and OR: 1.06, 95% CI: 0.90–1.25, P=0.49, respectively. These results have been illustrated in Fig. 6.

3.6. Sensitivity analysis

After visually assessing the funnel plots (Fig. 7A–D), a low or moderate publication bias was observed among several subgroups analyzing ST in these patients with T2DM. However, when analyzing the other cardiovascular outcomes, an increased risk of bias was observed in certain but not all of the subgroups.

4. Discussion

Controversies have been observed when comparing SES with other DES such as PES, EES, or ZES in patients with T2DM. This analysis showed that SES were neither inferior nor superior to non-SE DES in patients with T2DM. Between 6 months and 5 years, total, definite, and probable STs were not significantly different in these 2 groups. Other adverse cardiovascular outcomes such as mortality, cardiac death, MI, stroke, TVR, TLR, and MACEs were also similarly manifested among patients treated with SES and non-SE DES.

Similarly, the meta-analysis involving 11,000 patients with T2DM showed no significant difference in MACEs reported

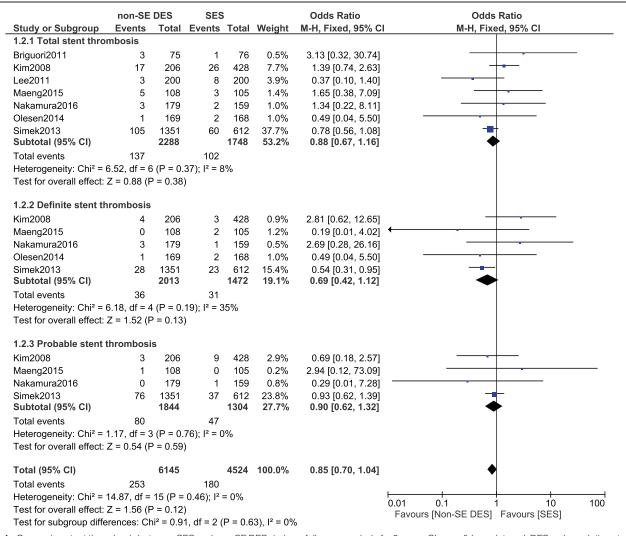


Figure 4. Comparing stent thrombosis between SES and non-SE DES during a follow-up period of >2 years. CI = confidence interval, DES = drug-eluting stent, df = degree of freedom, SES = sirolimus-eluting stent.

between SES and PES.^[40] Moreover, another meta-analysis involving 7370 patients obtained from 5 randomized trials showed no significant difference between EES and SES in terms of safety and clinical efficacy.^[7] The results were consistent with the current analysis, even though PES, EES, and ZES were combined together.

In contrast, Bundhun et al recently showed EES to be associated with significantly better adverse clinical outcomes in patients with diabetes when compared with non-EE DES.^[6] However, a 1-year follow-up period might not be sufficient to analyze ST and other cardiovascular outcomes if a long-term follow-up was to be considered. Another meta-analysis that compared SES and PES in patients with diabetes with coronary artery diseases showed SES to be associated with a significantly reduced TLR compared to PES.^[41] However, the risks of MI, ST, and death were similar. Furthermore, the analysis comparing SES with PES in patients with diabetes again showed SES to be superior compared to PES in terms of TLR and restenosis; however, SES were noninferior to PES in terms of ST, cardiac death, and MI.^[42] The meta-analysis published by Yan et al comparing second-generation DES (EES) with first-generation DES showed the former to be highly effective in reducing the risk of MACEs in patients with T2DM.^[43] However, their study compared EES with SES separately, which was different when compared to the current study, whereby SES were compared with the other DES combined together (non-SE DES).

In the mixed treatment comparison analysis including 22,844 patients with diabetes obtained from randomized trials, all DES were effective when compared to bare metal stents.^[44] Moreover, when SES were compared with PES, they were superior in lowering late lumen loss. However, the current study did not analyze lumen loss. Also, when EES were compared to other DES, EES were associated with better outcomes in these patients with T2DM. In this analysis PES were dominating. Therefore, other DES such as EES that could most probably be more effective than SES could not efficiently show their effectiveness. Lee et al also compared SES with PES in patients with T2DM.^[4] Their results showed SES to be superior compared to PES in improving clinical outcomes. However, their study had a follow-up period of only 9 months, whereas the current analysis involved a follow-up period ranging from 6 months to 5 years. Moreover, even if the SORT OUT III substudy showed SES to be associated with better

