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# Impact of Modifiable Cardiovascular Risk Factors on Mortality After Percutaneous Coronary Intervention

A Systematic Review and Meta-Analysis of 100 Studies

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**Abstract:** Modifiable cardiovascular risk factors such as obesity, hypertension, dyslipidemia, smoking, diabetes mellitus, and metabolic syndrome can easily give rise to coronary heart disease (CHD). However, due to the existence of the so-called "obesity paradox" and "smoking paradox," the impact of these modifiable cardiovascular risk factors on mortality after percutaneous coronary intervention (PCI) is still not clear.

Therefore, in order to solve this issue, we aim to compare mortality between patients with low and high modifiable cardiovascular risk factors after PCI.

Medline and EMBASE were searched for studies related to these modifiable cardiovascular risk factors. Reported outcome was all-cause mortality after PCI. Risk ratios (RRs) with 95% confidence intervals (CIs) were calculated, and the pooled analyses were performed with RevMan 5.3 software.

A total of 100 studies consisting of 884,190 patients (330,068 and 514,122 with high and low cardiovascular risk factors respectively) have been included in this meta-analysis. Diabetes mellitus was associated with a significantly higher short and long-term mortality with RR 2.11; 95% CI: (1.91–2.33) and 1.85; 95% CI: (1.66–2.06), respectively, after PCI. A significantly higher long-term mortality in the hypertensive and metabolic syndrome patients with RR 1.45; 95% CI: (1.24–1.69) and RR 1.29; 95% CI: (1.11–1.51), respectively, has also been observed. However, an unexpectedly, significantly lower mortality risk was observed among the smokers and obese patients.

Certain modifiable cardiovascular risk subgroups had a significantly higher impact on mortality after PCI. However, mortality among the obese patients and the smokers showed an unexpected paradox after coronary intervention.

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**Abbreviations**: BMI = body mass index, CAD = coronary artery disease, DM = diabetes mellitus, LDL = low-density lipoprotein, MS = metabolic syndrome, PCI = percutaneous coronary intervention.

## INTRODUCTION

oronary heart disease, also known as coronary artery disease (CAD), is the most common type of heart disease in the elderly. Almost all over the world, it is the number 1 cause of death in both men and women. From the year 1990 to 2013, there has been a rise from 5.74 to 8.14 million deaths from CAD globally.<sup>1</sup> There are many risk factors associated with CAD. These risk factors include hypertension, dyslipidemia, smoking, obesity, old age, family history, diabetes mellitus (DM), and metabolic syndrome (MS).<sup>2</sup> These risk factors can still be subdivided into modifiable and nonmodifiable risk factors. Modifiable risk factors are those that can be changed; or simply, if careful precautions are taken, the risk for developing CAD will be lower in the susceptible population. For example, eating a healthy diet, doing regular exercises, avoiding smoking, and maintaining a healthy weight are all safety measures which can help to prevent CAD.<sup>3,4</sup> Except old age and a family history with cardiovascular disorders, factors such as a high body mass index (BMI), hypertension, dyslipidemia, smoking, DM, and MS are all considered as modifiable cardiovascular risk factors.

Unfortunately, because of the unhealthy lifestyle adopted by people nowadays, they finally end up with conditions which expose them to a high risk for CAD. When symptoms become more severe, or intolerable, and when medications become ineffective, percutaneous coronary intervention (PCI) proves to be the most common invasive treatment in these patients.<sup>5</sup> However, due to the presence of the so-called phenomenon "obesity paradox" and "smoking paradox" whereby the mortality rate in the obese patients and smokers is unexpectedly lower compared to the normal weight patients and nonsmokers, respectively, the impact of these modifiable cardiovascular risk factors on mortality after PCI is still not clear. Therefore, in order to solve this issue, we aim to compare the short- and longterm mortality in patients with low and high modifiable cardiovascular risk factors after PCI.

## **METHODS**

## **Data Sources and Search Strategy**

Medline and EMBASE were searched for randomized controlled trials (RCTs) and observational studies by typing the words or phrases "X and percutaneous coronary intervention/PCI" whereby X was interchangeable with these modifiable cardiovascular risk factors such as smoking, overweight/obesity/high BMI, hypertension, hyperlipidemia/hypercholesterolemia/high-density lipoprotein (HDL)/low-density lipoprotein (LDL), DM, and MS. To further enhance this search, the term "angioplasty" has also been used to replace PCI and the words "smoking paradox" and "obesity paradox" have been used to replace smoking and obesity, respectively. No language restriction was applied.

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#### Inclusion and Exclusion Criteria

Studies were included if:

- (1) They were RCTs or observational studies relating these modifiable cardiovascular risk factors with PCI.
- (2) They reported mortality among their clinical endpoints.
- (3) They included data for both the experimental and the control groups. For example, DM and non-DM, smokers and nonsmokers, overweight/obese and nonobese/normal weight, MS and non-MS, hypertensive and normotensive patients, increased LDL and normal/low LDL, or decreased high density lipoprotein (HDL) and increased HDL.

Studies were excluded if:

- (1) They did not include these modifiable cardiovascular risk factors.
- (2) They were meta-analyses, case studies, or letter to editors.
- (3) No control group was present.
- (4) Mortality was not among the reported endpoints.
- (5) Duplicates.

## **Types of Participants**

All the patients were >18 years old and suffered from CAD. Enrolled patients in the experimental group had at least 1 modifiable cardiovascular risk factor (diabetes, MS, high BMI, dyslipidemia, cigarette smoking, or hypertension) whereas those patients in the control group did not suffer from the risk factor being analyzed in the corresponding subgroups. All patients underwent PCI.

## Definitions, Outcomes, and Follow-Up Periods

Modifiable Cardiovascular Risk Factors: defined as cardiovascular risk factors that can be controlled or if prevented, can result in a lower risk of suffering from CAD. In our studies, these patients were considered as high risk patients. Low risk patients, who acted as controls for this meta-analysis, were those without these modifiable cardiovascular risk factors.

DM: defined as a fasting blood glucose (FBG) level of >7.0 mmol/L or an oral glucose tolerance test (OGTT) >11.1 mmol/L observed at least on 2 different occasions.

Overweight and obese: BMI of >25 and  $>30 \text{ kg/m}^2$ , respectively.

Hypertension: a blood pressure of >130/80 mmHg on at least 2 separate occasions.

Dyslipidemia: defined as an LDL level of (>130 mg/dL) or an HDL level of (<40 mg/dL). A borderline value was already considered as dyslipidemia in this study.

MS: a condition diagnosed if at least 3 of the followings were present: central obesity, high blood pressure, high fasting plasma glucose, high serum triglyceride, and low-highdensity lipoproteins.

Smoking: included current smokers and late nonsmokers. Quitters, former smokers, pre- and post-PCI smoking quitters have not been included in the study.

In-hospital mortality: included all-cause deaths during the hospital stay ( $\leq$ 30 days).

Short-term mortality: included all-cause deaths during a follow-up period from 30 days to 1 year after PCI.

Long-term mortality: included all-cause deaths during a follow-up period at 1 year or more than 1 year after PCI.

## Data Extraction and Quality Assessment

Two authors (PKB and ZW) independently reviewed the data and assessed the eligibility and methodological quality of each eligible study. Information and data regarding the number of patients and patient characteristics, associated risk factors, intervention strategies, and the clinical outcomes, and respective follow-up periods (in-hospital, short-term, and long-term) were systematically extracted. If any of the 2 authors disagreed about the information or data extracted, disagreements were discussed between the authors, and if the authors could not reach a final decision, disagreements were resolved by the 3rd author (MHC). The bias risk of trials was assessed with the components recommended by the Cochrane Collaboration.<sup>6</sup>

#### Methodological Quality and Statistical Analysis

Study selection, data collection, analysis, and reporting of the results were performed using the recommendations of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. Heterogeneity across trials was assessed using the Cochrane Q-statistic ( $P \le 0.05$  was considered significant) and I<sup>2</sup>-statistic. I<sup>2</sup> described the percentage of total variation across studies, that is, due to heterogeneity rather than chance. A value of 0% indicated no heterogeneity, and larger values indicated increased heterogeneity. If I<sup>2</sup> was <50%, fixed effect model was used. However, if I<sup>2</sup> was >50%, a random effect model was used. Publication bias was visually estimated by assessing funnel plots. We calculated risk ratios (RRs) and 95% confidence intervals (CIs) for categorical variables. The pooled analyses were performed with RevMan 5.3 software. Since this is a systematic review and metaanalysis, ethical approval was not required.

## RESULTS

#### Selection of Studies for This Meta-Analysis

A total of 7456 articles were identified from search databases, and 32 articles were identified from references. After excluding the 1120 duplicates, 6030 articles were excluded by title and abstract since they were not related to our topic. Among the remaining articles, 79 were related to obesity, 142 to diabetes, 25 to MS, 36 to dyslipidemia, 29 to smoking, and 27 were related to hypertension. A total of 338 full text articles were assessed for eligibility. More articles were excluded since they were meta-analyses, case studies, data for the control group were not available, outcomes of interest were not reported and also dichotomous data which were very important for our statistical analysis were not provided. The flow diagram for the selection of studies has been represented in Figure 1.

A total number of 100 articles from randomized controlled trials and observational studies have been included in this metaanalysis with a total number of 844,190 patients to be analyzed; among which, 330,068 patients were in the experimental group while 514,122 were in the control group. The total number of patients associated with the corresponding risk factors from this whole study have been given in Tables 1 and 2 shows the total number of patients in all the different subgroups (for both the experimental and control groups) as well as their follow-up periods.

Among these 330,068 patients analyzed in the experimental group, 76.2% had hypertension, 24% were smokers, 50.3% had dyslipidemia, 65.5% were overweight or obese, 1.5% had MS, and 47.6% had DM.

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FIGURE 1. Shows the flow diagram for the study selection.

Considering this whole study, pure data for only 27,415 (10.9%) hypertensive patients, 14,507 (18.3%) smokers, 15,008 (9.03%) patients with dyslipidemia, 215,834 (99.9%) patients with high BMI, 4741 (94.8%) patients with MS, and 52,563 (33.4%) patients with DM were available for subgroup analysis. Note that data which were not available in the original articles have been omitted.

Table 2 has been divided into different subgroups of modifiable cardiovascular risk factors. Total number of patients in the experimental group, control group as well as the total number of patients in each study with their follow-up periods have been given in Table 2. Five studies dealt with hypertension, 8 studies dealt with smoking, 6 studies dealt with dyslipidemia, 9 studies dealt with MS, 23 studies dealt with high

**TABLE 1.** An Approximation<sup>\*</sup> of the number of patients corresponding to these modifiable risk factors throughout this whole meta-analysis

Features	Number of Patients (n)			
Patients in this study	844,190			
Patients in the experimental group	330,068	39.1%		
Patients in the control group	514,122	60.9%		
Modifiable cardiovascular risk factors in the experiment group	Number of patients analyzed/number of patients with corresponding risk factor in whole study			
Hypertension	27,415/251,567	10.9%		
Smoking	14,507/79,205	18.3%		
Dyslipidemia	15,008/166,173	9.03%		
Overweight and obesity	215,834/216,041	99.9%		
Metabolic syndrome	4741/4999	94.8%		
Diabetes	52,563/157,160	33.4%		

\* These data were calculated according to data provided in these 100 studies. The data concerning the number of patients with their corresponding risk factor in the whole study were also obtained from the baseline features of each study. However, studies without dichotomous data at baseline, or if corresponding data were not available, have been omitted from this count. Therefore, except the data analyzed, the count for "modifiable cardiovascular risk factors for the whole study" is just an approximation for this study.