Study or Subgroup .1.1 All-cause mortalit	Events	DES	SES Events		Weight	Odds Ratio M-H, Fixed, 95% C	Odds Ratio M-H, Fixed, 95% Cl
		rotal	Events	rotal	weight	m-n, rixea, 95% C	MI-II, FIXED, 95% CI
Balducelli2010	35	339	59	606	3.1%	1.07 [0.69, 1.66]	+-
Billinger2008	10	93	9	108	0.6%	1.33 [0.51, 3.42]	
Briguori2011	7	150	5	76	0.5%	0.70 [0.21, 2.27]	
Buch2008	12	189	31	405	1.5%	0.82 [0.41, 1.63]	
3uja2012 Chiu2009	57 757	637 835	85 765	780 835	5.8% 5.9%	0.80 [0.56, 1.14]	<u> </u>
Chong2008	4	209	2	79	0.2%	0.89 [0.63, 1.25] 0.75 [0.13, 4.18]	
Daemen2007	29	250	27	206	2.2%	0.87 [0.50, 1.52]	
Desch2011	3	114	6	118	0.5%	0.50 [0.12, 2.07]	
ranzone2015	9	229	13	257	1.0%	0.77 [0.32, 1.83]	
ang2013	15	513	3	247	0.3%	2.45 [0.70, 8.54]	
eong2013	1	285	9	516	0.5%	0.20 [0.03, 1.57]	
esen2012	7	194	16	196	1.3%	0.42 [0.17, 1.05]	
Kedhi2012	158	3301	35	717	4.5%	0.98 [0.67, 1.43]	
(im m2008 (im2008	1 12	84 206	1 37	85 428	0.1% 1.9%	1.01 [0.06, 16.45]	
(im2008 (im2011	2	206	5	428	0.4%	0.65 [0.33, 1.28] 0.40 [0.08, 2.08]	
Kuchulakanti2006	15	221	44	630	1.8%	0.97 [0.53, 1.78]	
.ee2011	10	200	6	200	0.5%	1.70 [0.61, 4.77]	
Maeng2009	1	77	2	76	0.2%	0.49 [0.04, 5.48]	
Aaeng2015	13	108	10	105	0.7%	1.30 [0.54, 3.11]	_
akamura2016	37	859	41	846	3.3%	0.88 [0.56, 1.39]	-+
Diesen2014	18	169	22	168	1.6%	0.79 [0.41, 1.54]	-+
Simek2013	198	1351	91	612	8.8%	0.98 [0.75, 1.29]	
Stankovic2006	1	113	3	147	0.2%	0.43 [0.04, 4.18]	
Volf2010 Subtotal (95% CI)	35	328	56	677 9271	2.7%	1.32 [0.85, 2.07]	1
oubtotal (95% CI)	1447	11203	1383	9271	50.1%	0.92 [0.82, 1.03]	٦
otal events leterogeneity: Chi ² = 18		25 (P -		= 0%			
est for overall effect: Z				v /0			
		50,					
.1.2 Cardiac death							
Billinger2008	7	93	7	108	0.5%	1.17 [0.40, 3.48]	
Costa2015	22	413	5	380	0.4%	4.22 [1.58, 11.26]	
Desch2011	3	114	4	118	0.3%	0.77 [0.17, 3.52]	
ranzone2015	7	229	9	257	0.7%	0.87 [0.32, 2.37]	
ang2013	11	513	2	247	0.2%	2.68 [0.59, 12.20]	
eong2013	1	285	8	516	0.5%	0.22 [0.03, 1.80]	
esen2012 Kim2008	6 10	194 206	9 24	196 428	0.7% 1.2%	0.66 [0.23, 1.90]	
(im2008 (im2011	1	200	24	420	0.2%	0.86 [0.40, 1.83] 0.50 [0.05, 5.61]	
.ee2011	5	200	1	200	0.2%	5.10 [0.59, 44.07]	
laeng2009	1	77	1	76	0.1%	0.99 [0.06, 16.07]	
Aaeng2015	9	108	5	105	0.4%	1.82 [0.59, 5.62]	
lakamura2016	16	859	17	846	1.4%	0.93 [0.46, 1.84]	
Diesen2014	7	169	10	168	0.8%	0.68 [0.25, 1.84]	
Simek2013	133	1351	59	612	6.1%	1.02 [0.74, 1.41]	+
	100	1551					
Subtotal (95% CI)		4960		4408	13.5%	1.09 [0.88, 1.35]	•
oubtotal (95% CI) otal events leterogeneity: Chi ² = 16 est for overall effect: Z	239 6.91, df = = 0.77 (F	4960 : 14 (P =	163 0.26); l² =	4408			•
Subtotal (95% CI) Total events Heterogeneity: Chi ² = 16 Test for overall effect: Z .1.3 Myocardial Infarc	239 6.91, df = = 0.77 (f	4960 = 14 (P = P = 0.44)	163 0.26); l² =	4408 = 17%	13.5%	1.09 [0.88, 1.35]	•
Subtotal (95% CI) Total events Heterogeneity: Chi ² = 16 Test for overall effect: Z .1.3 Myocardial Infarc Balducelli2010	239 3.91, df = = 0.77 (f tion 35	4960 : 14 (P = P = 0.44) 339	163 0.26); I² = 56	4408 = 17% 606	13.5% 3.0%	1.09 [0.88, 1.35]	•
Subtotal (95% CI) Total events leterogeneity: Chi ² = 16 Test for overall effect: Z .1.3 Myocardial Infarc Balducelli2010 Billinger2008	239 6.91, df = = 0.77 (f tion 35 6	4960 : 14 (P = P = 0.44) 339 93	163 0.26); I ² = 56 2	4408 = 17% 606 108	13.5% 3.0% 0.1%	1.09 [0.88, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57]	
Subtotal (95% CI) Total events Heterogeneity: Chi ² = 16 rest for overall effect: Z .1.3 Myocardial Infarc Balducelli2010 Billinger2008 Briguori2011	239 3.91, df = = 0.77 (f tion 35 6 5	4960 = 14 (P = P = 0.44) 339 93 150	163 0.26); l² = 56 2 0	4408 = 17% 606 108 76	3.0% 0.1% 0.1%	1.09 [0.88, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.98]	+
Subtotal (95% CI) Total events teterogeneity: Chi ² = 16 Test for overall effect: Z .1.3 Myocardial Infarc Balducelli2010 Sillinger2008 Sriguori2011 Such2008	239 6.91, df = = 0.77 (f tion 35 6	4960 : 14 (P = P = 0.44) 339 93	163 0.26); l² = 56 2 0 43	4408 = 17% 606 108	13.5% 3.0% 0.1%	1.09 [0.88, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.98] 1.00 [0.57, 1.75]	
Subtotal (95% CI) Total events Heterogeneity: Chi ² = 16 rest for overall effect: Z .1.3 Myocardial Infarc Balducelli2010 Billinger2008 Briguori2011	239 3.91, df = = 0.77 (f tion 35 6 5 20	4960 = 14 (P = P = 0.44) 339 93 150 189	163 0.26); l² = 56 2 0	4408 = 17% 606 108 76 405	3.0% 0.1% 0.1% 2.0%	1.09 [0.88, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.98] 1.00 [0.57, 1.75] 0.60 [0.31, 1.16]	
Subtotal (95% CI) Total events deterogeneity: Chi ² = 16 Test for overall effect: Z 1.3 Myocardial Infarc Salducelli2010 Sillinger2008 Briguor2011 Such2008 Buja2012	239 5.91, df = = 0.77 (f tion 35 6 5 20 14	4960 = 14 (P = P = 0.44) 339 93 150 189 637	163 0.26); l ² = 56 2 0 43 28	4408 = 17% 606 108 76 405 780	3.0% 0.1% 0.1% 2.0% 2.0%	1.09 [0.88, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.98] 1.00 [0.57, 1.75]	
Subtotal (95% CI) Total events deterogeneily: Chi ² = 16 rest for overall effect: Z sladucelli2010 slillinger2008 slillinger2008 sluja2011 Suba2009 Subja2012 Shub2009	239 5.91, df = = 0.77 (f tion 35 6 5 20 14 764	4960 = 14 (P = P = 0.44) 339 93 150 189 637 835	163 0.26); I ² = 56 2 0 43 28 769	4408 = 17% 606 108 76 405 780 835	3.0% 0.1% 0.1% 2.0% 2.0% 5.4%	1.09 [0.88, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.98] 1.00 [0.57, 1.75] 0.60 [0.31, 1.16] 0.92 [0.65, 1.31]	
Jubtotal (95% CI) Total events leterogeneily: Chi ² = 16 rest for overall effect: Z .1.3 Myocardial Infarc Jalducelli2010 Jillinger2008 Jilguori2011 Jiluch2008 Julg2012 Jhlu2009 Chong2008 Josta2015	239 3.91, df = = 0.77 (f ition 35 6 5 20 14 764 11	4960 14 (P = P = 0.44) 339 93 150 189 637 835 209	163 0.26); l ² = 56 2 0 43 28 769 7	4408 = 17% 606 108 76 405 780 835 79	3.0% 0.1% 2.0% 2.0% 5.4% 0.8%	1.09 [0.88, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.98] 1.00 [0.57, 1.75] 0.60 [0.31, 1.16] 0.92 [0.65, 1.31] 0.57 [0.21, 1.53]	
slubtotal (95% CI) 'otal events letercogeneily: Chi ² = 16 'est for overall effect: Z .1.3 Myocardial Infarc laducelli2010 Billinger2008 birguor2011 such2008 birguor2012 birguor2012 birguor2015 besch2011	239 5.91, df = = 0.77 (f tion 35 6 5 20 14 764 11 26 1 1 26 1 0	4960 14 (P = P = 0.44) 339 93 150 189 637 835 209 413	163 0.26); ² = 56 2 0 43 28 769 7 16	4408 = 17% 606 108 76 405 780 835 79 380	3.0% 0.1% 0.1% 2.0% 5.4% 0.8% 1.3% 0.3% 1.1%	1.09 [0.88, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.88] 1.00 [0.57, 1.75] 0.60 [0.31, 1.16] 0.57 [0.21, 1.53] 1.53 [0.81, 2.90] 0.25 [0.03, 2.29] 0.74 [0.32, 1.67]	
Jubtotal (95% CI) 'otal events 'otal events 'otal events 'est for overall effect: Z .1.3 Myocardial Infarc Jaiduceili201	239 5.91, df = = 0.77 (f tion 35 6 5 20 14 764 11 26 1 10 36	4960 14 (P = P = 0.44) 339 93 150 189 637 835 209 413 114 229 513	163 0.26); ² = 56 2 0 43 28 769 7 6 9 7 6 9 7 6 4 4 15	4408 = 17% 606 108 76 405 780 835 79 380 118 257 247	3.0% 0.1% 0.1% 2.0% 5.4% 0.8% 1.3% 0.3% 1.1% 1.5%	1.09 [0.86, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 1.857] 5.78 [0.32, 105.98] 1.00 [0.57, 1.75] 0.60 [0.31, 1.16] 0.92 [0.65, 1.31] 0.57 [0.21, 1.53] 1.53 [0.81, 2.90] 0.25 [0.03, 2.29] 0.74 [0.32, 167] 1.26 [0.66, 2.37]	
subtotal (95% CI) total events leterogeneity: Chi ² = 16 sest for overall effect: Z .1.3 Myocardial Infarc ladiducelli2010 lillinger2008 singuori2011 such2008 lya2012 chug2009 chong2008 costa2015 besch2015 besch2015 ang2013 eong2013	239 5.91, df = = 0.77 (f tion 35 6 5 20 14 764 11 26 1 10 36 1	4960 14 (P = P = 0.44) 339 93 150 189 637 835 209 413 114 229 513 285	163 0.26); ² = 56 2 0 43 28 769 7 16 4 15 14	4408 = 17% 606 108 76 405 780 835 79 380 118 257 247 516	3.0% 0.1% 0.1% 2.0% 2.0% 5.4% 0.3% 1.3% 0.3% 1.5% 0.0%	1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.98] 1.00 [0.57, 175] 0.60 [0.31, 1.16] 0.92 [0.65, 1.31] 1.53 [0.81, 2.90] 0.25 [0.03, 2.29] 0.74 [0.32, 167] 1.26 [0.66, 3.37] 3.46 [0.66, 2.37]	
Jubtotal (95% CI) otala events leterogeneity: Chi ² = 16 est for overall effect: Z .1.3 Myocardial Infarc Jalducelli2010 Jillinger2008 Jinguori2011 Jupacital Jupacit	239 3.91, df = = 0.77 (f tion 35 6 5 20 14 764 11 26 1 10 36 1 1 1 1 1	4960 = 14 (P = P = 0.44) 339 93 150 189 637 835 209 413 114 229 513 285 194	163 0.26); l ² = 56 2 0 43 28 769 7 16 4 15 14 15 14 0 7	4408 = 17% 606 108 76 405 780 835 79 380 118 257 247 516 196	3.0% 0.1% 0.1% 2.0% 5.4% 0.3% 1.3% 0.3% 1.1% 0.0% 0.6%	$\begin{array}{c} 1.09 \left[0.86, 1.35 \right] \\ \hline \\ 1.13 \left[0.72, 1.76 \right] \\ 3.66 \left[0.72, 1.657 \right] \\ 5.78 \left[0.32, 10559 \right] \\ 1.00 \left[0.57, 1.75 \right] \\ 0.57 \left[0.32, 10559 \right] \\ 1.53 \left[0.811, 2.90 \right] \\ 0.25 \left[0.32, 2.18 \right] \\ 1.53 \left[0.811, 2.90 \right] \\ 0.74 \left[0.32, 167 \right] \\ 1.26 \left[0.66, 2.37 \right] \\ 5.45 \left[0.22, 1341 \right] \\ 5.45 \left[0.22, 1341 \right] \\ 0.14 \left[0.02, 1.15 \right] \\ \end{array}$	
iubtotal (95% CI) iotal events leterogeneity: Chi ² = 16 est for overall effect: Z .1.3 Myocardial Infarc Iaduacelli2010 illinger2008 lupia2012 biug2012 biug2012 biug2012 biug2015 besch2011 ranzone2015 aeong2013 eeong2013 eeong2013 esen2012 im m2008	239 3.91, df = = 0.77 (f ition 35 6 5 20 14 764 11 26 1 10 36 1 1 1 1 1	4960 : 14 (P = P = 0.44) 339 93 150 189 637 835 209 413 114 229 513 285 194 84	163 0.26); ² = 56 2 0 43 28 769 7 16 4 15 14 0 7 7 1	4408 = 17% 606 108 76 405 780 835 79 380 118 257 247 516 196 85	13.5% 3.0% 0.1% 0.1% 2.0% 2.0% 5.4% 0.8% 1.3% 0.3% 0.3% 0.3% 0.6% 0.6%	1.09 [0.88, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.98] 0.92 [0.65, 1.31] 0.57 [0.21, 1.53] 1.53 [0.81, 2.90] 0.74 [0.32, 1.67] 1.26 [0.66, 2.37] 1.26 [0.66, 2.37] 5.45 [0.22, 134.13] 0.14 [0.02, 1.15] 1.40 [0.6, 18.45]	
subtotal (95% CI) 'otal events teterogeneity: Chi ^p = 16 test for overall effect: Z .1.3 Myocardial Infarc Jalducelii/2011 Jillinger2008 striguori2011 Jupi2012 Jupi2012 Jupi2012 Jupi2012 Jupi2013 Jesch2011 renzone2015 Jesch2011 seng2013 eong2013 eong2013 eong2013 eong2013 im 2008 Jim 2008 Jim 2008	239 3.91, df = = 0.77 (f ition 35 6 5 20 14 764 11 26 1 10 36 1 1 7	4960 14 (P = P = 0.44) 339 93 150 189 637 835 209 413 114 229 513 285 194 84 206	163 0.26); ² = 56 2 0 43 28 769 7 16 4 15 14 0 7 1 14 0 7 1 1 6	4408 = 17% 606 108 76 405 780 835 79 380 118 257 247 516 196 85 428	3.0% 0.1% 0.1% 2.0% 2.0% 5.4% 0.8% 1.3% 0.8% 1.1% 1.5% 0.0% 0.1% 0.3%	1.09 [0.86, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.88] 1.00 [0.57, 1.75] 0.60 [0.31, 1.16] 0.52 [0.65, 1.31] 0.57 [0.21, 1.53] 0.51 [0.21, 1.53] 0.52 [0.32, 2.14] 1.53 [0.81, 2.90] 0.25 [0.62, 2.34] 1.54 [0.22, 1.34] 1.01 [0.06, 1645] 0.14 [0.02, 1.15] 1.01 [0.06, 1645] 0.247 [0.82, 7.46]	
Jubtota (95% CI) Total events Total events Total events Test for overall effect: Z .1.3 Myocardial Infarc Jalducelli201 Jillinger2008 Juja2012 Jula2008 Juja2012 Jhua2009 Jhong2008 Josta2015 Seesch2011 Farazone2015 Seesch2011 Seesch2013 Seenc2013 Seenc2012 Jillinger2008 Jillinger2008 Jillinger2008 Jillinger2018	239 6.91, df = = 0.77 (f tion 35 6 5 20 14 764 11 26 1 10 36 1 1 1 7 0	4960 14 (P = P = 0.44) 339 93 150 189 637 835 209 413 114 229 513 285 194 84 206 149	163 0.26); ² = 56 2 0 43 28 769 7 16 4 15 14 0 7 1 5 14 0 7 1 6 2	4408 = 17% 606 108 76 405 780 835 79 380 118 257 247 516 196 85 428 151	3.0% 0.1% 0.1% 2.0% 5.4% 0.8% 1.3% 0.3% 1.1% 0.0% 0.6% 0.1% 0.3% 0.2%	1.09 [0.86, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.98] 0.92 [0.65, 1.31] 0.57 [0.21, 1.53] 0.57 [0.21, 1.53] 0.57 [0.21, 1.53] 0.52 [0.82, 2.39] 0.74 [0.32, 1.61] 1.51 [0.82, 2.43] 1.51 [0.82, 1.45] 1.51 [0.82, 1.45] 2.47 [0.82, 7.46] 0.21 [0.07, 4.20]	
subtotal (95% C)) idal events idetrogeneity: Chi ² = 16 est for overall effect: 2 .1.3 Myocardial Infarc .1.3 Myocardial Infarc Jaduceili2010 Jillinger2008 juga2012 chiu2009 chong2008 costa2015 Josta2015 Josta2015 Josta2015 esen2013 esen2013 esen2013 esen2013 esen2013 esen2013 esen2013 esen2013 esen2013 esen2013 esen2014 Lindowski and the senatory of the senatory o	239 3.91, df = = 0.77 (f ition 35 6 5 20 14 764 11 26 1 10 36 1 1 10 36 1 1 7 0 44	4960 14 (P = P = 0.44) 339 93 150 189 637 835 209 413 114 229 513 285 194 84 206 194 241	163 0.26); ² = 56 2 0 43 28 769 7 16 4 15 14 15 14 0 7 7 1 6 2 107	4408 = 17% 606 108 76 405 780 835 79 380 118 257 516 196 85 428 151 630	3.0% 0.1% 0.1% 2.0% 2.0% 5.4% 0.3% 1.3% 0.8% 0.3% 0.1% 0.3% 0.3% 0.3%	1.09 [0.86, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.98] 1.00 [0.57, 1.75] 0.60 [0.31, 1.16] 0.92 [0.65, 1.31] 0.57 [0.21, 1.53] 1.53 [0.81, 2.90] 0.25 [0.32, 2.87] 1.54 [0.62, 2.37] 1.64 [0.02, 1.163] 0.14 [0.02, 1.163] 1.01 [0.06, 16.45] 2.47 [0.82, 7.46] 0.20 [0.01, 4.20] 1.22 [0.82, 7.49]	
Jubtotal (95% CI) 'otal events 'otal events 'otal events 'otal events' 'est for overall effect: Z .1.3 Myocardial Infarc Jaiduceili201 Jaiduceili201 Jaiduceili201 Jaiduceili201 Jaiduceili201 Jaiduceili201 Jaiduceili201 Jaiduceili201 Jaiduceili201 Josta2012 Josta2015 Jasch2011 Jasch2013 J	239 6.91, df = = 0.77 (f tion 35 6 5 20 14 764 11 26 1 10 36 1 1 1 7 0	4960 14 (P = P = 0.44) 339 93 150 189 637 835 209 413 114 229 513 285 194 84 206 149	163 0.26); ² = 56 2 0 43 28 769 7 16 4 15 14 0 7 1 5 14 0 7 1 6 2	4408 = 17% 606 108 76 405 780 835 79 380 118 257 247 516 196 85 428 151	3.0% 0.1% 0.1% 2.0% 5.4% 0.8% 1.3% 0.3% 1.1% 0.0% 0.6% 0.1% 0.3% 0.2%	1.09 [0.86, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 1.857] 5.78 [0.32, 105.98] 1.00 [0.57, 1.75] 0.60 [0.31, 1.16] 0.92 [0.65, 1.31] 0.57 [0.21, 1.53] 0.51 [0.21, 1.53] 0.51 [0.22, 1.341] 1.26 [0.66, 2.37] 1.26 [0.27, 1.46] 1.26 [0.27, 1.46] 1.27 [0.32, 1.47] 1.27 [0.32, 1.47] 1.28 [0.32, 1.46] 1.29 [0.32, 1.46] 1.29 [0.32, 1.46] 1.29 [0.32, 1.46] 1.20 [0.32, 1.46] 1.20 [0.32, 1.46] 1.20 [0.32, 1.46] 1.20 [0.32, 1.46] 1.20 [0.32, 1.46] 1.21 [0.3	
subtotal (95% CI) total events teterogeneity: Chi ² = 16 est for overall effect: 2 .1.3 Myocardial Infarc .1.3 Myocardial Infarc salducelii2011 sillinger2008 singuori2011 such2008 sosta2015 besch2011 ranzone2015 ang2013 eseng2013 eseng2013 eseng2013 eseng2013 eseng2013 eseng2013 eseng2013 eseng2013 eseng2013 eseng2013 eseng2013 eseng2013 eseng2013 eseng2013 eseng2014 eseng2009 eseng2014 eseng2009	$\begin{array}{c} 239\\ 5.91, df =\\ = 0.77 \ (f\\ tion\\ 35\\ 6\\ 5\\ 20\\ 14\\ 764\\ 11\\ 26\\ 1\\ 1\\ 10\\ 36\\ 1\\ 1\\ 1\\ 7\\ 7\\ 0\\ 44\\ 2\end{array}$	4960 = 14 (P = P = 0.44) 339 93 150 189 637 209 413 114 229 513 285 194 84 206 149 221 200	163 0.26); ² = 56 2 0 43 28 769 7 16 4 15 14 4 15 14 0 7 1 6 2 107 3	4408 606 108 76 405 780 835 780 835 780 118 257 247 516 85 428 151 196 85 428 151 200	3.0% 0.1% 2.0% 5.4% 0.3% 1.3% 0.3% 1.5% 0.0% 0.6% 0.1% 0.3% 0.2% 3.7%	1.09 [0.86, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.98] 1.00 [0.57, 1.75] 0.60 [0.31, 1.16] 0.92 [0.65, 1.31] 0.57 [0.21, 1.53] 1.53 [0.81, 2.90] 0.25 [0.32, 2.87] 1.54 [0.62, 2.37] 1.64 [0.02, 1.163] 0.14 [0.02, 1.163] 1.01 [0.06, 16.45] 2.47 [0.82, 7.46] 0.20 [0.01, 4.20] 1.22 [0.82, 7.49]	