Study	Hypertensive Patients (n)	Normotensive Patients (n)	Total No of Patients (n)	Follow-Up Period
Lee 2012 <sup>7</sup>	1218	1220	2438	In hospital, short and Long-term
Lingman 20118	22,499	20,673	43,172	Short-term
Luca 20139	700	962	1662	Short-term
Luca 2014 <sup>10</sup>	2764	3522	6286	Long-term
Rembek 2010 <sup>11</sup>	234	132	366	In hospital
Study	Smoker (n)	Nonsmoker (n)	Total no of patients (n)	Follow-up period
Arbel 2014 <sup>12</sup>	3201	1363	4564	Short and long-term
Chen 2012 <sup>13</sup>	4049	7611	11 660	Long-term
Goto 2011 <sup>14</sup>	1563	1765	3328	Short and long-term
Lin 2013 <sup>15</sup>	147	226	373	Long term
Mahamadali 2012 <sup>16</sup>	259	501	750	Short torm
Robertson 2014 <sup>17</sup>	2042	0614	12 557	Short and long town
Top 2014 <sup>18</sup>	3943	9014	15,557	Short and long-term
Tan 2014	448	603	1051	Short and long-term
weisz 2015	898	638	1536	Short and long-term
Study	Dyslipidemia (n)	Normal lipids (n)	Total no of patients (n)	Follow-up period
Cho 2010 <sup>20</sup>	3284	6287	9571	In hospital, short and Long-term
Ghazzal 2009 <sup>21</sup>	2113	1975	4088	Long-term
Izuhara 2015 <sup>22</sup>	3838	6553	10,391	Long-term
Ji 2015 <sup>23</sup>	4030	5026	9056	In hospital, short-term
Kini 2009 <sup>24</sup>	1521	2095	3616	Long-term
Seo 2011 <sup>25</sup>	1585	1108	2693	Long-term
Study	Metabolic syndrome (n)	Nonmetabolic syndrome (n)	Total no of patients (n)	Follow-up period
Butler 2006 <sup>26</sup>	1169	1866	3035	Short-term
Kasai 2006 <sup>27</sup>	318	430	748	Long-term
Kasai 2008 <sup>28</sup>	318	430	748	Long-term
Kim 2010 <sup>29</sup>	170	168	338	Short and long-term
Lee $2015^{30}$	570	333	903	Long-term
Maron 2011 <sup>31</sup>	1262	996	2249	Long term
Marca 2012 <sup>32</sup>	220	424	672	Long-term
Marso $2012$	239	434	0/3	Long-term
Patsa 2013 $^{-1}$	14/	364	511	Long-term
Rana 2005	448	453	901	Short-term
Study	Overweight and obese (n)	Normal and underweight (n)	Total no of patients (n)	Follow-up period
Akin 2012 <sup>33</sup>	4370	1436	5806	In hospital, short-term
Ellis 1996 <sup>30</sup>	2841	614	3455	In hospital
Gruberg 2002 <sup>37</sup>	7710	1923	9633	In hospital and long-term
Gruberg 2005 <sup>38</sup>	431	168	599	Long-term
Gurm 2002 <sup>39</sup>	1553	537	2090	Long-term
He 2015 <sup>40</sup>	528	549	1077	In hospital and long-term
Kaneko 201341	473	732	1205	Long-term
Kang 200942	2442	1382	3824	In hospital, short and Long-term
Kosuge 2008 <sup>43</sup>	980	2096	3076	In hospital
Lancefield 201044	3442	1320	4762	In hospital, short and long-term
Mehta 200745	1622	703	2325	In hospital and long-term
Minutello 200446	69 501	25 934	95 435	In hospital
Nikolsky 2005 <sup>47</sup>	1074	233	1307	Long-term
Numacawa 2015 <sup>48</sup>	3735	6407	10.142	In hospital
Port 2012 <sup>49</sup>	10 740	12 422	22 181	Long term
Paik 2013	10,749	12,452	25,181	
Payvar 2015	85,801	217,010	301,477	
Poludasu 2008	631	146	///	In nospital
Poston 2004	1211	391	1602	Long-term
Powell 2003	4763	1269	6032	In hospital
Sarno 2010	1204	497	1701	Long-term
Shubair 2006 <sup>33</sup>	3645	986	4631	In hospital
Wang 2012 <sup>56</sup>	4491	1592	6083	Long-term
Witassek 201457	4577	2361	6938	In hospital
Study	Diabetics (n)	Non-diabetics (n)	Total no of patients (n)	Follow-up period
Abizaid 199858	248	706	954	In hospital and short-term
Akin 201059	1659	3559	5218	In hospital and long-term
Antoniucci 200460	166	895	1061	Short-term
Banning 2010 <sup>61</sup>	225	662	887	Long-term
Billinger 200862	201	811	1012	Long-term
Blondal 2012 <sup>63</sup>	201	1255	1652	In hosnital and long term
Classen 2011 <sup>64</sup>	271	1333	1032	Long term
Deamon 2000 <sup>65</sup>	203	440	1123	Long torm
Elozi 100066	109	448 2020	007	Long-term
EICZI 1998	/15	2839	3334	m-nospitai

# TABLE 2. The Number of Patients in These Different Subgroups and the Corresponding Follow-Up Periods

Study	Hypertensive Patients (n)	Normotensive Patients (n)	Total No of Patients (n)	Follow-Up Period
Fernandez 2011 <sup>67</sup>	141	103	334	Long-term
$Garg 2008^{68}$	5051	12 742	17 793	Long-term
El Ghannudi 2011 <sup>69</sup>	163	273	436	Short-term
Hariai 2003 <sup>70</sup>	626	3116	3742	In hospital and short-term
Hasdai $2000^{71}$	99	466	565	In hospital and short term
Hermillier 2005 <sup>72</sup>	318	906	1314	Short term
Jain 2015 <sup>73</sup>	2563	5269	7832	Short term
Jani 2015	1575	10 772	12 247	Short and long term
Januar 2010 <sup>75</sup>	200	2284	2774	
Version 2012 <sup>76</sup>	390	2384	2/74	Long-term
Kassalali 2012 Kadhi 2014 <sup>77</sup>	703	2181	2004	Short-term
Kedili 2014 Kanajakan 2010 <sup>78</sup>	5107	2408	0554	
Kerelakes 2010	1185	2496	2114	Long-term
Kip 1996	281	1855	2114	In nospital and long-term
	827	2080	3513	Long-term
Kirtane 2009	4//	10/1	1548	Long-term
Kutner 2014 <sup>32</sup>	162	288	450	Long-term
Kumar 2007 <sup>05</sup>	297	541	838	Short-term
Kuramitsu 2013°4	452	140	592	Long-term
Lee 2006 <sup>35</sup>	263	965	1228	Long-term
Lee 2012'	921	1517	2438	In hospital, short and long-term
Lenzen 2006°	1877	947	2824	Short-term
Lima 2013°	64	141	205	Long-term
Lingman 2011°	9415	34,278	43,693	In-hospital
Maeng 2011 <sup>88</sup>	337	1995	2332	Long-term
Marui 2015 <sup>89</sup>	1065	1123	2188	Long-term
Mathew 2004 <sup>90</sup>	2684	8798	11,482	Short-term
Mehran 2004 <sup>91</sup>	195	560	755	In hospital
Muhlestein 2003 <sup>92</sup>	394	630	1024	Long-term
Muramatsu 201493	136	415	551	Long-term
Norhammar 2004 <sup>94</sup>	299	2158	2457	Long-term
Onuma 2011 <sup>95</sup>	271	957	1228	Long-term
Overgaard 201396	203	898	1101	Long-term
Park 2009 <sup>97</sup>	865	2295	3160	Long-term
Silber 201398	878	1903	2781	Long-term
Sohrabi 201199	34	129	163	In hospital and short-term
Stein 1995100	1133	9300	10,433	In hospital
Stone 2011 <sup>101</sup>	1869	4911	6740	Long-term
Syed 2010 <sup>102</sup>	161	395	556	Long-term
Tada 2011 <sup>103</sup>	3404	6378	9782	Long-term
Weber 2008 <sup>104</sup>	1948	4707	6655	In hospital and short-term
Wilson 2004 <sup>105</sup>	1142	3142	4284	In hospital
Witzenbichler 2011 <sup>106</sup>	593	3006	3599	Short-term

BMI, and 51 studies dealt with DM. Two studies were common in both the hypertension and the diabetic groups since they analyzed both diabetic and hypertensive patients together. Follow-up periods were classified as in-hospital, short-term, and long-term follow-ups as mentioned in the "definition" section.

The baseline characteristics of all the included studies have been represented in Table 3.

Patients in the hypertensive group were older than the normotensive patients. There were more male patients in the control group compared to the experimental group. DM and dyslipidemia were more prominent among the hypertensive patients whereas cigarette smoking was more common in the control group.

Majority of the smokers were males and they were younger than the nonsmokers. Apart from 1 study, hypertension was more prominent among the nonsmokers. Most of the nonsmokers suffered from DM too.

Patients from both the experimental and the control groups were almost similar in age. If analyzed as a whole, there was no significant differences between genders, hypertension, and smoking between these 2 groups. However, except from 1 study, DM was more prominent among those with dyslipidemia.

There was no significant difference in age between these 2 groups. Majority of those patients in the control group were males. Hypertension was more prominent in the experimental group. Smoking was almost similar in both groups. Except from 1 study which had no diabetic patients and 1 which had less patients with DM, DM was more common in the MS group.

The overweight and obese patients were younger than the normal weight and underweight patients. There were more males than females in the experimental group. Hypertension, dyslipidemia, and DM were more prominent in the experimental group. Most of the patients in the high BMI category were nonsmokers.

There was no significant difference in age between the diabetic and nondiabetic patients. Most of the patients in the control group were males. Hypertension and dyslipidemia were more prominent in the DM group. Most of the patients in the experimental group were nonsmokers.

Studies	Age	Men	HT	Ds	Cs	DM
Hypertension group	E/C	E/C	E/C	E/C	E/C	E/C
Lee 2012 <sup>7</sup>	67.8/61.6	59.7/78.7	100.0/0.0	5.9/4.0	46.1/68.5	_
Lingman 2011 <sup>8</sup>	68.0/65.5	68.5/74.5	100.0/0.0	_	15.0/24.0	29.4/13.1
Luca 2013 <sup>9</sup>	63.0/59.5	71.6/81.3	100.0/0.0	45.6/30.0	43.0/58.1	23.6/12.1
Luca 2014 <sup>10</sup>	62.9/59.0	72.4/80.3	100.0/0.0	50.0/27.4	41.0/53.9	21.7/10.6
Rembek 2010 <sup>11</sup>	_	_	100.0/0.0	56.4/43.2	57.3/72.2	26.5/13.6
Smoking group	E/C	E/C	E/C	E/C	$E/C^*$	E/C
Arbel 2014 <sup>12</sup>	59.7/68.0	79.0/37.0	43.7/55.0	56.3/44.0	100.0/0.0	26.3/35.0
Chen 2012 <sup>13</sup>	53.1/60.9	96.0/55.6	44.7/54.3	32.0/31.7	100.0/0.0	17.2/20.6
Goto 2011 <sup>14</sup>	55.0/66.0	79.7/75.1	44.5/60.1	39.0/46.5	100.0/0.0	12.5/19.7
Liu 2013 <sup>15</sup>	53.8/61.0	-	61.2/58.2	60.5/48.8	100.0/0.0	25.9/29.1
Mohamedali 2013 <sup>16</sup>	61.0/68.0	99.2/98.4	-	50.0/41.0	100.0/0.0	30.0/44.0
Robertson 2014 <sup>17</sup>	55.7/65.3	74.8/68.1	55.7/71.4	48.1/60.8	100.0/0.0	20.6/31.0
Tan 2014 <sup>18</sup>	54.0/60.0	82.4/77.4	25.2/38.8	26.1/29.0	100.0/0.0	10.0/18.2
Weisz 2015 <sup>19</sup>	53.0/65.0	76.6/61.9	41.0/51.7	35.2/40.9	100.0/0.0	13.4/18.8
Dyslipidemia group	E/C	E/C	E/C	E/C	$E/C^*$	E/C
Cho 2010 <sup>20</sup>	60.5/64.0	67.5/75.0	45.0/50.3	100.0/0.0	58.0/60.0	23.5/30.0
Ghazzal 2009 <sup>21</sup>	63.4/66.2	82.9/58.4	77.8/79.7	100.0/0.0	20.7/14.9	33.7/25.6
Izuhara 2015 <sup>22</sup>	68.4/67.6	63.0/77.0	83.0/82.0	100.0/0.0	34.0/31.0	41.0/35.0
Ji 2015 <sup>23</sup>	65.4/62.1	61.3/81.5	53.3/45.8	100.0/0.0	53.5/65.2	33.3/23.6
Kini 2009 <sup>24</sup>	66.1/69.5	79.2/57.3	89.7/88.7	100.0/0.0	18.1/14.2	44.6/41.4
Seo 2011 <sup>23</sup>	62.7/62.2	59.7/75.2	62.6/56.8	100.0/0.0	23.6/26.2	41.0/30.7
Metabolic syndrome group	E/C	E/C	E/C	E/C	E/C	E/C
Butler $2006^{20}$	73.5/73.7	48.5/43.0	51.4/64.7	29.5/62.2	10.3/7.8	15.3/30.7
Kasai 2006 <sup>-7</sup>	59.0/59.0	85.2/88.4	/8.3/54.9	-	/8.3//6./	59.4/25.3
Kasal 2008	59.1/60.3	85.1/8/.4	/8.2/52.8	_	/8.2//6.3	59.4/25.5
$\lim_{n \to \infty} 2015^{30}$	03.3/02.3	60.0//1.4	80.0/31.0	_	43.5/52.4	4/.1/18.5
Lee 2015	04.8/04.8	01.0//0.9	09.1/40.8	_	21.0/23.8	4/.4/14.4
Marco $2011^{32}$	01.2/03.7	83.1/88.7 71.1/76.2	/9.0/30.3 60.0/47.7	-	28.2/23.9	4/.4/13./
Pates $2012^{33}$	50.0/59.9	78 2/84 6	65 3/50 1	76 2/66 5	74 8/72 5	40.8/26.9
Rana $2015^{34}$	61 0/63 0	71.0/72.0			21 0/18 0	24 0/7 0
High BML group	E/C	F/C	F/C	E/C	E/C	E/C
$\Delta kin 2012^{35}$	64 6/66 1	75 3/69 8	87 7/75 4	82 3/75 9	20.9/26.3	38 1/21 5
Filis 1996 <sup>36</sup>	60 5/65 0	65 4/65 0	55 4/45 3	21 0/14 5	20.3/20.8	16 4/10 1
Gruberg $2002^{37}$	62 5/68 0	69.8/59.7	67 7/55 6	72 5/63 1	58 2/54 3	31 8/17 4
Gruberg 2005 <sup>38</sup>	60.5/61.0	76.5/70.8	49.1/37.5	60.8/51.8	24.3/37.0	24.8/8.90
Gurm 2002 <sup>39</sup>	_	69.3/61.0	56.7/43.0	_	20.7/37.0	26.3/11.0
He 2015 <sup>40</sup>	_	63.0/64.7	74.6/53.1	50.8/46.9	14.2/19.1	25.6/22.9
Kaneko 2013 <sup>41</sup>	59.2/68.7	90.4/71.2	70.7/55.1	69.1/47.9	52.1/29.2	42.0/27.1
Kang 2009 <sup>42</sup>	58.0/67.2	78.0/66.9	50.7/36.6	11.6/8.40	65.2/59.6	26.1/19.9
Kosuge 2008 <sup>43</sup>	60.0/70.0	74.5/67.0	64.0/53.5	47.0/26.5	51.5/43.0	37.5/26.0
Lancefield 2010 <sup>44</sup>	62.5/68.1	72.2/66.8	70.0/58.3	74.3/63.7	22.1/25.2	29.8/14.8
Mehta 2007 <sup>45</sup>	58.5/63.0	76.0/67.0	51.0/39.0	40.5/33.0	42.0/47.0	19.0/11.0
Minutello 2004 <sup>46</sup>	59.4/66.1	62.8/55.4	68.0/57.6	_	26.2/25.9	29.2/14.3
Nikolsky 2005 <sup>47</sup>	61.7/65.8	73.5/65.2	72.1/68.3	67.5/60.7	22.4/22.7	26.9/10.3
Numasawa 2015 <sup>48</sup>	62.3/72.1	81.1/68.0	82.5/69.8	75.7/55.7	41.7/29.8	52.5/36.9
Park 2013 <sup>49</sup>	60.0/65.0	65.7/67.0	64.3/47.3	46.7/34.3	29.3/32.5	33.0/25.5
Payvar 2013 <sup>50</sup>	60.0/69.0	53.0/63.0	90.0/76.0	83.0/75.0	—	61.0/33.0
Poludasu 2008 <sup>51</sup>	61.8/66.0	53.1/56.8	88.8/89.7	_	23.3/33.5	51.5/45.9
Poston 2004 <sup>52</sup>	63.0/69.0	72.2/44.2	69.7/65.9	_	23.3/33.5	29.8/17.8
Powell 2003 <sup>53</sup>	64.7/70.5	69.3/54.0	65.3/55.5	67.7/49.5	19.3/28.5	28.0/15.0
Sarno 2010 <sup>54</sup>	63.9/65.9	75.5/71.0	77.5/65.0	70.5/60.0	24.5/27.0	30.0/15.0
Shubair 2006 <sup>55</sup>	58.9/65.2	65.9/64.5	65.8/54.5	84.1/77.6	23.7/20.6	29.0/14.9
Wang 2012 <sup>56</sup>	57.8/60.9	65.6/62.7	65.9/58.0	34.5/30.3	41.3/44.4	36.0/34.6
Witassek 2014 <sup>37</sup>	61.4/66.0	76.8/50.5	65.8/50.6	54.6/38.8	43.3/53.4	25.8/10.0
Diabetic group	E/C	E/C	E/C	E/C	E/C	E/C
Abizaid 1998 <sup>3°</sup>	63.0/61.0	56.6/73.3	70.4/54.2	62.0/69.1	48.8/49.1	100.0/0.0
Akin 2010 <sup>39</sup>	66.7/64.4	71.6/76.5	92.5/79.9	82.6/79.9	17.9/24.5	100.0/0.0

TABLE J. SHOWS THE DASENNE LEATHES OF LACH OF THE INCLUDED STUD	TABLE 3.	Shows the	Baseline	Features	of Each	of the	Included	Studies
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Studies	Age	Men	HT	Ds	Cs	DM
Antoniucci 200460	68.5/64.0	69.0/78.0	41.5/36.0	30.0/36.0	23.0/39.0	100.0/0.0
Banning 2010 <sup>61</sup>	65.4/65.0	71.0/79.9	_	81.5/76.7	15.8/21.7	100.0/0.0
Billinger 2008 <sup>62</sup>	_	70.7/78.8	80.7/56.7	60.8/58.5	20.2/40.0	100.0/0.0
Blondal 2012 <sup>63</sup>	67.2/67.5	52.2/66.8	86.2/69.2	66.1/68.5	18.7/29.2	100.0/0.0
Claessen 2011 <sup>64</sup>	61.9/61.3	87.2/82.5	70.6/56.5	75.0/61.2	33.0/24.5	100.0/0.0
Daemen 2008 <sup>65</sup>	64.5/62.1	66.7/80.1	79.9/62.7	74.1/74.0	11.9/21.9	100.0/0.0
Elezi 1998 <sup>66</sup>	66.7/62.5	68.1/79.1	75.0/63.0	39.0/37.1	23.8/35.5	100.0/0.0
Fernandez 2011 <sup>67</sup>	71.7/68.7	70.2/80.3	78.0/68.9	51.8/50.8	38.3/44.6	100.0/0.0
Garg 2008 <sup>68</sup>	65.6/64.3	62.6/70.0	87.2/70.2	84.4/71.9	15.6/22.9	100.0/0.0
El Ghannudi 2011 <sup>69</sup>	63.9/65.6	_	75.5/41.8	63.3/45.2	38.3/52.7	100.0/0.0
Hariai 2003 <sup>70</sup>	64.0/60.0	63.0/75.0	63.0/43.0	8.80/4.60	28.0/43.0	100.0/0.0
Hasdai $2000^{71}$	64.8/62.2	66.7/79.1	56.5/35.8	36.2/35.1	31.8/45.6	100.0/0.0
Hermillier 2005 <sup>72</sup>	62.2/62.6	63.5/74.8	81.1/64.0	71.5/67.4	_	100 0/0 0
Jain 2015 <sup>73</sup>	65.3/62.3	69.3/80.2	78.6/63.7	67.7/60.8	17.0/25.4	100.0/0.0
Jensen 2010 <sup>74</sup>	_	68.1/72.8	61.0/39.7	61.4/47.7	30.8/41.5	100.0/0.0
Jensen 2012 <sup>75</sup>	63 6/64 3	74 4/75 8	76.9/51.6	85 3/68 7	26 0/30 4	100.0/0.0
Kassajan 2012 <sup>76</sup>	59 0/57 4	53 0/75 8	61 4/46 1	78 7/61 5	26 4/47 0	100.0/0.0
Kedbi $2014^{77}$	63 1/63 2	63 6/64 6	82 7/82 9	78 3/78 7	24.0/29.5	100.0/0.0
Kerejakes 2010 <sup>78</sup>	63 3/63 3	63 3/70 0	87 0/71 9	82 5/72 6	18 3/24 0	100.0/0.0
Kin 1996 <sup>79</sup>	59 8/57 2	61 6/76 5	63 4/42 9	36 2/33 9	21 2/29 9	100.0/0.0
Kip 1990 Kirtana 2008 $^{80}$	63 0/62 1	64 7/75 0	82 1/64 5	74.0/69.6	18 4/24 0	100.0/0.0
Kirtane $2008^{81}$	64.0/63.3	60 4/71 0	00 6/76 7	87 1/81 /	5/ 1/6/ 8	100.0/0.0
Kutane 2009 Kufnor $2014^{82}$	66 6/66 8	74 5/78 0	74.0/71.5	70 5/72 5	8 0/14 5	100.0/0.0
Kumer 2014 Kumer 2007 <sup>83</sup>	65.0/66.0	65 0/73 0	94.0/77.0	91.0/80.0	0.0/14.0	100.0/0.0
Kumar $2007$ Kuramitsu $2012^{84}$	70.0/60.0	05.0/75.0	94.0/74.2	91.0/80.0 65.2/72.1	26 2/24 2	100.0/0.0
$L_{20} = 2006^{85}$	65.0/62.0	70.7773.3 58 4/71 1	71 0/52 0	40 2/42 1	15 6/22 0	100.0/0.0
Lee 2000	67.8/61.6	50 7/78 7	60 2/42 7	5 0/4 0	15.0/25.9	100.0/0.0
Let $2012$	66 5/62 0	59.7770.7	60.5/45.7	5.9/4.0 74.5/70.0	40.1/08.3	100.0/0.0
$L_{\rm max}^{\rm 2000} 2012^{87}$	61.0/50.0	56 0/71 0	72 0/57 0	/4.5//9.0	20.3/20.0	100.0/0.0
Line 2015 Line 2011 $^8$	01.0/39.0	50.0/71.0	72.0/37.0	—	17.0/37.0	100.0/0.0
Magna 2011 <sup>88</sup>	08.0/03.3	08.3/74.3	70.9/40.9	-	15.0/24.0	100.0/0.0
Maeni $2015^{89}$	68.2/70.2	71.3/74.0	/2.0/49.0	80.0/00.3	29.0/32.3	100.0/0.0
Marul 2015	08.3/70.3	70.0/73.0	80.0/83.0	-	25.0/24.0	100.0/0.0
Mathew 2004 $M_{\rm el}$	01.8/39.8	/0.0/80.0	73.0/57.0	64.0/05.0	10.0/25.0	100.0/0.0
Mehran 2004 Mahlastain 2002 $^{92}$	64.5/64.0	56.5/76.0	//.0/56.0	69.0/70.0	11.5/15.0	100.0/0.0
Munlestein 2003	63.0/61.0	65.0/80.0	08.0/55.0 75.0/61.4	55.0/53.0	18.0/29.0	100.0/0.0
Muramatsu 2014	61.6/61.9	73.5/73.7	/5.0/61.4	0/.0/03.0	19.9/21.0	100.0/0.0
Norhammar $2004^{\circ}$	66.0/64.0	/2.0/69.0	49.0/28.0	-	19.0/32.0	100.0/0.0
Onuma 2011	64.0/61.0	/0.0//9.0	/2.0/51.5	64.5/66.5	16.5/26.0	100.0/0.0
Overgaard 2013	60.0/58.0	68.5/80.5	68.5/43.5	57.2/50.5	28.4/41.8	100.0/0.0
Park 2009	62.7/59.7	63.9/73.0	61.6/46.4	— 	23.2/31.3	100.0/0.0
Silber 2013 <sup>56</sup>	65.2/63.5	66.4/74.4	87.673.1	86.2/76.0	18.2/22.1	100.0/0.0
Sohrabi 2011	58.1/58.2	64.7/80.6	58.8/38.0	38.2/29.5	20.6/36.4	100.0/0.0
Stein 1995 <sup>100</sup>	60.0/58.0	62.0/75.3	61.1/41.1	—	_	100.0/0.0
Stone 2011 <sup>101</sup>	63.0/63.8	71.3/63.2	62.5/83.1	64.0/79.4	27.1/19.6	100.0/0.0
Syed 2010 <sup>102</sup>	63.6/61.0	57.1/70.9	92.5/76.2	89.9/79.1	24.2/38.7	100.0/0.0
Tada 2011 <sup>103</sup>	67.3/68.8	71.5/76.0	77.0/73.0	-	18.5/20.0	100.0/0.0
Weber 2008 <sup>104</sup>	66.6/63.2	69.3/76.8	90.4/78.3	89.6/87.1	_	100.0/0.0
Wilson 2004 <sup>105</sup>	63.6/63.4	57.0/73.0	78.0/67.0	-	8.80/15.0	100.0/0.0
Witzenbichler 2011	64.5/59.6	73.4/77.2	72.3/49.8	60.3/39.7	56.8/64.9	100.0/0.0

C = control/low risk group, Cs = current smoker, DM = diabetes mellitus, Ds = dyslipidemia, E = experimental/high risk group, HT = hyperten-hypertension.

\* Late nonsmokers have been included in the same category as smokers; 100% smokers have been considered.

#### **Result of the Main Analysis**

Results from this meta-analysis showed that during the inhospital follow-up, mortality in the hypertensive and DM patients were significantly higher with RR 1.43; 95% CI: (1.05–1.94); P = 0.02 and RR 1.86; 95% CI: (1.68–2.06); P < 0.00001, respectively. The in-hospital mortality for the patients with dyslipidemia did not reach statistical significance RR 1.39; 95% CI: (0.32–5.94); P = 0.66. However, surprisingly, the inhospital mortality significantly favored patients with high BMI with RR 0.61; 95% CI: (0.58–0.64); P < 0.00001.

Short-term mortality was significantly higher in the DM group with RR 2.11; 95% CI: (1.91-2.33); P < 0.00001. The result was not significant in the hypertensive group with RR 1.40; 95% CI: (0.95-2.06); P = 0.09; dyslipidemia group with

TABLE 4	Summarizes	the	Results (	of This	Meta-Analysis
IADLL T.	Juimanzes	uie	Nesults (		ivieta-Analysis

In-I Mo	Hospital ortality	Sho Ma	rt-Term ortality	Long-Term Mortality		
RR	P Value	RR	P Value	RR	P Value	
1.43	0.02	1.40	0.09	1.45	0.00001	
1.39	0.66	0.91	0.77	1.21	0.27	
1.86	0.00001	2.11	0.00001	1.85	0.00001	
0.61	0.00001	0.67	0.002	0.64	0.00001	
_	_	0.53	0.00001	0.49	0.00001	
_	-	1.05	0.61	1.29	0.0009	
	In-l Mo RR 1.43 1.39 1.86 0.61 - -	In-Hospital Mortality           RR         P Value           1.43         0.02           1.39         0.66           1.86         0.00001           0.61         0.00001           -         -           -         -	In-Hospital Mortality         Sho Mathematical Sho Sho Sho Sho Sho Sho Sho Sho Sho Sho	In-Hospital Mortality         Short-Term Mortality           RR         P Value         RR         P Value           1.43         0.02         1.40         0.09           1.39         0.66         0.91         0.77           1.86         0.00001         2.11         0.0001           0.61         0.00001         0.67         0.002           -         -         0.53         0.00001           -         1.05         0.61	In-Hospital Mortality         Short-Term Mortality         Lon Mortality           RR         P Value         RR         P Value         RR           1.43         0.02         1.40         0.09         1.45           1.39         0.66         0.91         0.77         1.21           1.86         0.00001         2.11         0.00001         1.85           0.61         0.00001         0.67         0.002         0.64           -         -         0.53         0.00001         0.49           -         -         1.05         0.61         1.29	

RR 0.91; 95% CI: (0.47–1.76); P = 0.77 and MS group with RR 1.05; 95% CI: (0.88–1.25); P = 0.61. Unexpectedly, the short-term mortality significantly favored the smokers and high BMI groups with RR 0.53; 95% CI: (0.45–0.62); P < 0.00001 and 0.67; 95% CI: (0.52–0.86); P = 0.002, respectively.