Jubtotal (95% C)) folal events leterogeneity: Chi ² = 16 fest for overall effect: Z .1.3 Myocardial Infarc Jalducelii/2011 Jillinger2008 Jinguori2011 Jiuguori2011 Jiuguori2012 Jinguori2012 Jinguori2013 Josta2015 Josta2015 Josta2013 Seen2011 Gunzol08 Gunzol03 Seen2011 Gunzol08 Gunzol03 Seen2012 Jillinguori2006 ee2011 Jaeng2009 Jaeng2015	239 3.91, df = 0.77 (f tion 35 6 5 200 14 764 11 266 1 1 10 366 1 1 1 7 0 44 2 3	4960 = 14 (P = P = 0.44) 339 93 150 189 637 835 209 413 114 229 513 114 229 513 114 229 513 194 84 206 149 221 200 77	163 0.26); ² = 56 2 0 43 28 769 7 16 4 15 14 0 7 1 5 14 0 7 1 1 6 2 107 3 0	4408 6066 1088 76 405 7800 380 118 835 79 380 118 257 247 516 196 85 428 151 6300 200 76 428 151 151 151 151 151 151 151 15	3.0% 0.1% 0.1% 2.0% 2.0% 2.0% 3.4% 0.8% 1.3% 0.8% 0.3% 0.1% 0.6% 0.1% 0.2% 3.7% 0.2% 3.7%	1.09 [0.86, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.76 [0.32, 015.98] 1.00 [0.57, 1.75] 0.60 [0.31, 1.16] 0.52 [0.65, 1.31] 0.57 [0.21, 1.53] 0.54 [0.22, 1.67] 1.25 [0.66, 2.37] 0.74 [0.32, 1.67] 1.26 [0.66, 2.37] 0.41 [0.22, 1.64] 1.01 [0.06, 16.45] 1.22 [0.82, 1.79] 0.66 [0.11, 4.01] 1.28 [0.61, 14.15]	
subtotal (95% CI) total events leterogeneity: Chi ² = 16 ses for overall effect: Z .1.3 Myocardial Infarc .1.3 Myocardial Infarc salducelli2010 sillinger2008 singuot2011 such2008 sociat2015 besch2011 ranzone2015 sesen2013 sesen2013 sesen2013 sesen2013 sesen2013 sesen2013 sesen2013 sesen2013 sesen2013 sesen2013 sesen2014 Such2008 Sum2008 Sum2014 Such2008 Sum2014 Such2009 Sum2009 Such2009 Suc	239 9.91, df = 1 35 6 5 5 20 0 4 11 1 10 36 6 1 1 1 1 1 1 7 7 4 4 2 3 3 2 2	4960 : 14 (P = 0.44) 339 93 150 189 93 150 189 403 189 413 114 229 513 194 84 245 194 84 421 200 77 70 108	163 0.26); ² = 56 2 0 0 43 28 769 7 16 4 5 14 0 7 1 6 2 107 3 0 8	4408 4408 606 606 108 76 405 780 835 79 380 118 257 247 516 196 428 151 630 200 76 105	3.0% 0.1% 0.1% 2.0% 2.0% 3.4% 0.3% 1.1% 1.3% 0.3% 0.6% 0.3% 0.3% 0.2% 0.2% 0.2% 0.7%	1.09 [0.86, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 16.57] 5.78 [0.32, 105.98] 1.00 [0.57, 1.75] 0.60 [0.31, 1.16] 0.57 [0.21, 1.53] 0.57 [0.21, 1.53] 0.51 [0.21, 1.53] 0.74 [0.32, 167] 1.26 [0.66, 2.37] 5.45 [0.22, 134.13] 0.14 [0.02, 1.15] 1.01 [0.06, 16.45] 2.47 [0.82, 7.46] 0.22 [0.01, 4.20] 1.22 [0.82, 1.79] 0.66 [0.11, 4.01] 1.29 [0.86, 1.13] 1.29 [0.36, 14.15] 0.23 [0.05, 1.10]	
Lubtota (95% CI) otal events leterogeneity: Chi ^a = 16 est for overall effect: Z .1.3 Myocardial Infarc laiducelli201 lillinger2008 luija2012 luich2008 luija2012 luich2008 luija2012 licha2009 losta2015 losta2015 losta2013 eeng2013 eeng2013 eeng2013 eeng2013 luich2008 lim2008 lim2008 lim2008 lim2018 luich2008 losta2015 laim2009 leteng2015 laikamura2016 losen2014	$\begin{array}{c} 239\\ 9.91, df=0.77 \ (f)\\ 5.5\\ 6.5\\ 5.5\\ 7.64\\ 1.4\\ 1.1\\ 1.1\\ 1.6\\ 1.6\\ 1.6\\ 1.6\\ 1.6\\ 1.6$	4960 14 (P = 0.44) 339 93 150 637 189 637 189 637 209 413 114 229 513 285 513 285 5194 44 206 64 49 221 200 77 108 859	163 0.26); ² = 56 2 0 43 28 769 7 16 4 15 14 0 7 15 14 0 7 1 1 6 2 107 7 3 0 8 21	4408 6066 108 76 405 79 380 835 79 380 835 79 380 835 79 380 835 79 380 835 79 380 835 79 380 835 18 846 846 846 846 846 846 846 84	13.5% 3.0% 0.1% 2.0% 5.4% 0.3% 1.3% 1.3% 0.6% 0.1% 0.3% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2	$\begin{array}{c} 1.09 \left[0.86, 1.36 \right] \\ \hline \\ 1.13 \left[0.72, 1.76 \right] \\ 3.66 \left[0.72, 16.57 \right] \\ \hline \\ 5.76 \left[0.32, 105.98 \right] \\ 1.00 \left[0.57, 1.75 \right] \\ 0.20 \left[0.65, 1.31 \right] \\ \hline \\ 0.57 \left[0.21, 15.31 \right] \\ \hline \\ 1.53 \left[0.81, 2.90 \right] \\ 0.25 \left[0.03, 2.29 \right] \\ \hline \\ 7.4 \left[0.32, 167 \right] \\ 1.26 \left[0.66, 2.37 \right] \\ \hline \\ 2.47 \left[0.82, 164 \right] \\ 0.21 \left[0.66, 2.37 \right] \\ 0.17 \left[0.82, 164 \right] \\ 0.22 \left[0.01, 4.20 \right] \\ 1.22 \left[0.82, 179 \right] \\ 0.23 \left[0.05, 1.19 \right] \\ 0.18 \left[0.21, 179 \right] \\ 0.23 \left[0.05, 1.19 \right] \\ 0.23 \left[0.05, 1.19 \right] \\ 0.23 \left[0.05, 1.19 \right] \\ 0.33 \left[1.29 \right] \\ 0.35 \left[1.33, 1.29 \right] \\ \end{array}$	
ubtotal (95% CI) otal avents leterogeneity: Chi ^a = 16 est for overall effect: Z .1.3 Myocardial Infarc alducelli/2011 iillinger2008 iuja2012 uch2008 uja2012 bito2009 thong2008 osta2015 esch2011 ranzone2015 escn2013 esen2012 escn2013 esen2013 esen2013 esen2013 esen2014 im2008 im2008 im2001 lateng2009 taeng2015 alacmura2016 lesen2014 imeks2013 tankovic2006	$\begin{array}{c} 239\\ 35.91, df = = 0.77 \ (f\\ tion\\ 35\\ 6\\ 6\\ 5\\ 20\\ 14\\ 11\\ 10\\ 36\\ 6\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 0\\ 36\\ 44\\ 4\\ 2\\ 3\\ 2\\ 2\\ 14\\ 6\\ 8\\ 8\\ 8\\ 8\\ 8\\ 8\\ 8\\ 8\\ 8\\ 8\\ 8\\ 8\\ 8\\$	4960 14 (P = 0.44) 339 93 3150 189 637 209 413 113 229 513 285 209 414 229 513 285 194 84 84 84 84 84 85 93 105 105 105 105 105 105 105 105	163 0.26); l ² = 56 2 2 0 43 28 8 7 69 7 7 16 4 4 15 14 15 14 15 10 7 7 1 6 2 2 107 7 3 0 8 8 21 107 11 11	4408 606 108 76 108 76 79 380 118 257 79 380 118 257 516 196 65 428 151 163 0200 76 85 428 151 428 153 428 153 429 163 105 105 105 105 105 105 105 105	13.5% 3.0% 0.1% 2.0% 2.0% 2.0% 2.0% 0.8% 1.3% 0.3% 0.3% 0.3% 0.3% 0.1% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2	$\begin{array}{c} 1.09 \left[0.86, 1.35 \right] \\ \hline \\ 1.13 \left[0.72, 1.76 \right] \\ 3.66 \left[0.72, 16.57 \right] \\ 5.78 \left[0.32, 105.98 \right] \\ 1.00 \left[0.57, 1.75 \right] \\ 0.60 \left[0.31, 1.16 \right] \\ 0.52 \left[0.65, 1.31 \right] \\ 0.57 \left[0.21, 1.53 \right] \\ 0.51 \left[0.22, 1.53 \right] \\ 0.51 \left[0.23, 1.23 \right] \\ 0.51 \left[0.33, 1.29 \right] \\ 0.51 \left[0.33, 1.29 \right] \\ 0.51 \left[0.24, 1.15 \right] \\ 0.51 \left[0.24, 1.15 \right] \\ 0.51 \left[0.23, 1.16 \right] \\ 0.51 \left[0.24, 1.51 \right] \\ 0.51 \left[0.24, 1.53 \right] \\ 0.51$	
subtotal (95% CI) 'otal events 'otal events 'otal events 'otal events 'est for overall effect: Z .1.3 Myocardial Infarc Jaiduceili201	$\begin{array}{c} 239\\ 3.91, df = 0.77 \ (f\\ tion \\ 355 \\ 6 \\ 520 \\ 14 \\ 111 \\ 266 \\ 1 \\ 111 \\ 266 \\ 1 \\ 111 \\ 266 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 2 \\ 2 \\ 2 \\ 14 \\ 4 \\ 2 \\ 2 \\ 14 \\ 8 \\ 59 \end{array}$	4960 114 (P = 0.44) 339 93 150 189 93 150 189 93 150 189 93 150 189 93 150 189 93 150 189 93 150 189 93 150 189 93 150 189 93 150 189 193 150 189 193 150 189 193 150 189 193 150 189 193 150 189 193 150 189 193 150 189 193 193 150 189 193 193 193 193 193 193 193 19	$\begin{array}{c} 163\\ 0.260; \ l^{2}=\\ 566\\ 0\\ 0\\ 43\\ 38\\ 769\\ 7\\ 7\\ 166\\ 4\\ 4\\ 15\\ 14\\ 4\\ 0\\ 7\\ 7\\ 1\\ 6\\ 2\\ 2\\ 107\\ 7\\ 3\\ 0\\ 8\\ 21\\ 11\\ 11\\ 11\\ 142\\ 42\\ \end{array}$	4408 606 108 76 108 76 780 835 780 835 780 118 257 516 196 846 196 800 76 105 846 612 147	13.5% 3.0% 0.1% 0.1% 2.0% 5.4% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.2% 0.3% 0.2% 0.3% 0.2% 0.3% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2	$\begin{array}{c} 1.09 \ [0.86, \ 1.36] \\ \hline \\ 1.13 \ [0.72, \ 1.76] \\ 3.66 \ [0.72, \ 1.857] \\ 5.78 \ [0.32, \ 105.98] \\ 1.00 \ [0.57, \ 1.75] \\ 0.60 \ [0.31, \ 1.16] \\ 0.92 \ [0.65, \ 1.31] \\ 0.57 \ [0.21, \ 1.53] \\ 0.15 \ [0.61, \ 2.16] \\ 0.25 \ [0.03, \ 2.29] \\ 0.74 \ [0.32, \ 1.35] \\ 1.53 \ [0.81, \ 2.90] \\ 0.25 \ [0.03, \ 2.29] \\ 0.74 \ [0.32, \ 1.35] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.65, \ 1.40] \\ 0.23 \ [0.06, \ 1.40] \\ 0.25 \ [0.05, \ 1.40] \\ 0.25 \ [0.05, \ 1.40] \\ 0.25 \ [0.05, \ 1.40] \\ 0.26 \ [0.41, \ 0.33] \\ 0.26 \ [0.67, \ 1.40] \\ 0.66 \ [0.33, \ 1.29] \\ 0.71 \ (0.28, \ 1.41) \\ 0.66 \ [0.67, \ 2.34] \\ 0.86 \ [0.52, \ 1.49] \\ 0.88 \ [0.52, \ 1.49] \end{array}$	