Long-term mortality was significantly higher in the DM, hypertensive, and MS groups with RR 1.85; 95% CI: (1.66–

2.06); P < 0.00001, 1.45, 95% CI: (1.24–1.69); P < 0.00001, and 1.29; 95% CI: (1.11–1.51); P = 0.0009, respectively. The result for dyslipidemia was still not significant. However, the long-term mortality still significantly favored the smokers and high BMI patients with RR 0.49; 95% CI: (0.39–0.63); P < 0.00001 and 0.64; 95% CI: (0.54–0.75), P < 0.00001, respectively. The mortality risks within these subgroups have been summarized in Table 4, and the detailed results for mortality among these different subgroups have been shown in Figures 2–7.

For all of the above analyses, sensitivity analyses yielded consistent results. Based on a visual inspection of the funnel plots, there has been no evidence of publication bias for the included studies that assessed the subgroup mortality risk. Figure 8 shows the corresponding funnel plots.

#### DISCUSSION

Among these 844,190 patients who participated in this meta-analysis, an unexpected result has been obtained in certain subgroups of patients. A significantly higher mortality risk has been observed among the DM patients. A significantly higher in-hospital and long-term mortality risks have also been

	Hypertensive group		Normotensive	group		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I M-H, Fixed, 95% CI
1.1.1 In-hospital mor	tality						
Lee2012	81	1218	57	1220	17.8%	1.42 [1.02, 1.98]	
Rembek2010	18	234	7	132	2.8%	1.45 [0.62, 3.38]	
Subtotal (95% CI)		1452		1352	20.6%	1.43 [1.05, 1.94]	◆
Total events	99		64				
Heterogeneity: Chi <sup>2</sup> =	0.00, df = 1 (P =	: 0.97); l² :	= 0%				
Test for overall effect:	Z = 2.27 (P = 0.	02)					
1.1.3 Long-term Mort	tality						
Lee2012	104	1218	71	1220	22.2%	1.47 [1.10, 1.96]	
Luca2014	235	2764	208	3522	57.2%	1.44 [1.20, 1.72]	
Subtotal (95% CI)		3982		4742	79.4%	1.45 [1.24, 1.69]	◆
Total events	339		279				
Heterogeneity: Chi <sup>2</sup> =	0.01, df = 1 (P =	: 0.91); l <sup>2</sup> :	= 0%				
Test for overall effect:	Z = 4.74 (P < 0.	00001)					
Total (95% CI)		5434		6094	100.0%	1.44 [1.26, 1.65]	•
Total events	438		343				
Heterogeneity: Chi <sup>2</sup> =	0.02, df = 3 (P =	: 1.00); l <sup>2</sup> :	= 0%				
Test for overall effect:	Z = 5.25 (P < 0.	00001)					0.01 0.1 1 10 100
Test for subgroup diffe	erences: Chi <sup>2</sup> = (	0.01  df = 100000000000000000000000000000000000	$1 (P = 0.94)  ^2 =$	0%			Favours [nypertensive] Favours [normotensive]

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FIGURE 2. (A) Forest plot showing the in-hospital and long-term mortality risk in Hypertensive patients. (B) Forest plot showing the short-term mortality risk in hypertensive patients.

	Dyslipidemia group		Non-dyslipidemia group		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
1.2.1 In-hospital Mort	ality						
Cho2010	67	3284	194	6287	11.4%	0.66 [0.50, 0.87]	
Ji2015	151	4181	63	5089	11.3%	2.92 [2.18, 3.90]	
Subtotal (95% CI)		7465		11376	22.7%	1.39 [0.32, 5.94]	
Total events	218		257				
Heterogeneity: Tau <sup>2</sup> =	1.08; Chi <sup>2</sup> = 52	.87, df = 1	(P < 0.00001); l <sup>2</sup>	= 98%			
Test for overall effect:	Z = 0.44 (P = 0	.66)					
1.2.2 Short-term Mort	ality						
Cho2010	90	2969	261	5634	11.7%	0.65 [0.52, 0.83]	-
Ji2015	67	4030	65	5026	10.9%	1.29 [0.92, 1.80]	
Subtotal (95% CI)		6999		10660	22.5%	0.91 [0.47, 1.76]	-
Total events	157		326				
Heterogeneity: Tau <sup>2</sup> =	0.21; Chi <sup>2</sup> = 10	.30, df = 1	(P = 0.001); I <sup>2</sup> = 9	90%			
Test for overall effect:	Z = 0.29 (P = 0	.77)					
1.2.3 Long-term Mort	ality						
Cho2010	122	2566	351	4919	11.9%	0.67 [0.55, 0.81]	-
Ghazzal2009	100	2113	73	1975	11.2%	1.28 [0.95, 1.72]	
Izuhara2015	690	3838	909	6553	12.4%	1.30 [1.18, 1.42]	
Kini2009	53	1521	49	2095	10.5%	1.49 [1.02, 2.18]	
Seo2011	45	1585	16	1108	8.8%	1.97 [1.12, 3.46]	
Subtotal (95% CI)		11623		16650	54.8%	1.21 [0.86, 1.71]	•
Total events	1010		1398				
Heterogeneity: Tau <sup>2</sup> =	0.13; Chi <sup>2</sup> = 40	.35, df = 4	(P < 0.00001); l <sup>2</sup>	= 90%			
Test for overall effect:	Z = 1.11 (P = 0	.27)					
Total (95% CI)		26087		38686	100.0%	1.18 [0.87, 1.60]	•
Total events	1385		1981				*
Heterogeneity: Tau <sup>2</sup> =	$0.20^{\circ}$ Chi <sup>2</sup> = 11	846 df=	8 (P < 0.00001)· F	<sup>2</sup> = 93%			· · · · · · · · · · · · · · · · · · ·
Test for overall effect:	7 = 1.04 (P = 0)	30)	s (	0070			0.01 0.1 1 10 100
Test for subgroup diffe	rences: Chi <sup>2</sup> =	0.66 df =	$2(P = 0.72)  ^2 = 0$	1%			Favours [dyslipidemia] Favours [no-dyslipidemia]

FIGURE 3. Forest plot showing the mortality in dyslipidemia patients.

observed among the hypertensive patients. Moreover, a significantly higher long-term mortality has been observed in patients with MS whereas an almost similar mortality rate has been observed in patients with and without dyslipidemia.

However, smokers and those patients with high BMI had an unexpectedly lower short and long-term mortality risk compared to non-smokers and low-BMI/normal weight patients, respectively, after PCI. Several possible reasons could be responsible for such an outcome.

DM is associated with a higher risk of mortality after PCI.<sup>59</sup> A total of 3.02%, 4.12%, and 9.24% in-hospital, short-, and long-term deaths, respectively, occurred in these DM patients compared to 1.59%, 2.46%, and 5.35% in-hospital, short-, and long-term deaths in nondiabetics patients in our study. These patients have worse adverse clinical outcomes including mortality due to severe stent thrombosis, stroke, silent myocardial infarction, or other major adverse cardiac effects. Conditions such as multicoronary vessel diseases and chronic total occlusion which are associated with DM patients partly contribute to these worse clinical outcomes after PCI. The risk of restenosis after stent implantation is also higher in diabetic patients. DM patients also have platelet dysfunction which contribute to this expected increased risk of mortality in these patients.<sup>107</sup> A poor response to antiplatelet agents such as aspirin and clopidogrel after drug eluting stents implantation could be another reason for such a result.<sup>108</sup> The use of insulin could also be another reason for this higher mortality risk in these diabetic patients.<sup>109</sup> Comorbidities and severe diabetic complications are associated with these insulin-treated diabetic patients which finally result in a higher mortality in this category of patients after PCI.

MS which is considered to be a modifiable cardiovascular risk factor, includes patients who can be obese, may have diabetes, may suffer from hypertension, and may also have dyslipidemia. The long-term mortality in these patients was significantly higher compared to those without MS after PCI. A significant increase in long-term mortality from 8.21% in non-MS to 12.1% in MS has been found in our study. Its association with comorbidities such as DM and hypertension maybe one of the reasons that lead to a higher mortality in these patients after PCI.<sup>31</sup>

Hypertension is another major modifiable risk factor for CAD and acute coronary syndrome. Hypertensive patients had a higher mortality risk compared to normotensive patients after PCI. A significant long-term mortality of 8.51% has been observed in the hypertensive group, compared to the normotensive group which was only 5.88% after PCI. The reasons associated with this result could be an increased in diastolic dysfunction in these hypertensive patients which could lead to severe heart failure. Moreover, by hypertension, we refer to essential hypertension which is a disease that occurs in advanced age. Other comorbid conditions such as diabetic mellitus may be present in these hypertensive patients thus, strengthening/increasing the mortality risk in these patients after PCI.<sup>8</sup> Patients with high blood pressure are even prone to cerebral hemorrhage if their antiplatelet dosages are not adjusted after PCI. This can also contribute to death in these patients.

Dyslipidemia is another well-known modifiable risk factor for coronary heart disease. It was expected to be associated with a higher mortality after PCI but however, the results were not significant in our study. A few studies have shown the existence of a "cholesterol paradox" whereby the mortality rate in hypercholesterolemia patients was lower compared to those with normal cholesterol levels.<sup>20</sup> The reasons for such a phenomenon is still not clear. However, even such a result was not evident in our study. Several factors could have been responsible for this insignificant result. The use of statin (lipidlowering drugs) has not been studied in our meta-analysis.<sup>110</sup>

	Diabe	etic	Non-dia	betics		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
1.6.1 In-hospital Mortal	lity	040		700	0.49/	0.05 (0.40, 00.40)	
Abiazid1998 Akin2012	13	248	2	706	0.1%	2.85 [0.40, 20.10]	
Blondal2012	23	297	74	1355	2.9%	1.42 [0.90, 2.23]	<b>—</b>
Elezi1998	19	715	40	2839	1.7%	1.89 [1.10, 3.24]	
Harjai2003	29	626	81	3116	2.9%	1.78 [1.18, 2.70]	
Hasdai 2000	9	99	23	466	0.9%	1.84 [0.88, 3.86]	
Kip1996	9	281	9	1833	0.3%	6.52 [2.61, 16.29]	
Lee2012	242	921	54 730	1017	4.4%	2.00 [1.84, 3.07]	
Mehran2004	343	195	2	560	0.1%	4 31 [0 73 25 59]	
Sohrabi2011	1	34	0	129	0.0%	11.14 [0.46, 267.62]	
Stein1995	5	1133	24	9300	0.6%	1.71 [0.65, 4.47]	
Weber2008	12	1948	9	4707	0.6%	3.22 [1.36, 7.63]	
Wilson2004	11	1142	9	3142	0.5%	3.36 [1.40, 8.09]	
Subtotal (95% CI)	560	18632	1069	67067	49.4%	1.86 [1.68, 2.06]	•
Heterogeneity: Chi <sup>2</sup> = 20	200 126 df=	= 13 (P =	1000 : 0 09)· 12	= 36%			
Test for overall effect: Z	= 11.93	(P < 0.0	0001)	00,0			
1.6.2 Short-term Morta	lity	0.40		700	0.0%	4 55 10 50 4 451	
Abiazid1998 Antoniucci2004	25	248	11	706	2.0%	1.55 [0.58, 4.15]	
Ghannudi2011	14	163	11	273	0.9%	2.21 [1.43, 3.41]	
Harjai2003	48	626	128	3116	4.6%	1.87 [1.35, 2.57]	
Hasdai 2000	8	99	24	466	0.9%	1.57 [0.73, 3.39]	+
Hermillier2005	7	318	10	996	0.5%	2.19 [0.84, 5.71]	
Jain2015	104	2563	87	5269	6.1%	2.46 [1.86, 3.25]	
Jensen2010 Kassais=2012	136	1575	507	10772	13.9%	1.83 [1.53, 2.20]	*
⊾assaian∠012 Kedhi2014	5	703	25	2181	1.3%	0.02 [0.24, 1.61] 1.83 [0.01 - 3.70]	·
Kumar2007	22 5	297	12	541	0.5%	1.52 [0.47. 4 93]	
Lee2012	103	921	66	1517	5.3%	2.57 [1.91, 3.46]	<del></del>
Lenzen2006	134	1877	21	947	3.0%	3.22 [2.05, 5.07]	
Mathew2004	57	2684	75	8798	3.8%	2.49 [1.77, 3.51]	
Sohrabi2011	0	34	2	129	0.1%	0.74 [0.04, 15.12]	
Weber2008	41	1948	56	4707	3.5%	1.77 [1.19, 2.64]	
Subtotal (95% CI)	21	17982	00	47486	2.3%	2.07 [1.34, 3.22]	•
Total events	742		1168				
Heterogeneity: Chi <sup>2</sup> = 18	3.83, df =	= 16 (P =	0.28); l <sup>2</sup>	= 15%			
Test for overall effect: Z	= 14.78	(P < 0.0	0001)				
Total (95% CI)		36614		11/553	100.0%	1 00 [1 85 2 13]	
Total (95% CI)	1205	30014	2226	114000	100.0%	1.99 [1.05, 2.15]	•
Heterogeneity: Chi <sup>2</sup> = 41	156 df=	= 30 (P =	2230 = 0.08)· l <sup>2</sup>	= 28%		⊢	
riotorogeneity: en			0.00//			0.04	0.1 1 10 100
Test for overall effect: Z	= 18.95	(P < 0.0	0001)			0.01	Envoure (diabatica) Envoure (non diabatica)
Test for overall effect: Z Test for subgroup differe	= 18.95 ences: C	(P < 0.0 hi² = 2.9	0001) 2, df = 1 (	P = 0.09	), l² = 65.7	7%	Favours [diabetics] Favours [non-diabetics]
Test for overall effect: Z Test for subgroup differe A	= 18.95 ences: C	(P < 0.0 hi <sup>2</sup> = 2.9	0001) 2, df = 1 (	P = 0.09	), I² = 65.7	7%	Favours [diabetics] Favours [non-diabetics]
Test for overall effect: Z Test for subgroup differe A	= 18.95 ences: C	(P < 0.0 hi <sup>2</sup> = 2.9	0001) 2, df = 1 (	P = 0.09	), I² = 65.7	7% Pisk Patio	Favours [diabetics] Favours [non-diabetics]
Test for overall effect: Z Test for subgroup differe A Study or Subgroup	= 18.95 ences: C Diabe Events	(P < 0.0 hi <sup>2</sup> = 2.9 tic Total	0001) 2, df = 1 ( Non-dial Events	P = 0.09 petics Total	), I² = 65.7 Weight	Risk Ratio M-H, Random, 95% Cl	Risk Ratio M-H, Random, 95% Cl
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal	= 18.95 ences: C Diabe Events ity	(P < 0.0 hi <sup>2</sup> = 2.9 ttic Total	0001) 2, df = 1 ( Non-dial Events	P = 0.09 petics Total	), I² = 65.7 Weight	Risk Ratio M-H, Random, 95% Cl	Favours [diabetics] Favours [non-diabetics] Risk Ratio M-H, Random, 95% Cl
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012	= 18.95 ences: C Diabe Events ity 93	(P < 0.0 hi <sup>2</sup> = 2.9 tic Total 1659	00001) 2, df = 1 ( Non-dial <u>Events</u> 121	P = 0.09 petics Total 3559	), I <sup>2</sup> = 65.7 <u>Weight</u> 4.5%	7% Risk Ratio M-H, Random, 95% Cl 1.65 [1.27, 2.15]	Risk Ratio
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010	= 18.95 ences: C Diabe Events ity 93 16	(P < 0.0 hi <sup>2</sup> = 2.9 ttic Total 1659 227	00001) 2, df = 1 ( Non-dial Events 121 20	P = 0.09 Detics Total 3559 664	), I <sup>2</sup> = 65.7 Weight 4.5% 2.0%	Risk Ratio M-H, Random, 95% Cl 1.65 [1.27, 2.15] 2.34 [1.23, 4.44]	Risk Ratio
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008	= 18.95 ences: C Diabe Events ity 93 16 19 00	(P < 0.0 hi <sup>2</sup> = 2.9 ttic Total 1659 227 201	00001) 2, df = 1 ( Non-dial Events 121 20 33	P = 0.09 petics Total 3559 664 811	), I <sup>2</sup> = 65.7 Weight 4.5% 2.0% 2.4% 2.4%	Risk Ratio M-H, Random, 95% Cl 1.65 [1.27, 2.15] 2.34 [1.23, 4.44] 2.32 [1.35, 4.00] 4.14 (4.15)	Favours [diabetics] Favours [non-diabetics]
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Baining2010 Billinger2008 Billinger2008 Billinger2018	= 18.95 ences: C Diabe Events ity 93 16 19 69 54	(P < 0.0 hi <sup>2</sup> = 2.9 tic Total 1659 227 201 297 395	00001) 2, df = 1 ( Non-dial Events 121 20 33 224 89	P = 0.09 petics Total 3559 664 811 1355 1347	), I <sup>2</sup> = 65.7 <u>Weight</u> 4.5% 2.0% 2.4% 4.8% 4.0%	Risk Ratio M-H, Random, 95% Cl 1.65 [1.27, 2.15] 2.34 [1.23, 4.44] 2.32 [1.35, 4.00] 1.44 [1.11, 1.78] 2.07 [1.50, 2.85]	Favours [diabetics] Favours [non-diabetics]
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Bilondai2012 Claessen2011 Daemen2008	= 18.95 ences: C Diabe <u>Events</u> ity 93 16 19 69 54 8	(P < 0.0 hi <sup>2</sup> = 2.9 tic Total 1659 227 201 297 395 159	0001) 2, df = 1 ( Non-dial Events 121 20 33 224 89 10	P = 0.09 petics Total 3559 664 811 1355 1347 448	), I <sup>2</sup> = 65.7 <u>Weight</u> 4.5% 2.0% 2.4% 4.8% 4.0% 1.1%	Risk Ratio M-H, Random, 95% CI 1.65 [1.27, 2.15] 2.34 [1.23, 4.44] 2.32 [1.35, 4.00] 1.44 [1.11, 1.78] 2.07 [1.50, 2.85] 2.25 [0.91, 5.61]	Risk Ratio M-H, Random, 95% Cl
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Bilondal2012 Claessen2011 Daemen2008 Fernandez2011	= 18.95 ences: C Diabe Events ity 93 16 19 69 54 8 23	(P < 0.0 hi <sup>2</sup> = 2.9 ttic 1659 227 201 297 395 159 141	0001) 2, df = 1 ( Non-dial <u>Events</u> 121 20 33 224 89 10 14	P = 0.09 petics Total 3559 664 811 1355 1347 448 193	), I <sup>2</sup> = 65.7 Weight 4.5% 2.0% 2.4% 4.8% 4.0% 1.1% 2.0%	Risk Ratio M-H, Randorn, 95% CI 1.65 [1.27, 2.15] 2.34 [1.23, 4.44] 2.32 [1.35, 4.00] 1.44 [1.11, 1.78] 2.07 [1.50, 2.85] 2.25 [0.91, 5.61] 2.25 [1.20, 4.21]	Favours [diabetics] Favours [non-diabetics]
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008	= 18.95 ences: C Diabe <u>Events</u> ity 93 16 19 69 54 8 23 862	(P < 0.0 hi <sup>2</sup> = 2.9 ttic 1659 227 201 297 395 159 141 5051	0001) 2, df = 1 ( Non-dial Events 121 20 33 224 89 10 14 1246	P = 0.09 petics Total 3559 664 811 1355 1347 448 193 12742	), l <sup>2</sup> = 65.7 Weight 4.5% 2.0% 2.4% 4.8% 4.0% 1.1% 2.0% 6.0%	Risk Ratio M-H, Random, 95% Cl 1.65 [1.27, 2.15] 2.34 [1.23, 444] 2.32 [1.25, 4.00] 1.41 [1.11, 1.78] 2.07 [1.50, 2.85] 2.25 [0.91, 5.61] 2.25 [1.20, 4.21] 1.75 [1.61, 1.89]	Favours [diabetics] Favours [non-diabetics]
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Bilondai2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2010	= 18.95 ences: C Diabe <u>Events</u> ity 93 16 19 69 54 8 23 862 60	(P < 0.0 hi <sup>2</sup> = 2.9 tic Total 1659 227 201 297 395 159 141 5051 1575	0001) 2, df = 1 ( Non-dial Events 121 20 33 224 89 10 14 1246 217 7	P = 0.09 <b>Detics</b> <b>Total</b> 3559 664 811 1355 1347 448 193 12742 10772	), I <sup>2</sup> = 65.7 Weight 4.5% 2.0% 2.4% 4.8% 4.0% 1.1% 2.0% 6.0% 4.4%	Risk Ratio M-H, Random, 95% CI 1.65 [1.27, 2.15] 2.34 [1.23, 4.44] 2.32 [1.35, 4.00] 1.41 [1.11, 1.78] 2.07 [1.50, 2.85] 2.25 [0.91, 5.61] 2.25 [1.20, 4.21] 1.75 [1.61, 1.89] 1.85 [1.43, 2.50]	Risk Ratio M-H, Random, 95% Cl
Test for overall effect: Z Test for subgroup differe A Study or Subgroup 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondai2012 Claessen2011 Daemen2008 Fermandez2011 Garg2008 Jensen2010 Jensen2012 Kortkrott J	= 18.95 ences: C Diabe <u>Events</u> ity 93 16 19 69 54 8 23 862 60 23 70	(P < 0.0 hi <sup>2</sup> = 2.9 tic Total 1659 227 207 297 395 159 141 5051 1575 390 2467	0001) 2, df = 1 ( Non-dial Events 121 20 33 224 89 10 14 1246 217 84 422	P = 0.09 <b>Detics</b> <b>Total</b> 3559 664 811 1355 1347 448 193 12742 10772 2384 2467	), I <sup>2</sup> = 65.7 Weight 4.5% 2.0% 2.4% 4.8% 4.0% 1.1% 2.0% 6.0% 4.4% 3.0% 2.6%	Risk Ratio M-H, Random, 95% Cl 1.65 [1.27, 2.15] 2.34 [1.23, 4.44] 2.32 [1.35, 4.00] 1.41 [1.11, 1.78] 2.07 [1.50, 2.85] 2.25 [0.91, 5.61] 2.25 [0.91, 5.61] 2.25 [0.91, 5.61] 2.25 [1.20, 4.21] 1.75 [1.61, 1.89] 1.89 [1.43, 2.50] 1.67 [1.07, 2.52] 1.67 [1.07, 2.52]	Favours [diabetics] Favours [non-diabetics]
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2010 Jensen2012 Kedhi2014 Kereiakes2010	= 18.95 ences: C Diabe <u>Events</u> ity 93 16 19 69 54 8 23 862 60 23 79 15	(P < 0.0 hi <sup>2</sup> = 2.9 tic Total 1659 227 201 297 395 159 141 5051 1575 390 3167 1140	0001) 2, df = 1 ( <b>Non-dial</b> <b>Events</b> 121 20 33 224 89 10 14 1246 217 84 42 25	P = 0.09 <b>Total</b> 3559 664 811 1355 1347 448 193 12742 10772 2384 3167 2467	),  2 = 65.7 Weight 4.5% 2.0% 2.4% 4.8% 4.0% 1.1% 6.0% 4.4% 3.0% 3.6% 2.0%	Risk Ratio M-H, Random, 95% Cl 1.65 [1.27, 2.15] 2.34 [1.23, 4.44] 2.32 [1.35, 4.00] 1.41 [1.11, 1.78] 2.07 [1.50, 2.85] 2.25 [1.50, 2.85] 2.25 [1.50, 2.85] 2.25 [1.50, 2.85] 1.57 [1.61, 1.89] 1.89 [1.43, 2.50] 1.67 [1.07, 2.62] 1.88 [1.30, 2.73] 1.30 [0.69, 2.45]	Favours (diabetics) Favours (non-diabetics)
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Baining2010 Biondal2012 Claessen2011 Daemer2008 Fernandez2011 Garg2008 Jensen2010 Jensen2012 Kedhi2014 Kerlaikes2010 Kip1996	= 18.95 ences: C Diabe Events ity 93 16 19 69 54 8 23 862 60 23 79 15 101	(P < 0.0 hi <sup>2</sup> = 2.9 ttic Total 1659 227 201 297 395 159 141 5051 1575 390 3167 1140 281	0001) 2, df = 1 ( Non-dial Events 121 20 33 224 89 10 14 1246 217 84 42 25 328	P = 0.09 <b>Total</b> 3559 664 811 1355 1347 448 193 12742 10772 2384 3167 2467 1833	),  2 = 65.7 Weight 4.5% 2.0% 2.4% 4.0% 1.1% 2.0% 6.0% 4.4% 3.0% 3.6% 2.0% 5.3%	Risk Ratio M-H, Random, 95% CI 1.65 [1.27, 2.15] 2.34 [1.23, 4.44] 2.32 [1.23, 4.44] 2.32 [1.25, 4.00] 1.41 [1.11, 1.78] 2.07 [1.50, 2.85] 2.25 [0.91, 5.61] 2.25 [1.20, 4.21] 1.75 [1.61, 1.89] 1.89 [1.43, 2.50] 1.67 [1.07, 2.62] 1.86 [1.30, 2.73] 1.30 [0.69, 2.45] 2.01 [1.67, 2.42]	Risk Ratio M-H, Random, 95% Cl