Liubtotal (95% CI) cital events leterogeneity: Chi ² = 16 est for overall effect: 2 .1.3 Myocardial Infarc inducelii2011 lillinger2008 inguon2011 Luch2008 L	$\begin{array}{c} 239\\ 35,91,df=\\ =0.77\ (f\\ tion\\ 35\\ 6\\ 5\\ 20\\ 0\\ 14\\ 764\\ 11\\ 10\\ 36\\ 6\\ 1\\ 1\\ 1\\ 1\\ 1\\ 7\\ 7\\ 0\\ 3\\ 3\\ 2\\ 2\\ 14\\ 8\\ 8\\ 9\\ 1\\ 21\\ \end{array}$	4960 114 (P = 0.44) 339 93 3150 189 637 209 413 113 229 513 285 209 414 229 513 285 194 84 84 84 84 84 85 93 105 105 105 105 105 105 105 105	$\begin{array}{c} 163\\ 0.266); \ P=\\ 566\\ 2\\ 0\\ 0\\ 328\\ 769\\ 7\\ 7\\ 16\\ 4\\ 4\\ 15\\ 14\\ 10\\ 7\\ 7\\ 1\\ 6\\ 2\\ 2\\ 107\\ 7\\ 3\\ 0\\ 0\\ 8\\ 21\\ 111\\ 14\\ 2\\ 2\\ 49 \end{array}$	4408 606 108 76 108 76 79 380 118 257 79 380 118 257 516 196 65 428 151 163 0200 76 85 428 151 428 153 428 153 429 163 105 105 105 105 105 105 105 105	13.5% 3.0% 0.1% 2.0% 2.0% 2.0% 2.0% 0.8% 1.3% 0.3% 0.3% 0.3% 0.3% 0.1% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2	$\begin{array}{c} 1.09 \left[0.86, 1.35 \right] \\ \hline \\ 1.13 \left[0.72, 1.76 \right] \\ 3.66 \left[0.72, 16.57 \right] \\ 5.78 \left[0.32, 105.98 \right] \\ 1.00 \left[0.57, 1.75 \right] \\ 0.60 \left[0.31, 1.16 \right] \\ 0.52 \left[0.65, 1.31 \right] \\ 0.57 \left[0.21, 1.53 \right] \\ 0.51 \left[0.22, 1.53 \right] \\ 0.51 \left[0.23, 1.23 \right] \\ 0.51 \left[0.33, 1.29 \right] \\ 0.51 \left[0.33, 1.29 \right] \\ 0.51 \left[0.24, 1.15 \right] \\ 0.51 \left[0.24, 1.15 \right] \\ 0.51 \left[0.23, 1.16 \right] \\ 0.51 \left[0.24, 1.51 \right] \\ 0.51 \left[0.24, 1.53 \right] \\ 0.51$	
iubtota (95% C)) iotal events iotal events iotal events ieterogeneity: Chi ² = 16 est for overall effect: Z .1.3 Myocardial Infarc ialducelii2001 uinja2011 uinja2012 injuori2011 uinja2012 bihaz0009 bihaz009 bihaz015 sesh2011 ranzone2015 ang2013 seens2011 uinhulakanti2006 ee2011 taeng2009 taeng2015 takamura2016 bisesh2014 immeX2013 taeng2015 takamura2016 oti2010 uintota(16%% C1) vibita vents	$\begin{array}{c} 239\\ 35.91, df=\\ =0.77 \ (fr\ 355\\ 6\\ 5\\ 5\\ 200 \ 14\\ 1764\\ 11\\ 16\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\$	4960 4960 339 93 150 189 93 150 189 93 150 189 93 150 189 93 150 189 93 150 189 93 150 189 93 150 189 93 150 189 93 150 189 193 150 189 193 150 189 193 150 189 193 150 189 193 193 150 189 193 193 150 189 193 193 193 193 193 193 193 19	$\begin{array}{c} 163 \\ 0.26); {}^{p} = \\ 56 \\ 2 \\ 0 \\ 0 \\ 3 \\ 28 \\ 28 \\ 28 \\ 28 \\ 28 \\ 769 \\ 7 \\ 16 \\ 16 \\ 15 \\ 114 \\ 4 \\ 15 \\ 16 \\ 2 \\ 2 \\ 2 \\ 10 \\ 7 \\ 7 \\ 1 \\ 1 \\ 6 \\ 2 \\ 2 \\ 2 \\ 10 \\ 1 \\ 1 \\ 4 \\ 2 \\ 2 \\ 49 \\ 1213 \end{array}$	4408 606 108 76 405 780 805 805 805 805 805 818 8257 79 380 118 257 79 380 118 257 247 516 196 805 815 815 800 800 815 815 815 815 815 815 815 815 815 815	13.5% 3.0% 0.1% 0.1% 2.0% 5.4% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.2% 0.3% 0.2% 0.3% 0.2% 0.3% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2	$\begin{array}{c} 1.09 \ [0.86, \ 1.36] \\ \hline \\ 1.13 \ [0.72, \ 1.76] \\ 3.66 \ [0.72, \ 1.857] \\ 5.78 \ [0.32, \ 105.98] \\ 1.00 \ [0.57, \ 1.75] \\ 0.60 \ [0.31, \ 1.16] \\ 0.92 \ [0.65, \ 1.31] \\ 0.57 \ [0.21, \ 1.53] \\ 0.15 \ [0.61, \ 2.16] \\ 0.25 \ [0.03, \ 2.29] \\ 0.74 \ [0.32, \ 1.35] \\ 1.53 \ [0.81, \ 2.90] \\ 0.25 \ [0.03, \ 2.29] \\ 0.74 \ [0.32, \ 1.35] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.65, \ 1.40] \\ 0.23 \ [0.06, \ 1.40] \\ 0.25 \ [0.05, \ 1.40] \\ 0.25 \ [0.05, \ 1.40] \\ 0.25 \ [0.05, \ 1.40] \\ 0.26 \ [0.41, \ 0.33] \\ 0.26 \ [0.67, \ 1.40] \\ 0.66 \ [0.33, \ 1.29] \\ 0.71 \ (0.28, \ 1.41) \\ 0.66 \ [0.67, \ 2.34] \\ 0.86 \ [0.52, \ 1.49] \\ 0.88 \ [0.52, \ 1.49] \end{array}$	
Jubtotal (95% CI) Total events leterogeneity: Chi ² = 16 est for overall effect: 2 .1.3 Myocardial Infarc .1.3 Myocard .1.3	239 3.91, df = = 0.77 (f 100 355 5 200 14 764 1 1 1 26 6 1 4 764 1 1 1 1 7 0 36 6 1 4 1 1 1 7 0 36 1 4 1 1 1 1 1 1 1 1 1 1 1 1 1	4960 1: 14 (P = 0.44; 339 93 150 189 637 635 229 213 229 513 229 513 229 513 249 221 194 84 84 229 194 194 221 194 195 194 195 194 195 195 195 195 195 195 195 195	163 0.26); ² = 566 2 2 0 3 288 769 9 7 16 4 15 14 0 0 7 7 1 16 2 2 107 7 3 0 8 8 21 111 12 2 2 107 3 3 0.26); ² = 2 (1) 2 (1)	4408 606 108 76 405 780 805 805 805 805 805 818 8257 79 380 118 257 79 380 118 257 247 516 196 805 815 815 800 800 815 815 815 815 815 815 815 815 815 815	13.5% 3.0% 0.1% 0.1% 2.0% 5.4% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.2% 0.3% 0.2% 0.3% 0.2% 0.3% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2	$\begin{array}{c} 1.09 \ [0.86, \ 1.36] \\ \hline \\ 1.13 \ [0.72, \ 1.76] \\ 3.66 \ [0.72, \ 1.857] \\ 5.78 \ [0.32, \ 105.98] \\ 1.00 \ [0.57, \ 1.75] \\ 0.60 \ [0.31, \ 1.16] \\ 0.92 \ [0.65, \ 1.31] \\ 0.57 \ [0.21, \ 1.53] \\ 0.15 \ [0.61, \ 2.16] \\ 0.25 \ [0.03, \ 2.29] \\ 0.74 \ [0.32, \ 1.35] \\ 1.53 \ [0.81, \ 2.90] \\ 0.25 \ [0.03, \ 2.29] \\ 0.74 \ [0.32, \ 1.35] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.65, \ 1.40] \\ 0.23 \ [0.06, \ 1.40] \\ 0.25 \ [0.05, \ 1.40] \\ 0.25 \ [0.05, \ 1.40] \\ 0.25 \ [0.05, \ 1.40] \\ 0.26 \ [0.41, \ 0.33] \\ 0.26 \ [0.67, \ 1.40] \\ 0.66 \ [0.33, \ 1.29] \\ 0.71 \ (0.28, \ 1.41) \\ 0.66 \ [0.67, \ 2.34] \\ 0.86 \ [0.52, \ 1.49] \\ 0.88 \ [0.52, \ 1.49] \end{array}$	
subtotal (95% CI) otala events leterogeneity: Chi ² = 16 lest for overall effect: Z .1.3 Myocardial Infarc laiducelii/2011 lillinger2008 singuori2011 buch2009 bulg2012 buch2009 bulg2012 buch2009 bulg2013 leong2013 leong2013 leong2013 leong2013 leong2013 leong2013 leong2013 leong2013 leong2013 leong2013 leong2013 leong2013 leong2014 lim2008 lim2008 lim2008 lim2008 lim2008 lim2008 lim2008 lim2008 lim2008 lim2008 lim2008 lim2008 lim2008 lim2008 lim2008 lim2008 lim2011 logsm2015 lakamur2016 lakamur2016 lakankovic2006 Volf2010 logtbotal (95% CI) 'otal events leterogeneity: Chi ² = 32 set for overall effect: Z .1.4 Stroke	239 239 35 6 5 5 200 14 11 26 6 5 20 14 11 10 36 6 1 1 10 36 6 1 1 10 36 6 1 1 1 1 7 7 4 4 4 2 3 3 2 2 11 11 10 11 10 11 10 11 10 10 10 10 10	4960 1: 14 (P = 0.44; 339 93 150 189 637 635 229 213 229 513 229 513 229 513 249 221 194 84 84 229 194 194 221 194 195 194 195 194 195 195 195 195 195 195 195 195	163 0.26); ² = 566 2 2 0 3 288 769 9 7 16 4 15 14 0 0 7 7 1 16 2 2 107 7 3 0 8 8 21 111 12 2 2 107 3 3 0.26); ² = 2 (1) 2 (1)	4408 606 108 76 405 780 805 805 805 805 805 818 8257 79 380 118 257 79 380 118 257 247 516 196 805 815 815 800 800 815 815 815 815 815 815 815 815 815 815	13.5% 3.0% 0.1% 0.1% 2.0% 5.4% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.2% 0.3% 0.2% 0.3% 0.2% 0.3% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2	$\begin{array}{c} 1.09 \ [0.86, \ 1.36] \\ \hline \\ 1.13 \ [0.72, \ 1.76] \\ 3.66 \ [0.72, \ 1.857] \\ 5.78 \ [0.32, \ 105.98] \\ 1.00 \ [0.57, \ 1.75] \\ 0.60 \ [0.31, \ 1.16] \\ 0.92 \ [0.65, \ 1.31] \\ 0.57 \ [0.21, \ 1.53] \\ 0.15 \ [0.61, \ 2.16] \\ 0.25 \ [0.03, \ 2.29] \\ 0.74 \ [0.32, \ 1.35] \\ 1.53 \ [0.81, \ 2.90] \\ 0.25 \ [0.03, \ 2.29] \\ 0.74 \ [0.32, \ 1.35] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.66, \ 2.37] \\ 1.26 \ [0.65, \ 1.40] \\ 0.23 \ [0.06, \ 1.40] \\ 0.25 \ [0.05, \ 1.40] \\ 0.25 \ [0.05, \ 1.40] \\ 0.25 \ [0.05, \ 1.40] \\ 0.26 \ [0.41, \ 0.33] \\ 0.26 \ [0.67, \ 1.40] \\ 0.66 \ [0.33, \ 1.29] \\ 0.71 \ (0.28, \ 1.41) \\ 0.66 \ [0.67, \ 2.34] \\ 0.86 \ [0.52, \ 1.49] \\ 0.88 \ [0.52, \ 1.49] \end{array}$	
Jubtotal (95% CI) Total events leterogeneity: Chi ² = 16 est for overall effect: 2 .1.3 Myocardial Infarc .1.3 Myocard .1.3	239 3.91, df = = 0.77 (f 100 355 5 200 14 764 1 1 1 26 6 1 4 764 1 1 1 1 7 0 36 6 1 4 1 1 1 1 7 0 36 1 4 1 1 1 1 1 1 1 1 1 1 1 1 1	4960 4960 339 93 150 189 637 635 239 241 229 513 229 513 249 221 194 84 84 229 513 209 229 513 328 84 84 84 84 85 85 85 85 85 85 85 85 85 85	163 0.26); ² = 566 2 2 0 3 288 769 9 7 16 4 15 14 0 0 7 7 1 16 2 2 107 7 3 0 8 8 21 111 12 2 2 107 3 3 0.26); ² = 2 (1) 2 (1)	4408 606 108 76 405 780 805 805 805 805 805 818 8257 79 380 118 257 79 380 118 257 247 516 196 805 815 815 800 800 815 815 815 815 815 815 815 815 815 815	13.5% 3.0% 0.1% 0.1% 2.0% 5.4% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.2% 0.3% 0.2% 0.3% 0.2% 0.3% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2	$\begin{array}{c} 1.09 \left[0.86, 1.36 \right] \\ \hline 1.13 \left[0.72, 1.76 \right] \\ 3.66 \left[0.72, 16.57 \right] \\ \hline 1.05 \left[0.32, 105.98 \right] \\ \hline 1.00 \left[0.57, 1.75 \right] \\ \hline 1.05 \left[0.21, 105.98 \right] \\ \hline 1.00 \left[0.57, 1.75 \right] \\ \hline 1.53 \left[0.81, 2.90 \right] \\ \hline 0.25 \left[0.65, 1.31 \right] \\ \hline 1.53 \left[0.81, 2.90 \right] \\ \hline 0.74 \left[0.32, 167 \right] \\ \hline 1.26 \left[0.66, 2.37 \right] \\ \hline 2.47 \left[0.82, 7.46 \right] \\ \hline 1.01 \left[0.06, 1.420 \right] \\ \hline 1.22 \left[0.82, 1.79 \right] \\ \hline 0.23 \left[0.51, 1.41 \right] \\ \hline 0.41 \left[0.28, 1.53 \right] \\ \hline 0.41 \left[0.28, 1.63 \right] \\ \hline 1.19 \left[0.36, 1.420 \right] \\ \hline 0.65 \left[0.33, 1.29 \right] \\ \hline 0.74 \left[0.32, 2.44 \right] \\ \hline 0.88 \left[0.52, 2.49 \right] \\ \hline 0.92 \left[0.80, 1.06 \right] \\ \hline 0.92 \left[0.80, 1.06 \right] \\ \hline 1.13 \left[0.32, 3.94 \right] \\ \hline \end{array}$	
subtotal (95% CI) telerogeneity: Chi ² = 16 test for overall effect: Z .1.3 Myocardial Infarc laiducelii201 sillinger2008 sillinger2008 sillinger2008 buja2012 buja2012 binog2008 costa2015 besch2011 ranzone2015 esen2012 sen2013 esen2013 esen2013 esen2013 esen2013 esen2014 sim2008 sim2018 sim2018 sim2008 sim2018 sim2018 sim2018 sim2008 sim2016 lakamura2016 lakam	$\begin{array}{c} 239\\ 239\\ 0.91, df = 0.77 \ (f\\ 0.51\\ 0.5$	4960 4960 339 93 350 93 150 93 150 93 150 93 189 637 209 93 189 637 114 229 913 245 515 515 515 515 515 515 515 5	163 0.26); F = 56 2 2 0 43 3 28 769 7 7 14 4 4 4 4 4 4 0 7 7 11 10 7 7 3 0 0 8 21 11 11 4 2 2 2 2 49 2 20 0.11; F =	4408 606 108 76 108 76 108 76 108 76 108 76 108 835 79 380 118 257 247 7516 85 151 67 828 151 166 168 846 161 2147 8728 5 200 200 76 168 5 846 612 147 8728 5 27%	13.5% 3.0% 0.1% 2.0% 2.0% 2.0% 5.4% 0.8% 1.5% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.4% 0.4% 0.4%	1.09 [0.86, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.98] 5.78 [0.32, 105.98] 1.00 [0.57, 1.75] 0.60 [0.31, 1.16] 0.52 [0.66, 1.31] 1.53 [0.81, 2.90] 0.25 [0.62, 2.31] 1.53 [0.81, 2.90] 0.74 [0.32, 1.67] 1.26 [0.66, 2.37] 0.14 [0.02, 11.51] 1.01 [0.06, 16.45] 0.24 [0.02, 1.41] 0.25 [0.31, 1.29] 0.66 [0.11, 4.01] 0.25 [0.31, 1.29] 0.66 [0.11, 4.01] 0.25 [0.31, 1.29] 0.66 [0.13, 4.15] 0.23 [0.64, 1.16] 0.23 [0.64, 1.23] 0.88 [0.52, 1.49] 0.65 [0.66, 7.23] 0.88 [0.52, 1.49] 0.92 [0.80, 1.06] 1.13 [0.32, 3.94] 1.13 [0.32, 3.94]	
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subtotal (95% CI) stal avents leterogeneity: Chi ² = 16 ses for overall effect: 2 .1.3 Myocardial Infarc .1.3 Myocardial Infarc .1.4 Stroke .1.4 Stro	239 0.91, df = [= 0.77 (f tion 35 6 5 200 14 764 11 1 7 7 7 44 4 8 5 9 5 9 1 21 1 1 1 1 1 1 1 1 1 1 1 1 1	4960 4960 114 (P = 0.44) 339 93 350 837 847 847 114 229 211 200 114 229 211 201 215 1351 115 1351 1351 1351 205 206 207 207 207 207 207 207 207 207	163 0.26); I ² = 56 2 2 0 43 3 88 769 7 7 16 4 4 4 4 4 4 14 0 7 7 16 6 2 2 107 3 0 0 8 8 21 11 11 4 2 2 2 49 1213 7 5 5 7 7 29	4408 4408 606 606 606 608 76 606 108 76 606 108 76 79 380 118 257 247 516 606 106 85 846 106 85 846 612 147 77 8728 227%	13.5% 3.0% 0.1% 2.0% 2.0% 2.0% 5.4% 0.8% 1.5% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.4% 0.4% 0.4%	1.09 [0.86, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.98] 5.78 [0.32, 105.98] 1.00 [0.57, 1.75] 0.60 [0.31, 1.16] 0.52 [0.66, 1.31] 1.53 [0.81, 2.90] 0.25 [0.62, 2.31] 1.53 [0.81, 2.90] 0.74 [0.32, 1.67] 1.26 [0.66, 2.37] 0.14 [0.02, 11.51] 1.01 [0.06, 16.45] 0.24 [0.02, 1.41] 0.25 [0.31, 1.29] 0.66 [0.11, 4.01] 0.25 [0.31, 1.29] 0.66 [0.11, 4.01] 0.25 [0.31, 1.29] 0.66 [0.13, 4.15] 0.23 [0.64, 1.16] 0.23 [0.64, 1.23] 0.88 [0.52, 1.49] 0.65 [0.66, 7.23] 0.88 [0.52, 1.49] 0.92 [0.80, 1.06] 1.13 [0.32, 3.94] 1.13 [0.32, 3.94]	
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iubtota (95% CI) otal events leterogeneity: Chi ² = 16 est for overall effect: Z .1.3 Myocardial Infarc laiduceili201 lillinger2008 iuja2012 liuch2008 luja2012 liuch2008 luja2012 liuch2008 luja2012 liuch2008 luja2013 esen2015 esen2015 esen2013 esen2013 esen2013 esen2013 esen2013 esen2014 limc2008 limc2008 lakamura2016 lakamura2016 lakamura2016 lakamura2016 lakamura2016 lakamura2016 lakamura2016 lakamura2016 lakamura2016 lakamura2016 lakamura2016 lakamura2016 lakamura2016 lakamura2016 lakamura2016 lakamura2016 lakamura2016 leterogeneity: Chi ² = 32 est for overall effect: Z 'total (95% CI) 'total events leterogeneity: Chi ² = 0.1 est for overall effect: Z 'total (95% CI)	239 0.91, df = 0.77 (f tion 35 5 20 0 14 11 1 7 6 5 20 0 14 11 1 7 6 1 1 1 1 1 1 1 1 1 1 1 1 1	$\begin{array}{r} 4960\\ +14 (P =\\ P = 0.44)\\ 339 \\ 93\\ 150\\ 150\\ 189\\ 209\\ 835\\ 209\\ 835\\ 209\\ 835\\ 194\\ 413\\ 114\\ 229\\ 513\\ 124\\ 229\\ 513\\ 2485\\ 194\\ 48\\ 866\\ 149\\ 221\\ 200\\ 1351\\ 113\\ 328\\ 859\\ 1351\\ 113\\ 328\\ 8065\\ 524 (P = 0.26)\\ 229\\ 229\\ 229\\ 2285\\ 859\\ 1373\\ 22(P = 0.26)\\ 137\\ 328\\ 24(P = 0.26)\\ 137\\ 328\\ 24(P = 0.26)\\ 137\\ 328\\ 24(P = 0.26)\\ 137\\ 338\\ 24(P = 0.26)\\ 137\\ 2$	163 0.26); I ² = 56 2 2 0.43 3 28 7 7 1 4 4 4 4 4 4 4 7 7 1 1 6 2 2 2 7 7 107 7 107 7 107 7 29 29 29 41 34); I ² = 0 21 21 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	4408 4408 606 108 76 108 76 108 76 0835 79 380 80 818 257 79 318 257 79 16 6 6 8 5 16 6 8 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6	13.5% 3.0% 0.1% 2.0% 2.0% 2.0% 0.4% 0.3% 0.3% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.4% 0.4% 0.4% 0.4%	1.09 [0.86, 1.35] 1.13 [0.72, 1.76] 3.66 [0.72, 18.57] 5.78 [0.32, 105.98] 1.00 [0.57, 1.75] 0.60 [0.31, 1.16] 0.92 [0.65, 1.31] 0.57 [0.21, 1.53] 1.53 [0.81, 2.90] 0.74 [0.32, 1.67] 1.26 [0.66, 2.37] 5.45 [0.22, 1.34] 1.21 [0.66, 2.37] 5.45 [0.22, 1.34] 1.21 [0.66, 2.37] 5.45 [0.22, 1.34] 1.21 [0.66, 2.37] 5.45 [0.22, 1.34] 1.21 [0.36, 1.45] 0.23 [0.05, 1.10] 0.25 [0.36, 1.410] 0.23 [0.05, 1.10] 0.25 [0.36, 1.40] 0.23 [0.36, 1.40] 0.24 [0.42, 1.30] 0.24 [0.42, 1.30] 0.25 [0.26, 1.40] 0.25 [0.2	
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Figure 5. Comparing the adverse cardiovascular outcomes (part 1). CI = confidence interval, DES = drug-eluting stent, df = degree of freedom, SES = sirolimuseluting stent.