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Biondal2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2012 Kedhi2014 Kedhi2014 Kerja96 Kirtane2008	= 18.95 ences: C Diabe Events ity 93 16 19 69 54 8 23 862 23 862 23 79 15 101 61	(P < 0.0 hi <sup>2</sup> = 2.9 tic Total 207 207 207 297 395 159 141 5051 1575 390 3167 1140 281 827	0001) 2, df = 1 ( Non-dial Events 121 20 33 224 89 10 14 1246 217 84 422 25 328 117	P = 0.09 <b>oetics</b> <b>Total</b> 3559 664 811 1355 1347 448 193 12742 10772 2384 3167 2467 1833 2686	),  2 = 65.7 Weight 4.5% 2.0% 2.4% 4.0% 1.1% 2.0% 6.0% 4.4% 3.0% 3.6% 2.0% 5.3% 4.2%	Risk Ratio M-H, Random, 95% CI 1.65 [1.27, 2.15] 2.34 [1.23, 4.44] 2.32 [1.36, 4.00] 1.41 [1.11, 1.78] 2.07 [1.50, 2.85] 2.25 [0.20, 4.21] 1.75 [1.61, 1.89] 1.89 [1.43, 2.50] 1.67 [1.07, 2.62] 1.88 [1.43, 2.51] 2.18 [1.43, 2.51] 1.69 [1.43, 2.51] 2.01 [1.67, 2.42] 2.01 [1.67, 2.42]	Risk Ratio M-H, Random, 95% Cl
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fermandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2010 Kerliakes2010 Kip1996 Kirtane2008 Kirtane2008	= 18.95 ences: C Diabe Events ity 93 16 19 69 54 8 23 862 60 023 79 15 101 61 22	(P < 0.0 hi <sup>2</sup> = 2.9 tic Total 227 207 297 395 159 141 5051 1575 390 3167 1140 281 827 456	0001) 2, df = 1 ( Non-dial Events 121 20 33 224 89 10 14 1246 217 84 42 25 328 117 14	P = 0.09 petics Total 3559 664 811 1355 1347 448 193 12742 10772 2384 3167 2467 1833 2686 1034	),   <sup>2</sup> = 65.7 Weight 4.5% 2.0% 2.4% 4.8% 4.0% 1.1% 2.0% 6.0% 4.4% 3.0% 5.3% 0.5% 0.5%	Risk Ratio M-H, Random, 95% Cl 1.65 [1.27, 2.15] 2.34 [1.23, 4.44] 2.32 [1.35, 4.00] 1.41 [1.11, 1.78] 2.07 [1.50, 2.85] 2.25 [0.91, 5.61] 2.25 [1.0, 4.21] 1.75 [1.61, 1.89] 1.89 [1.43, 2.50] 1.67 [1.07, 2.62] 1.88 [1.30, 2.73] 1.30 [0.69, 2.45] 2.01 [1.67, 2.42] 1.69 [1.26, 2.28] 0.32 [0.07, 1.42]	Risk Ratio M-H, Random, 95% Cl
Test for overall effect: Z Test for subgroup diffect A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Biondal2012 Claessen2010 Daemer2008 Fernandez2011 Garg2008 Jensen2010 Jensen2012 Kedhi2014 Kereiakes2010 Kirtane2008 Kirtane2008 Kirtane2009 Kurter2014	= 18.95 ences: C Diabe Events ity 93 16 19 69 54 8 23 862 60 23 79 15 101 61 2 4	(P < 0.0 hi <sup>2</sup> = 2.9 ttic Total 1659 227 201 297 395 159 141 5051 1575 390 3167 1140 281 827 456 162	0001) 2, df = 1 ( Non-dial Events 121 20 33 224 89 10 14 1246 217 84 42 25 328 117 84 42 25 328 117 14 12	P = 0.09 petics Total 3559 664 811 1355 1347 448 193 12742 10772 2384 3167 2467 1833 2686 1034 2686 1034	),   <sup>2</sup> = 65.7 Weight 4.5% 2.0% 2.4% 4.8% 4.0% 5.0% 6.0% 5.3% 4.2% 5.3% 4.2% 0.5% 0.5% 0.8% 0.2%	Risk Ratio M-H, Random, 95% Cl 1.65 [1.27, 2.15] 2.34 [1.23, 4.44] 2.32 [1.23, 4.44] 2.32 [1.25, 4.00] 1.41 [1.11, 1.78] 2.07 [1.50, 2.85] 2.25 [0.91, 5.61] 2.25 [1.20, 4.21] 1.75 [1.61, 1.89] 1.89 [1.43, 2.50] 1.67 [1.07, 2.62] 1.88 [1.30, 2.73] 1.30 [0.69, 2.45] 2.01 [1.67, 2.42] 1.69 [1.26, 2.28] 0.32 [0.07, 1.42] 0.59 [0.19, 1.81] 2.61 [0.9, 1.61]	Risk Ratio M-H, Random, 95% Cl
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Bilondal2012 Claessen2011 Daemen2008 Fernandez2011 Daeme2008 Jensen2010 Jensen2010 Jensen2012 Kedhi2014 Kereiakes2010 Kirtane2009 Kirtane2009 Kirtane2014 Kuramitsu2013 Lee2006	= 18.95 ences: C Diabe Events ity 93 16 19 69 93 54 862 23 862 23 862 23 79 915 101 61 2 4 37 16	(P < 0.0.4) hi <sup>2</sup> = 2.9 total 1659 227 201 297 395 141 5051 1575 390 3167 1140 281 144 5051 147 5051 147 5051 147 5051 147 5051 297 390 3167 297 297 201 297 201 201 207 201 207 207 201 207 207 201 207 207 207 207 207 207 207 207 207 207	0001) 2, df = 1 ( Non-dial Events 121 20 33 224 89 10 14 126 217 84 42 25 328 117 14 122 3 3 3 28 117 14 12 3 3 28 14 121 20 3 3 224 89 10 14 121 20 3 224 89 10 10 10 10 10 10 10 10 10 10	P = 0.09 Detics Total 3559 664 811 1355 1347 448 193 12742 10772 2384 3167 1833 2686 1034 288 140 966	),   <sup>2</sup> = 65.7 Weight 4.5% 2.0% 2.4% 4.8% 4.0% 3.0% 3.6% 2.0% 5.3% 4.2% 0.5% 0.8% 0.8% 0.8%	Risk Ratio M-H, Random, 95% CI 1.65 [1.27, 2.15] 2.34 [1.23, 4.44] 2.32 [1.23, 4.44] 2.32 [1.35, 4.00] 1.41 [1.11, 1.78] 2.07 [1.50, 2.85] 2.25 [0.91, 5.61] 2.25 [0.91, 5.61] 2.25 [1.20, 4.21] 1.75 [1.61, 1.89] 1.89 [1.43, 2.50] 1.67 [1.07, 2.42] 1.88 [1.30, 2.73] 1.30 [0.69, 2.45] 2.01 [1.69, 1.84] 0.52 [0.19, 1.81] 3.82 [1.20, 12.20] 1.40 [0.80, 2.45] 3.40 [0.80, 2.45]	Risk Ratio M-H, Random, 95% Cl
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fermandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2010 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2004 Kuramitsu2013 Lee2006 Lee2012	= 18.95 Certain Control Contro	(P < 0.0.4) hiP = 2.9 tic Total 1659 227 201 297 395 159 141 1575 390 3167 1140 281 827 3167 456 263 3167 2141 297 3167 207 207 207 207 207 207 207 20	0001) 2, df = 1 ( Non-dial Events 121 20 33 224 89 10 14 1246 247 84 42 25 328 117 14 12 3 3 42 25 328 117 14 26 3 3 3 26 4 4 26 3 26 26 26 26 26 26 26 26 26 26	P = 0.09 <b>Total</b> 3559 664 8111 1357 448 10772 2384 31677 2387 12742 2467 1833 2686 1034 2467 1034 2467 1034 2467 1034 1034 1034 1034 1034 1034 1034 1034 1034 1034 1034 1034 1034 1035 1034 1034 1035 1034 1034 1035 1034 1035 1034 1035 1034 1035 1034 1035 1034 1035 1034 1035 1034 1035 1034 1035 1034 1035 1037 1034 1037 1037 1037 1034 1035 1034 1035 1034 1035 1035 1035 1035 1035 1035 1035 1035 1035 1035 1035 1035 1035 1035 1035 1035 1035 1037	),   <sup>2</sup> = 65.7 Weight 4.5% 2.0% 2.4% 4.0% 1.1% 2.0% 6.0% 4.4% 3.0% 5.3% 4.2% 0.5% 0.8% 0.8% 2.3% 4.3%	Risk Ratio M-H, Random, 95% Cl 1.65 [1.27, 2.15] 2.34 [1.23, 4.44] 2.32 [1.35, 4.00] 1.41 [1.11, 1.78] 2.07 [1.50, 2.85] 2.25 [0.91, 5.61] 2.25 [1.0, 4.21] 1.75 [1.61, 1.89] 1.89 [1.43, 2.50] 1.67 [1.07, 2.62] 1.88 [1.30, 2.73] 1.30 [0.69, 2.45] 2.01 [1.67, 2.42] 1.69 [1.42, 2.43] 0.59 [0.19, 1.81] 3.82 [1.20, 12.20] 1.40 [0.80, 3.45] 2.53 [1.80, 3.39]	Risk Ratio M-H, Random, 95% Cl
Test for overall effect: Z Test for subgroup diffect A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Baining2010 Bilondal2012 Claessen2018 Demen2008 Fernandez2011 Garg2008 Jensen2010 Jensen2012 Kedhi2014 Kereiakes2010 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kuramitsu2013 Lee2006 Lee2012 Lima2013	= 18.95 5% Diabee Events ity 93 16 93 16 99 94 93 16 16 10 61 2 4 37 16 10 16 10 10 10 10 10 10 10 10 10 10	(P < 0.0.4) hi <sup>2</sup> = 2.9 <b>Total</b> 1659 227 201 297 201 297 159 141 1575 390 3167 1140 281 827 456 263 921 444	0001) 2, df = 1 ( <b>Non-dial</b> <b>Events</b> 121 20 33 224 89 9 10 14 1246 217 84 42 25 328 117 84 42 25 328 114 12 3 42 69 29	P = 0.09 Total 3559 664 811 1355 1347 448 193 12742 2384 3167 2384 3167 2384 3167 2384 3167 2384 10732 2686 1033 2686 1034 2384 1033 2686 1034 1035 1047 1055 1057 105	),   <sup>2</sup> = 65.7 Weight 4.5% 2.0% 2.4% 4.8% 4.0% 6.0% 4.4% 3.0% 5.3% 0.5% 0.8% 2.3% 4.2% 0.5% 0.8% 2.3% 4.3%	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.20, 4.21]           1.75 [1.61, 1.89]           1.41 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [0.91, 5.61]           2.25 [1.20, 4.21]           1.75 [1.61, 1.89]           1.89 [1.43, 2.50]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.01 [1.67, 2.42]           1.69 [1.26, 2.28]           0.32 [0.07, 1.42]           0.59 [0.19, 1.81]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.89, 3.39]           1.52 [0.39, 2.47]	Risk Ratio M-H, Random, 95% Cl 
Test for overall effect: Z Test for subgroup diffect A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Biondal2012 Claessen2010 Deemer2008 Fernandez2011 Daemer2008 Fernandez2011 Garg2008 Jensen2010 Jensen2012 Kedhi2014 Kereiakes2010 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2014 Kumer2014 Kumer2014 Kumer2014 Kumer2014 Kumer2014 Kumer2014 Kumer2014 Kumer2014 Kumer2014 Kumer2013 Maeng2011	= 18.95 C Diabe Events '' Diabe Events'' '' '' '' '' '' '' '' '' '' '' '' ''	(P < 0.0.0 h)P = 2.9 tic Total 1659 227 201 297 395 159 297 395 159 141 1575 5051 11575 390 3167 1140 281 1140 281 1422 263 3921 452 263 921 452 263 392	0001) 2, df = 1 ( Non-dial Events 121 20 33 224 89 10 14 1246 217 84 25 328 117 14 42 25 328 117 14 12 69 9 9 00	P = 0.09 Total 3559 664 4811 1355 1347 12742 10772 2384 12742 10772 2384 12742 10772 2384 1034 2467 1034 2880 1034 1034 2895 1034 1034 2805 1034 1034 1034 2805 1034 10	),   <sup>2</sup> = 65.7 Weight 4.5% 2.0% 2.4% 4.8% 4.0% 1.1% 2.0% 6.0% 4.4% 3.0% 3.6% 2.0% 5.3% 4.2% 0.8% 0.8% 0.8% 2.3% 4.3% 2.3%	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.20, 4.21]           1.75 [1.61, 1.89]           1.80 [1.43, 2.60]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.01 [1.67, 2.42]           1.69 [1.26, 2.28]           0.32 [0.07, 1.42]           0.59 [0.19, 1.81]           3.82 [1.20, 1.2.01]           1.40 [0.80, 2.45]           2.51 [1.89, 3.39]           1.52 [0.33, 2.47]           2.53 [1.89, 3.39]           1.52 [0.33, 2.47]           2.53 [1.49, 3.39]	Risk Ratio M-H, Random, 95% Cl
Test for overall effect: Z Test for subgroup diffect A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2010 Kirtane2008 Kirtane2009 Kufter2014 Kuramitsu2013 Lee2006 Lee2012 Lima2013 Maeng2011 Marui2015	= 18.95 Scale of the second se	(P < 0.0.0 h)P = 2.9 ttic Total 1659 227 201 297 395 5051 1595 1599 141 1575 3900 3167 1140 2811 827 456 64 452 263 2921 64 337 71065	0001) 2, df = 1 ( <b>Non-dial</b> <b>Events</b> 121 20 33 3224 224 225 238 8328 117 14 42 25 328 8328 117 14 42 25 29 9 60 222	P = 0.09 Total 3559 664 811 1355 1347 12742 2384 12772 2384 12772 2384 12772 2384 10772 2467 1033 2467 1034 2485 1034 1035 1037	),   <sup>2</sup> = 65.7 Weight 4.5% 2.0% 4.8% 4.0% 1.1% 2.0% 6.0% 3.6% 2.0% 5.3% 0.8% 2.3% 4.2% 0.5% 0.8% 2.8% 2.8% 2.8% 2.5%	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.35, 4.00]           1.41 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [0.91, 5.61]           2.25 [1.04, 2.41]           1.75 [1.61, 1.89]           1.89 [1.43, 2.50]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.01 [1.67, 2.42]           0.69 [1.26, 2.28]           1.69 [1.26, 2.28]           1.69 [1.26, 2.42]           0.59 [0.19, 1.81]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.40, 12.20]           1.40 [0.80, 2.45]           2.53 [1.40, 12.20]           1.40 [0.89, 3.39]           1.52 [0.93, 2.47]           2.27 [1.42, 3.62]           1.16 [0.99, 1.36]	Risk Ratio M-H, Random, 95% CI 