clinical outcomes compared to ZES,^[45] only a follow-up period of 18 months was considered.

4.1. Novelty

This study is new in several ways. First of all, it is among the first meta-analyses comparing SES with other DES using a large number

of patients with diabetes among whom ST is expected to be more prominent after coronary angioplasty. Therefore, this research represents a new idea in clinical medicine. Second, previous metaanalyses comparing different types of DES mainly included patients only from randomized trials. However, this analysis involved a mixture of patients obtained from randomized trials and

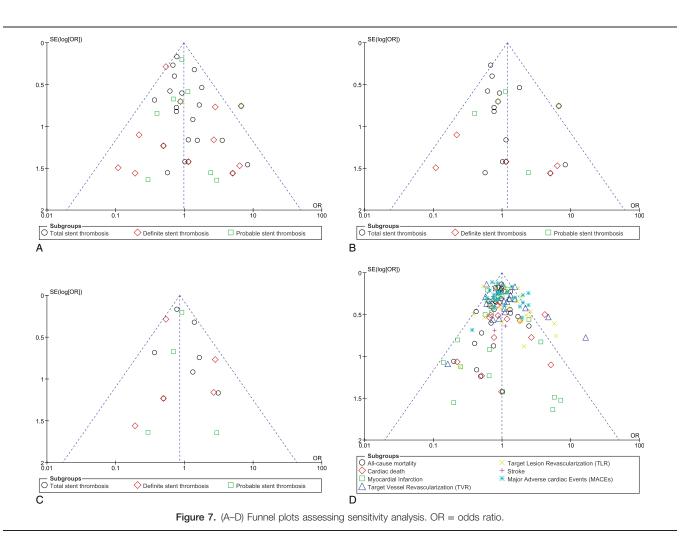
	non-SE	DES	SE	6		Odds Ratio	Odds Ratio
Study or Subgroup	Events		Events	Total	Weight	M-H, Random, 95% C	I M-H, Random, 95% CI
1.1.1 Target Vessel R Balducelli2010	evascular 48	ization 339	(IVR) 88	606	2.2%	0.97 [0.66, 1.42]	
Billinger2008	17	93	10	108	1.2%	2.19 [0.95, 5.06]	
Briguori2011	19	150	9	76	1.2%	1.08 [0.46, 2.52]	
Buch2008	14	189	28	405	1.5%	1.08 [0.55, 2.10]	
Chong2008 Daemen2007	12 24	209 250	5 32	79 206	0.9% 1.7%	0.90 [0.31, 2.65] 0.58 [0.33, 1.02]	
Desch2011	24	114	25	119	1.6%	1.28 [0.70, 2.36]	
Franzone2015	12	229	20	257	1.4%	0.66 [0.31, 1.37]	
Jang2013	37	513	4	247	0.9%	4.72 [1.66, 13.40]	
Jeong2013	25	285	35	516	1.8%	1.32 [0.77, 2.26]	
Jesen2012 Kim m2008	13 6	194 84	21 8	196 85	1.4% 0.8%	0.60 [0.29, 1.23] 0.74 [0.25, 2.23]	
Kim2008	14	206	25	428	1.5%	1.18 [0.60, 2.31]	
Kim2011	1	149	6	151	0.3%	0.16 [0.02, 1.37]	
Kuchulakanti2006	11	221	2	630	0.5%	16.45 [3.62, 74.81]	
Lee2011	28	200	19	200	1.6%	1.55 [0.84, 2.88]	
Maeng2015 Nakamura2016	13 96	108 859	17 64	105 846	1.3% 2.3%	0.71 [0.33, 1.54] 1.54 [1.10, 2.14]	
Olesen2014	10	169	9	168	1.1%	1.11 [0.44, 2.81]	
Simek2013	151	1351	107	612	2.4%	0.59 [0.45, 0.78]	
Stankovic2006	21	113	34	147	1.6%	0.76 [0.41, 1.40]	
Wolf2010	49	328	120	677	2.2%	0.82 [0.57, 1.17]	
Subtotal (95% CI)	650	6353	688	6864	31.7%	1.04 [0.83, 1.31]	Ť
Total events Heterogeneity: Tau ² =	650 0.17: Chi ²	= 62 21		P < 0.00	0001)· I ² =	66%	
Test for overall effect:				. 0.00			
1.1.2 Target Lesion R						0.00 // 00.0	
Billinger2008 Briguori2011	16 21	93 150	8 2	108 76	1.1% 0.5%	2.60 [1.06, 6.38] 6.02 [1.37, 26.41]	
Buja2012	58	637	∠ 65	780	2.2%	1.10 [0.76, 1.60]	
Costa2015	14	413	5	380	0.9%	2.63 [0.94, 7.38]	
Desch2011	14	114	12	118	1.2%	1.24 [0.55, 2.80]	
Franzone2015	11	229	18	257	1.3%	0.67 [0.31, 1.45]	
Jang2013	34	513	3	247	0.8%	5.77 [1.76, 18.99]	
Jeong2013 Jesen2012	26 6	285 194	26 15	516 196	1.7% 1.0%	1.89 [1.08, 3.33] 0.39 [0.15, 1.01]	
Kim m2008	4	84	2	85	0.4%	2.08 [0.37, 11.65]	
Kim2011	1	149	4	151	0.3%	0.25 [0.03, 2.25]	
Kuchulakanti2006	7	221	9	630	1.0%	2.26 [0.83, 6.13]	
Kufner2014	12	76	14	86	1.2%	0.96 [0.42, 2.24]	
Lee2011 Maang2000	24 9	200 77	15 5	200 76	1.5% 0.8%	1.68 [0.85, 3.31]	
Maeng2009 Maeng2015	9	108	10	105	0.8%	1.88 [0.60, 5.89] 0.56 [0.20, 1.60]	
Nakamura2016	81	859	49	846	2.2%	1.69 [1.17, 2.45]	
Olesen2014	6	169	6	168	0.8%	0.99 [0.31, 3.15]	
Sato2012	6	54	8	129	0.8%	1.89 [0.62, 5.74]	
Simek2013	92	1351	73	612	2.3%	0.54 [0.39, 0.75]	
Stankovic2006 Wolf2010	18 49	113 328	27 120	147 677	1.5% 2.2%	0.84 [0.44, 1.62] 0.82 [0.57, 1.17]	
Subtotal (95% CI)	40	6417	120	6590	26.9%	1.25 [0.95, 1.64]	
Total events	515		496				
Heterogeneity: Tau ² =				P < 0.00	0001); l² =	68%	
Test for overall effect:	∠ = 1.58 (F	- = 0.11	,				
1.1.3 Major Adverse	cardiac Ev	ents (M	IACEs)				
Balducelli2010	86	339	148	606	2.4%	1.05 [0.77, 1.43]	
Billinger2008	24	93	16	108	1.4%	2.00 [0.99, 4.05]	
Briguori2011	40 25	150 189	10 59	76 405	1.3%	2.40 [1.13, 5.12] 0.89 [0.54, 1.48]	
Buch2008 Buja2012	25 129	637	59 178	405 780	1.9% 2.5%	0.89 [0.54, 1.48]	
Chong2008	21	209	10	79	1.3%	0.77 [0.35, 1.72]	
Costa2015	62	413	26	380	1.9%	2.40 [1.49, 3.89]	
Daemen2007	53	250	60	206	2.1%	0.65 [0.43, 1.00]	
Franzone2015 Jang2013	29 74	229 513	41 19	257 247	1.9% 1.8%	0.76 [0.46, 1.28] 2.02 [1.19, 3.43]	
Jeong2013	26	285	50	247 516	1.8%	0.94 [0.57, 1.54]	
Jesen2012	20	194	31	196	1.7%	0.61 [0.34, 1.12]	
Kim2008	29	206	52	428	1.9%	1.18 [0.73, 1.93]	
Kim2011	3	149	8	151	0.6%	0.37 [0.10, 1.41]	
Kuchulakanti2006 Kufner2014	27	221	86 17	630	2.0%	0.88 [0.55, 1.40]	
Lee2011	16 32	76 200	17 22	86 200	1.3% 1.7%	1.08 [0.50, 2.33] 1.54 [0.86, 2.76]	
Maeng2009	11	77	6	76	0.9%	1.94 [0.68, 5.56]	
Maeng2015	22	108	25	105	1.6%	0.82 [0.43, 1.57]	
Nakamura2016	95	859	69	846	2.3%	1.40 [1.01, 1.94]	
Olesen2014 Sate2012	21	169	23	168	1.6%	0.89 [0.47, 1.69]	
Sato2012 Simek2013	13 245	54 1351	19 144	129 612	1.3% 2.5%	1.84 [0.83, 4.05] 0.72 [0.57, 0.91]	
Stankovic2006	245	113	36	147	2.5%	0.75 [0.41, 1.36]	
Subtotal (95% CI)		7084		7434	41.4%	1.06 [0.90, 1.25]	
Total events	1125		1155				
Heterogeneity: Tau ² = Test for overall effect:				P < 0.00	001); l ² = 6	2%	
rest for overall effect:	∠ = 0.70 (F	- = 0.49	,				
Total (95% CI)		19854		20888	100.0%	1.10 [0.97, 1.24]	•
Total events	2290		2339				
Heterogeneity: Tau ² =				(P < 0.0	00001); l² =	= 65%	0.01 0.1 1 10 100
Test for overall effect: Test for subgroup diffe				P = 0 54	3) $ ^2 = 0^{0/2}$		Favours [non-SE DES] Favours [SES]
. sacior subgroup une		a = 1.0	o, ui = 2 (. – 0.30	-,, - 0 /0		

Figure 6. Comparing the adverse cardiovascular outcomes (part 2). CI = confidence interval, DES = drug-eluting stent, df = degree of freedom, SES = sirolimuseluting stent.

observational studies representing another new feature. In addition, this meta-analysis compared ST and the other adverse cardiovascular outcomes between 6 months and 5 years follow-up. Total, definite, and probable STs were also analyzed during a follow-up period ranging from 6 months to 2 years, and a long-term follow-up >2 years showing another new feature in this study.

4.2. Limitations

This study also has several limitations. First of all, the inclusion of data from observational studies is believed to be associated with a high risk of bias. Therefore, an increased level of heterogeneity was observed when analyzing several subgroups of adverse cardiovascular outcomes. This could also have been due to the



comparison of SES with different types of DES (non-SE DES) combined together. Moreover, PES that were dominating among the non-SE DES could also represent a major limitation in this study.

5. Conclusions

During this particular follow-up period, SES were not associated with any increase in ST among these patients with T2DM. Mortality and other adverse cardiovascular outcomes were also not significantly different between these 2 groups. Hence, SES should be considered neither superior nor inferior to other DES. They are expected to be equally effective and safe to use in patients with T2DM.

References

- Wei CC, Shyu KG, Cheng JJ, et al. Diabetes and Adverse Cardiovascular Outcomes in Patients with Acute Coronary Syndrome - Data from Taiwan's Acute Coronary Syndrome Full Spectrum Data Registry. Zhonghua Minguo Xin Zang Xue Hui Za Zhi 2016;32:31–8.
- [2] Iijima R, Byrne RA, Dibra A, et al. Drug-eluting stents versus bare-metal stents in diabetic patients with ST-segment elevation acute myocardial infarction: a pooled analysis of individual patient data from seven randomized trials. Rev Esp Cardiol 2009;62:354–64.
- [3] De Luca G, Dirksen MT, Spaulding C, et al. for the DESERT cooperationImpact of diabetes on long-term outcome after primary angioplasty: insights from the DESERT cooperation. Diabetes Care 2013;36:1020–5.

- [4] Lee SW, Park SW, Kim YH, et al. A randomized comparison of sirolimusversus paclitaxel-eluting stent implantation in patients with diabetes mellitus. J Am Coll Cardiol 2008;52:727–33.
- [5] Ong AT, Aoki J, van Mieghem CA, et al. Comparison of short- (one month) and long- (twelve months) term outcomes of sirolimus- versus paclitaxel-eluting stents in 293 consecutive patients with diabetes mellitus (from the RESEARCH and T-SEARCH registries). Am J Cardiol 2005;96:358–62.
- [6] Bundhun PK, Pursun M, Teeluck AR, et al. Are everolimus-eluting stents associated with better clinical outcomes compared to other drug-eluting stents in patients with type 2 diabetes mellitus?: A systematic review and meta-analysis. Medicine (Baltimore) 2016;95:e3276.
- [7] de Waha A , Dibra A, Byrne RA, et al. Everolimus-eluting versus sirolimus-eluting stents: a meta-analysis of randomized trials. Circ Cardiovasc Interv 2011;4:371–7.
- [8] Cutlip DE, Windecker S, Mehran R, et al. Academic Research ConsortiumClinical end points in coronary stent trials: a case for standardized definitions. Circulation 2007;115:2344–51.
- [9] Wiley, Higgins JPT, Altman DG. Higgins JPT, Green S. Assessing risk of bias in included studies. Cochrane Handbook for Systematic Reviews of Interventions 2008;187–241.
- [10] Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 2009;339: b2700.
- [11] Billinger M, Beutler J, Taghetchian KR, et al. Two-year clinical outcome after implantation of sirolimus-eluting and paclitaxel-eluting stents in diabetic patients. Eur Heart J 2008;29:718–25.
- [12] Briguori C, Airoldi F, Visconti G, et al. Novel approaches for preventing or limiting events in diabetic patients (Naples-diabetes) trial: a randomized comparison of 3 drug-eluting stents in diabetic patients. Circ Cardiovasc Interv 2011;4:121–9.

- [13] Buch AN, Javaid A, Steinberg DH, et al. Outcomes after sirolimus- and paclitaxel-eluting stent implantation in patients with insulin-treated diabetes mellitus. Am J Cardiol 2008;101:1253–8.
- [14] Chong E, Poh KK, Liang S, et al. Eighteen-month clinical safety and efficacy outcomes of sirolimus-, paclitaxel- and zotarolimus-drug eluting stents in diabetic patients undergoing percutaneous coronary intervention for complex coronary artery stenosis. Ann Acad Med Singapore 2010;39:381–4.
- [15] Costa JRJr, Sousa A, Moreira AC, et al. Drug-eluting stents in the elderly: long-term (>one year) clinical outcomes of octogenarians in the DESIRE (Drug-Eluting Stents In the REal world) registry. J Invasive Cardiol 2008;20:404–10.
- [16] Desch S, Schloma D, Möbius-Winkler S, et al. Randomized comparison of a polymer-free sirolimus-eluting stent versus a polymer-based paclitaxel-eluting stent in patients with diabetes mellitus: the LIPSIA Yukon trial. JACC Cardiovasc Interv 2011;4:452–9.
- [17] Franzone A, Pilgrim T, Heg D, et al. Clinical outcomes according to diabetic status in patients treated with biodegradable polymer sirolimuseluting stents versus durable polymer everolimus-eluting stents: prespecified subgroup analysis of the BIOSCIENCE trial. Circ Cardiovasc Interv 2015;8:
- [18] Jensen LO, Thayssen P, Junker A, et al. Comparison of outcomes in patients with versus without diabetes mellitus after revascularization with everolimus- and sirolimus-eluting stents (from the SORT OUT IV trial). Am J Cardiol 2012;110:1585–91.
- [19] Kedhi E, Gomes ME, Lagerqvist B, et al. Clinical impact of secondgeneration everolimus-eluting stent compared with first-generation drugeluting stents in diabetes mellitus patients: insights from a nationwide coronary intervention register. JACC Cardiovasc Interv 2012;5:1141–9.
- [20] Kim JS, Lee BH, Ko YG, et al. Korean Multicenter Angioplasty Team (KOMATE) InvestigatorsComparison of sirolimus-eluting stent and paclitaxel-eluting stent for long-term cardiac adverse events in diabetic patients: the Korean Multicenter Angioplasty Team (KOMATE) Registry. Catheter Cardiovasc Interv 2008;72:601–7.
- [21] Kim WJ, Lee SW, Park SW, et al. ESSENCE-DIABETES Study InvestigatorsRandomized comparison of everolimus-eluting stent versus sirolimus-eluting stent implantation for de novo coronary artery disease in patients with diabetes mellitus (ESSENCE-DIABETES): results from the ESSENCE-DIABETES trial. Circulation 2011;124:886–92.
- [22] Kuchulakanti PK, Chu WW, Torguson R, et al. Sirolimus-eluting stents versus paclitaxel-eluting stents in the treatment of coronary artery disease in patients with diabetes mellitus. Am J Cardiol 2006;98:187–92.
- [23] Kufner S, Byrne RA, de Waha A, et al. Intracoronary Stenting and Angiographic Results: Drug Eluting Stents for In-Stent Restenosis 2 (ISAR-DESIRE 2) InvestigatorsSirolimus-eluting versus paclitaxel-eluting stents in diabetic and non-diabetic patients within sirolimus-eluting stent restenosis: results from the ISAR-DESIRE 2 trial. Cardiovasc Revasc Med 2014;15:69–75.
- [24] Lee SW, Park SW, Kim YH, et al. A randomized comparison of sirolimusversus paclitaxel-eluting stent implantation in patients with diabetes mellitus: 4-year clinical outcomes of DES-DIABETES (drug-eluting stent in patients with DIABETES mellitus) trial. JACC Cardiovasc Interv 2011;4:310–6.
- [25] Maeng M, Jensen LO, Galloe AM, et al. Comparison of the sirolimuseluting versus paclitaxel-eluting coronary stent in patients with diabetes mellitus: the diabetes and drug-eluting stent (DiabeDES) randomized angiography trial. Am J Cardiol 2009;103:345–9.
- [26] Maeng M, Baranauskas A, Christiansen EH, et al. A 10-month angiographic and 4-year clinical outcome of everolimus-eluting versus sirolimus-eluting coronary stents in patients with diabetes mellitus (the DiabeDES IV randomized angiography trial). Catheter Cardiovasc Interv 2015;86:1161–7.
- [27] Nakamura M, Muramatsu T, Yokoi H, et al. J-DESSERT Investigators-Three-year follow-up outcomes of SES and PES in a randomized controlled study stratified by the presence of diabetes mellitus: J-DESSERT trial. Int J Cardiol 2016;208:4–12.

- [28] Olesen KK, Tilsted HH, Jensen LO, et al. Long-term outcome of sirolimus-eluting and zotarolimus-eluting coronary stent implantation in patients with and without diabetes mellitus (a Danish organization for randomized trials on clinical outcome III substudy). Am J Cardiol 2015;115:298–302.
- [29] Simsek C, Räber L, Magro M, et al. Long-term outcome of the unrestricted use of everolimus-eluting stents compared to sirolimuseluting stents and paclitaxel-eluting stents in diabetic patients: the Bern-Rotterdam diabetes cohort study. Int J Cardiol 2013;170:36–42.
- [30] Stankovic G, Cosgrave J, Chieffo A, et al. Impact of sirolimus-eluting and paclitaxel-eluting stents on outcome in patients with diabetes mellitus and stenting in more than one coronary artery. Am J Cardiol 2006;98:362–6.
- [31] Wolf WM, Vlachos HA, Marroquin OC, et al. Paclitaxel-eluting versus sirolimus-eluting stents in diabetes mellitus: a report from the National Heart, Lung, and Blood Institute Dynamic Registry. Circ Cardiovasc Interv 2010;3:42–9.
- [32] Chiu M, Ko DT, Austin PC, et al. Paclitaxel versus sirolimus stents in diabetic and nondiabetic patients. Circ Cardiovasc Qual Outcomes 2009;2:96–107.
- [33] Daemen J, Garcia-Garcia HM, Kukreja N, et al. The long-term value of sirolimus- and paclitaxel-eluting stents over bare metal stents in patients with diabetes mellitus. Eur Heart J 2007;28:26–32.
- [34] Jang SJ, Park DW, Kim WJ, et al. Differential long-term outcomes of zotarolimus-eluting stents compared with sirolimus-eluting and paclitaxel-eluting stents in diabetic and nondiabetic patients: two-year subgroup analysis of the ZEST randomized trial. Catheter Cardiovasc Interv 2013;81:1106–14.
- [35] Sato T, Ono T, Morimoto Y, et al. Differences in clinical and angiographic outcomes with different drug-eluting stents in Japanese patients with and without diabetes mellitus. J Cardiol 2012;60: 361–6.
- [36] Balducelli M, Ortolani P, Marzaroli P, et al. Comparison of 2-year clinical outcomes with sirolimus and paclitaxel-eluting stents for patients with diabetes: results of the Registro Regionale AngiopLastiche Emilia-Romagna Registry. Catheter Cardiovasc Interv 2010;75: 327–34.
- [37] Buja P, Facchin M, Musumeci G, et al. Paclitaxel- and sirolimus-eluting stents in older patients with diabetes mellitus: results of a real-life multicenter registry. Catheter Cardiovasc Interv 2013;81:1117–24.
- [38] Jeong HS, Cho JY, Kim EJ, et al. Comparison of clinical outcomes between first-generation and second-generation drug-eluting stents in type 2 diabetic patients. Coron Artery Dis 2013;24:676–83.
- [39] Kim MH, Hong SJ, Cha KS, et al. Effect of paclitaxel-eluting versus sirolimus-eluting stents on coronary restenosis in Korean diabetic patients. J Interv Cardiol 2008;21:225–31.
- [40] Mahmud E, Bromberg-Marin G, Palakodeti V, et al. Clinical efficacy of drug-eluting stents in diabetic patients: a meta-analysis. J Am Coll Cardiol 2008;51:2385–95.
- [41] Kufner S, de Waha A, Tomai F, et al. A meta-analysis of specifically designed randomized trials of sirolimus-eluting versus paclitaxel-eluting stents in diabetic patients with coronary artery disease. Am Heart J 2011;162:740–7.
- [42] Zhang F, Dong L, Ge J. Meta-analysis of five randomized clinical trials comparing sirolimus- versus paclitaxel-eluting stents in patients with diabetes mellitus. Am J Cardiol 2010;105:64–8.
- [43] Yan P, Dong P, Li Z. Second- versus first-generation drug-eluting stents for diabetic patients: a meta-analysis. Arch Med Sci 2014;10:213–21.
- [44] Bangalore S, Kumar S, Fusaro M, et al. Outcomes with various drug eluting or bare metal stents in patients with diabetes mellitus: mixed treatment comparison analysis of 22,844 patient years of follow-up from randomised trials. BMJ 2012;345:e5170.
- [45] Maeng M, Jensen LO, Tilsted HH, et al. Outcome of sirolimus-eluting versus zotarolimus-eluting coronary stent implantation in patients with and without diabetes mellitus (a SORT OUT III substudy). Am J Cardiol 2011;108:1232–7.