Test for overall effect: Z Test for subgroup diffect A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Baning2010 Bilmiger2008 Biondal2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2010 Jensen2012 Kedhi2014 Kereiakes2010 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2014 Kuramitsu2013 Lee2006 Lee2012 Lima2013 Maeng2011 Marri2015 Muhostein2003	= 18.95 C Diabee Events 19 20 20 20 20 20 20 20 20 20 20 20 20 20	(P < 0.0.0 hi <sup>p</sup> = 2.9 tic Total 1659 227 201 297 395 201 297 395 5051 159 141 5051 159 346 390 3167 456 452 263 394 452 452 263 3921 642 3921 643 3921 643 3921 643 3921 643 263 263 263 263 263 263 263 263 263 26	0001) 2, df = 1 ( Non-dialate 224 89 121 20 33 3224 89 124 225 328 89 114 1246 89 114 1246 217 25 328 8117 14 122 99 90 00 222 222 222	P = 0.09 Total 3559 664 811 1355 664 811 1355 664 811 1355 664 811 1355 664 811 1355 8157 1347 2384 4288 140 965 1517 141 1995 1517 141 1123 630 647 141 1417 1418 1437 1418 1437 1437 1437 1438 1437 1438 1437 1438 1437 1438 1437 1438 1437 1438 1437 1438 1437 1438 1437 1448 1447 1448 1457 1448 1457	), l <sup>2</sup> = 65.7 Weight 4.5% 2.0% 4.8% 4.0% 4.0% 4.0% 4.0% 3.0% 5.3% 4.4% 0.5% 0.8% 2.0% 0.8% 2.3% 4.3% 0.8% 2.3% 0.8% 2.3% 0.8% 0.8% 0.8% 0.8% 0.8% 0.8% 0.9% 0.8% 0.9% 0.9% 0.0%	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.20, 4.21]           1.75 [1.61, 1.89]           1.41 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [0.91, 5.61]           2.25 [1.20, 4.21]           1.75 [1.61, 1.89]           1.89 [1.43, 2.50]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.01 [1.67, 2.42]           1.69 [1.26, 2.28]           0.32 [0.07, 1.42]           0.59 [0.19, 1.81]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.89, 3.39]           1.52 [0.39, 2.47]           2.53 [1.89, 3.39]           1.52 [0.39, 2.47]           2.77 [1.42, 3.62]           1.16 [0.99, 3.26]           5.86 [3.14, 10.96]           5.86 [3.14, 10.96]	Risk Ratio M-H, Random, 95% Cl 
Test for overall effect: Z Test for subgroup differe A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2010 Kirtane2009 Kirtane2009 Kirtane2009 Kufmer2014 Kuramitsu2013 Lee2014 Kuramitsu2013 Lee2012 Lima2013 Maeng2011 Marni2015 Muhlestein2003 Muramatsu2014	= 18.95 C Diabe Events : C Diabe Events : C Diabe Events : C Diabe Events : 19 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(P < 0.0.0 Total 1659 227 227 227 201 297 395 5051 15051 15051 15051 15051 15051 3167 1140 281 157 5031 201 283 3167 1140 281 263 3167 214 203 201 201 201 201 201 207 201 207 201 207 207 201 207 207 207 207 207 207 207 207 207 207	0001) 2, df = 1 ( <b>Non-dialate</b> 1211 200 33 3224 899 1246 899 1246 899 1246 217 247 245 253 217 442 245 217 33 369 292 69 292 692 292 692 292 692 292 692 292 2	P = 0.09 Total 3559 664 811 1355 1347 12742 10772 2384 12742 10772 2384 12742 10772 2386 1034 12742 10772 2467 1034 12742 10772 2467 1034 12742 10772 2467 1034 12742 10772 2467 1034 12742 10772 2467 1034 12742 10772 2467 1034 12742 10772 2467 1034 12742 10772 2467 1034 12742 10772 2467 1034 12742 10772 2467 1034 12742 10772 2467 1034 12742 10772 2467 1034 1267 1267 1267 12742 12742 10772 2467 1034 1267 12742 12742 12742 12742 12742 12742 12742 12742 12742 1267 1267 1274 1267 1274 12742 1274 12742 12742 12742 12742 12742 1274	),  2 = 65.7 Weight 4.5% 2.0% 2.0% 4.8% 4.0% 1.0% 4.	Risk Ratio M-H, Random, 95% Cl 1.65 [1.27, 2.15] 2.34 [1.23, 4.44] 2.32 [1.35, 4.00] 1.41 [1.11, 1.78] 2.07 [1.50, 2.85] 2.25 [0.91, 5.61] 2.25 [0.91, 5.61] 2.25 [1.20, 4.21] 1.56 [1.30, 2.73] 1.89 [1.43, 2.50] 1.67 [1.07, 2.62] 1.88 [1.30, 2.73] 1.30 [0.69, 2.45] 2.21 [1.67, 2.42] 1.69 [1.26, 2.28] 0.32 [0.07, 1.42] 0.59 [0.19, 1.81] 3.82 [1.20, 12.20] 1.40 [0.80, 2.45] 2.23 [1.89, 3.39] 1.52 [0.93, 2.47] 2.27 [1.42, 3.82] 1.66 [0.99, 1.36] 5.86 [3.14, 10.96] 0.58 [0.94, 14, 10.96] 0.58 [0.94, 14, 10.96] 0.58 [0.94, 14, 10.96] 0.58 [0.94, 2.35] 5.66 [2.12, 20, 0.00]	Risk Ratio M-H, Random, 95% Cl 
Test for overall effect: Z Test for subgroup diffect A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fermandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2010 Kirtane2008 Kirtane2009 Kufrer2014 Kuramitsu2013 Lee2006 Lee2012 Lima2013 Maeng2011 Marri2015 Multestein2003 Muramatu2014 Norhammar2004 Onuma2011	= 18.95 Construction of the second se	(P < 0.0.0 h)r = 2.9 ttic Total 1659 227 201 159 227 201 15051 15051 15051 15051 15051 1575 395 3167 2452 263 3921 64 452 263 3921 64 337 1065 394 136 6299 271	0001) 2, df = 1 ( <b>Non-dialate</b> <b>121</b> 200 33 32 224 89 9 124 89 9 124 124 6 217 84 227 25 328 227 124 124 225 328 328 42 24 25 328 328 42 29 9 0 222 21 22 33 30 0 222 222 23 30 0 222 222 33 30 35 33 30 224 30 224 222 222 222 33 30 30 224 33 3224 224 225 225 225 225 225 225 225 225	P = 0.09 Detics Total 3559 664 811 1355 147 448 193 12742 10772 2467 1833 2866 1034 448 140 288 103 286 1033 2866 1033 2866 1034 1033 2866 1034 1033 2865 1034 1033 2865 1033 2865 1034 1033 2865 1034 1033 2865 1034 1033 2865 1034 1033 2865 1034 1033 2865 1034 1035 11272 2467 1123 287 287 287 287 287 287 287 287	), P = 65.7 Weight 4.5% 2.0% 4.8% 4.8% 4.4% 0.0% 6.0% 4.4% 5.3% 5.3% 5.3% 2.8% 2.9% 5.3% 2.9% 5.3% 2.9% 5.3% 2.9% 5.3% 2.9% 5.3% 2.9% 5.3% 2.9% 5.3% 2.9% 5.3% 2.9% 5.3% 2.9% 5.3% 2.9% 5.3% 2.9% 5.3% 2.9% 5.3	Risk Ratio           M-H, Random, 95% Cl           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.35, 4.00]           1.41 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [0.91, 5.61]           2.25 [1.00, 4.21]           1.75 [1.61, 1.89]           1.89 [1.43, 2.50]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.01 [1.67, 2.42]           0.69 [1.26, 2.28]           1.69 [1.26, 2.28]           1.69 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.40, 11.20]           1.56 [0.34], 10.66]           0.43 [0.02, 8.35]           5.36 [3.14, 10.66]           0.43 [0.02, 8.35]           5.33 [2.66, 9.40]           2.01 [1.30, 3.10]	Risk Ratio M-H, Random, 95% CI 
Test for overall effect: Z Test for subgroup diffect A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2012 Kedhi2014 Kereiakes2010 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2009 Kurer2014 Kuramitsu2013 Maeng2011 Marui2015 Muhestein2003 Muramatsu2014 Norhammar2004 Onuma2011	= 18.95 5 ences: C Diabe Events 93 16 19 93 16 19 93 46 23 3862 23 3862 23 3862 23 379 95 44 37 101 16 102 23 37 101 16 22 23 23 20 20 23 23 20 20 23 20 20 20 20 20 20 20 20 20 20 20 20 20	(P < 0.0.0 h)P = 2.9 ttic Total = 2.9 1659 227 201 227 201 227 201 227 201 395 5051 1575 395 3167 3167 3167 3167 346 452 263 3167 1065 394 4337 1065 394 4136 299 271 1365 209 271 203 203 203 203 203 203 203 203 203 203	0001) 2, df = 1 ( Non-diala 121 220 121 20 121 20 121 20 122 20 124 42 205 20 124 42 205 20 205 20	P = 0.09 petics Total 3559 664 811 1355 1347 1355 1347 1372 2384 1077 2384 1077 2384 1077 2384 100 265 1034 288 140 965 1517 141 1995 2158 957 2158 957 898	),  ? = 65.7 Weight 4.5% 2.0% 4.8% 4.8% 4.8% 4.8% 4.8% 4.8% 4.8% 4.8% 4.8% 4.8% 4.2% 0.8% 0.8% 0.8% 0.8% 0.5% 0.8% 0.9% 0.5% 0.5% 0.8% 0.9% 0.5% 0.	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.25, 4.00]           1.41 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [1.50, 2.85]           2.25 [1.20, 4.21]           1.75 [1.61, 1.89]           1.89 [1.43, 2.50]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.20 [1.60, 7, 1.42]           0.59 [0.07, 1.42]           0.59 [0.07, 1.42]           0.59 [0.07, 1.42]           0.59 [0.07, 1.42]           0.59 [0.07, 1.42]           0.59 [0.07, 1.42]           0.58 [0.07, 1.42]           0.58 [0.31, 1.00, 12.00]           1.40 [0.80, 2.45]           2.53 [1.89, 3.39]           1.52 [0.93, 2.47]           2.27 [1.42, 3.62]           1.16 [0.90, 3.26]           5.86 [3.14, 10.96]           0.43 [0.02, 8.35]           5.53 [3.26, 9.40]           2.01 [1.30, 3.10]           1.90 [1.30, 3.10]	Risk Ratio M-H, Random, 95% Cl 
Test for overall effect: Z Test for subgroup differe A Study or Subgroup 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondai2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2010 Kirtane2009 Kirtane2009 Kufmer2014 Kuramitsu2013 Lee2014 Kuramitsu2013 Lee2012 Lima2013 Muhlestein2003 Muramatsu2014 Norhammar2004 Onuma2011 Overgaard2013 Park2009	= 18.95 C Diabe Events Ity 93 16 19 93 16 19 93 16 19 93 16 19 93 48 23 23 79 101 101 102 44 47 37 16 102 24 44 40 23 24 24 24 24 24 25 101 102 102 102 102 102 102 102	(P < 0.0.0 km s = 2.9	0001) 2, df = 1 ( <b>Non-diala</b> <b>Events</b> 121 20 33 3224 20 33 224 20 33 224 225 224 217 20 0 10 4 1246 217 1246 227 2328 2328 24 225 228 2328 20 99 00 00 2222 21 23 33 30 00 2222 23 23 30 30 30 30 32 32 4 24 25 26 26 20 27 20 20 20 20 20 20 20 20 20 20 20 20 20	P = 0.09 Detics Total 3559 664 811 1355 1347 448 193 12742 2384 3167 10772 2384 3167 10772 2467 1034 2467 1034 2467 1034 1037 2467 1034 1034 2467 1034 1035 1034 2467 11212 2467 11212 2467 11212 2467 11212 2467 11212 2467 11212 2467 11212 2467 11212 2467 11212 2467 11212 2467 11212 2467 11212 2458 11212 2458 11212 247 11212 2458 11212 2458 11212 2458 11212 2458 11212 2458 2458 11212 24588 24588 24588 24588 24588 24588 2458	), $P = 65.7$ <b>Weight</b> 4.5% 2.0% 2.4% 4.8% 4.4% 4.0% 4.4% 6.0%	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.35, 4.00]           1.41 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [0.91, 5.61]           2.25 [1.00, 4.21]           1.75 [1.61, 1.89]           1.89 [1.43, 2.60]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.01 [1.67, 2.42]           1.69 [1.26, 2.28]           0.52 [0.91, 1.61]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.89, 3.39]           1.52 [0.93, 2.47]           2.27 [1.42, 3.62]           1.68 [1.41, 10.66]           0.43 [0.02, 8.45]           2.53 [1.89, 3.39]           1.52 [0.93, 2.47]           2.27 [1.42, 3.62]           1.66 [0.99, 1.36]           5.86 [3.14, 10.06]           0.43 [0.02, 8.45]           5.58 [3.26, 9.40]           2.01 [1.7, 2.34]           1.50 [1.7, 2.34]	Risk Ratio M-H, Random, 95% Cl 
Test for overall effect: Z Test for subgroup diffect A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fermandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2010 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2014 Kuramitsu2013 Lee2012 Lima2013 Maeng2011 Maeng2011 Maria2013 Muramatsu2014 Norhammar2004 Onuma2013 Park2009 Silber2013	= 18.95 sences: C Diabe Events iity 93 16 93 16 9 9 9 16 9 9 9 16 8 9 9 9 54 4 8 23 38 862 23 37 9 15 101 61 61 24 4 37 106 107 107 107 107 107 107 107 107	(P < 0.0.0 km <sup>2</sup> = 2.9 tic Total 1659 227 201 1659 227 201 159 159 141 1505 159 141 1505 159 141 1505 390 3167 1140 281 827 1140 281 452 263 392 114 452 263 392 1165 263 394 1366 299 121 203 394 1366 5878 878 878 878 878 878 878 878 878 87	0001) 2, df = 1 ( <b>Non-diala</b> <b>Events</b> 121 20 33 3224 89 10 122 33 3224 89 10 14 1246 217 84 425 227 84 425 228 3288 117 14 129 29 90 0 2022 12 2 33 30 0 222 12 12 12 12 12 12 12 12 12 12 12 12	P = 0.09 petics Total 3559 664 8111 1355 1347 12742 10772 2384 1034 2686 1034 2888 140 965 1517 1411 1995 1123 630 415 1995 1129 2158 11995 119	), P = 65.7 Weight 4.5% 2.0% 4.8% 4.8% 4.4% 3.0% 3.0% 3.0% 5.3% 3.0% 2.8% 2.8% 2.8% 2.8% 2.8% 2.8% 2.8% 2.8% 2.8% 3.0	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.35, 4.00]           1.41 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [0.91, 5.61]           2.25 [1.00, 4.21]           1.75 [1.61, 189]           1.89 [1.43, 2.50]           1.75 [1.61, 189]           1.89 [1.43, 2.73]           1.30 [0.69, 2.45]           2.01 [1.67, 2.42]           0.69 [0.19, 1.81]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.40, 12.20]           1.40 [0.80, 2.45]           2.53 [1.40, 12.20]           1.40 [0.90, 1.36]           5.85 [3.14, 10.66]           0.43 [0.02, 8.35]           5.33 [3.26, 9.40]           2.01 [1.67, 2.34]           1.90 [1.38, 2.60]           1.36 [1.7, 2.34]           2.01 [1.30, 3.10]	Risk Ratio M-H, Random, 95% CI 
Test for overall effect: Z Test for subgroup diffect A Study or Subgroup 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2011 Kedhi2014 Kereiakes2010 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2014 Kuramitsu2013 Maeng2011 Marii2015 Muhestein2003 Muramatsu2014 Onuma2011 Overgaard2013 Park2009 Silber2013 Stone2011	= 18.95 spances: C Diabe Events: V 93 16 19 93 16 19 93 16 19 93 16 19 93 16 23 23 23 23 23 23 23 23 23 23 23 24 24 44 23 29 24 24 24 24 23 29 55 50 23 24 24 24 24 24 23 24 24 24 24 24 24 24 24 24 24 24 24 24	(P < 0.0.0 hi <sup>2</sup> = 2.9 tic Total 1659 227 201 159 159 141 1575 390 3167 1140 281 1140 281 1140 281 1140 281 1140 281 1140 281 1140 281 1140 281 1140 281 1140 281 1140 281 202 203 203 203 203 203 203 203 203 203	0001) 2, df = 1 ( Non-diala 121 220 121 20 121 20 121 20 122 20 124 42 205 20 124 42 205 20 207 20	P = 0.09 betics Total 3559 664 8111 1355 1347 448 11742 2384 3167 2384 3167 2384 3167 1333 2886 1034 2888 1034 2955 1034 2055 1034 2056 1034 1034 2056 1034 1034 2056 1034 1034 2056 1034 1034 2056 1034 1034 2056 1034 1034 2056 1034 1034 2056 1034 1034 2058 1034	),  ? = 65.7 Weight 4.5% 2.0% 4.8% 4.8% 4.8% 4.8% 4.8% 4.8% 4.8% 4.8% 2.0% 5.3% 0.8% 2.0% 2.8% 2.9% 2.8% 2.9% 2.8% 2.9% 2.9% 2.9% 2.9% 2.9% 2.9% 2.9% 2.9% 2.9% 2.9% 2.9% 2.9% 2.9% 2.9% 2.9% 2.9% 2.8% 2.	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.25, 4.00]           1.41 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [1.50, 2.85]           2.25 [1.20, 4.21]           1.75 [1.61, 1.89]           1.43 [1.30, 2.73]           1.30 [0.69, 2.45]           2.01 [1.67, 2.42]           1.69 [1.26, 2.28]           0.59 [0.19, 1.81]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.25 [0.93, 2.47]           2.27 [1.42, 3.62]           1.166 [1.70, 2.83]           5.53 [3.26, 9.40]           2.01 [1.30, 3.10]           1.90 [1.30, 3.10]           1.90 [1.30, 3.10]           1.91 [1.30, 2.07]           2.82 [1.71, 7.3.13]           1.53 [1.13, 2.07]	Risk Ratio M-H, Random, 95% Cl 
Test for overall effect: Z Test for subgroup differe A Study or Subgroup 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondai2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2010 Jensen2010 Kirtane2009 Kirtane2009 Kirtane2009 Kufmer2014 Kuramitsu2013 Lee2012 Lima2013 Maeng2011 Marni2014 Norhammar2004 Onuma2011 Overgaard2013 Stone2011 Stone2011 Stone2011	= 18,95 spances: C Diabe Events: C 93 16 16 93 16 16 16 16 16 16 16 16 16 16	(P < 0.0. h <sup>2</sup> = 2.9 tic Total 1659 227 201 297 395 201 297 159 141 15051 1575 3167 1140 3167 1140 3167 1140 3167 1243 325 457 457 457 457 457 457 457 45	0001) 2, df = 1 ( <b>Non-diala</b> <b>Events</b> 121 20 33 224 121 20 33 224 124 20 33 224 422 23 24 24 24 24 24 24 24 24 24 24	P = 0.09 petics Total 3559 664 8111 1355 1347 448 11347 2467 1337 2466 1034 2484 1472 2384 1077 2467 1033 2686 1034 288 140 034 288 111 1995 1113 268 2055 1034 288 2055 1034 288 2055 1034 288 2055 1034 288 2055 1034 288 2055 1034 2055 1034 2055 1034 2055 1034 2055 1034 2055 1034 2055 1037 2055	), $P = 65.7$ <b>Weight</b> 4.5% 2.0% 2.4% 4.8% 4.48% 4.48% 4.48% 6.0% 6	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.35, 4.00]           1.41 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [0.91, 5.61]           2.25 [1.00, 4.21]           1.75 [1.61, 1.89]           1.89 [1.43, 2.60]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.01 [1.67, 2.42]           1.69 [1.62, 2.28]           0.52 [0.91, 1.61]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.89, 3.39]           1.52 [0.93, 2.47]           2.27 [1.42, 3.62]           5.86 [3.44, 10.96]           5.86 [3.44, 10.96]           0.55 [0.23, 2.67]           1.30 [1.30, 2.07]           1.50 [1.33, 2.07]           1.50 [1.30, 3.10]           1.90 [1.38, 2.60]           1.66 [1.77, 2.34]           2.07 [1.73, 3.13]           1.53 [1.53, 5.77]           1.40 [1.23, 4.67]	Risk Ratio M-H, Random, 95% Cl
Test for overall effect: Z Test for subgroup diffect A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fermandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2010 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2009 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2014 Kuramitsu2013 Lee2012 Lima2013 Maeng2011 Marui2015 Muhlestein2003 Muramatsu2014 Norhammar2004 Onuma2011 Overgaard2013 Stone2011 Syed2010 Tada2011 Subtotal (95% CI)	= 18.95 spances: C Diabe Events: V 93 16 19 69 954 8 8 23 862 60 0 23 79 101 61 2 4 4 37 79 101 61 2 4 4 37 79 101 61 2 4 4 4 4 0 0 0 23 244 4 4 0 23 244 4 4 0 23 29 4 5 5 5 5 5 6 5 7 7 7 9 10 10 10 10 10 10 10 10 10 10 10 10 10	(P < 0.0.0 hi <sup>2</sup> = 2.9 tic Total 1659 2277 201 297 395 297 395 159 141 5051 1157 5051 11575 390 281 83167 211 456 62 293 263 921 62 263 921 166 263 921 166 263 921 166 263 921 166 263 277 1140 281 281 263 277 1140 281 281 281 281 281 281 281 281 281 281	0001) 2, df = 1 ( <b>Non-diala</b> <b>Events</b> 121 20 33 3224 89 10 4 1246 217 84 422 233 84 117 14 1246 217 84 425 3288 117 14 123 3422 290 00 2022 12 3 300 202 21 12 12 12 12 12 12 12 12 12 12 12 12	P = 0.09 betics Total 3559 664 811 1355 4811 1347 448 11347 448 11347 448 11347 448 11347 448 1347 2384 3167 2384 1034 2886 1034 2955 2055 2056 20	), P = 65.7 <b>Weight</b> 4.5% 2.0% 4.8% 4.8% 4.4% 6.0% 6	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.35, 4.00]           1.41 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [0.91, 5.61]           2.25 [1.00, 4.21]           1.75 [1.61, 189]           1.89 [1.43, 2.50]           1.75 [1.61, 189]           1.80 [1.43, 2.50]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.01 [1.67, 2.42]           0.69 [0.19, 1.81]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.40, 12.20]           2.41 [1.53, 5.17]           2.27 [1.42, 3.62]           1.66 [1.7, 2.34]           1.69 [1.7, 3.43]           1.60 [0.92, 3.55]           5.53 [3.26, 9.40]           2.01 [1.7, 3.13]           1.53 [1.13, 2.07]           2.81 [1.53, 5.17]           1.40 [1.23, 1.60]	Risk Ratio M-H, Random, 95% CI 
Test for overall effect: Z Test for subgroup diffect A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2010 Jensen2010 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2009 Kirtane2009 Kirtane2009 Kuramisu2013 Daeng2011 Marvi2015 Muhastein2003 Muramatsu2014 Norhammar2004 Onuma2011 Overgaard2013 Park2009 Silber2013 Stone2011 Syd2010 Tada2011 Subtotal (95% CI)	= 18.95 spances: C Diabe Events: W 93 16 19 69 54 8 8 3 862 60 0 23 3 60 23 3 79 9 54 8 8 3 862 60 0 23 3 60 23 3 79 9 101 61 22 4 4 4 4 3 8 22 9 24 4 4 4 0 23 32 9 22 54 24 4 22 54 24 54 24 54 24 54 24 54 24 54 24 54 54 54 54 54 54 54 54 54 54 54 54 54	(P < 0.0. hi <sup>2</sup> = 2.9 tic Total 1659 227 201 297 201 297 201 297 395 5051 1575 5051 1575 5051 1575 390 3167 1140 281 8281 8281 8452 263 394 1452 452 452 452 452 452 878 81868 299 271 105 1365 291 207 207 207 207 207 207 207 207 207 207	0001) 2, df = 1 ( <b>Non-diala</b> <b>121</b> 200 30 3224 489 10 11 203 3224 489 10 11 203 3224 489 10 11 203 3224 489 10 11 203 3224 489 10 11 203 3224 489 10 203 203 204 203 203 204 203 203 204 203 203 204 203 203 204 203 203 204 203 203 204 203 203 204 203 203 204 203 203 204 203 203 203 203 203 203 203 203 203 203	P = 0.09 betics Total 3559 664 811 1355 1347 483 12742 2384 3167 2384 3167 2384 3167 2384 3167 2384 3167 2384 3167 2384 3167 2384 3167 2384 3167 2384 3167 2384 3167 2384 3167 2467 3167 2467 3167 2467 3167 2467 3167 2467 3167 2467 3167 2467 3167 2467 3167 2467 3167 2467 3167 2467 3167 2467 3167 2467 3167 2467 3167 2467 2467 2467 2467 2467 2467 2467 24	), P = 65.7 Weight 4.5% 2.0% 4.8% 4.8% 4.4% 4.8% 4.4% 5.3% 0.5	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.25, 4.00]           1.41 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [1.20, 4.21]           1.57 [1.61, 1.89]           1.43 [1.30, 2.73]           1.30 [0.69, 2.45]           2.201 [1.67, 2.42]           1.69 [1.26, 2.28]           0.52 [0.07, 1.42]           0.59 [0.19, 1.81]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.49, 3.39]           1.52 [0.93, 2.47]           2.27 [1.42, 3.62]           1.66 [1.17, 2.34]           0.04 [0.02, 8.35]           5.33 [3.26, 9.40]           2.01 [1.30, 3.10]           1.90 [1.38, 2.60]           1.66 [1.17, 7.31]           1.20 [1.33, 2.07]           2.81 [1.33, 2.07]           2.81 [1.33, 2.07]           2.81 [1.35, 5.17]           1.40 [1.23, 1.60]           1.85 [1.66, 2.06]	Risk Ratio M-H, Random, 95% CI 
Test for overall effect: Z Test for subgroup diffect A Study or Subgroup 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondai2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2012 Kedhi2014 Kurealekes2010 Kiptane2009 Kithane2009 Kufner2014 Kuramitsu2013 Lee2006 Lee2012 Lima2013 Muhlestein2003 Muramatsu2014 Norhamma2004 Onuma2011 Overgaard2013 Park2009 Sibner2013 Stone2011 Syad2010 Tada2011 Subtotal (95% CI) Total events Heterogeneily: Tau <sup>2</sup> = 0.	= 18.95 spances: C Diabe Events ity 93 16 93 16 93 16 93 16 93 16 93 16 93 16 93 16 93 16 93 16 93 16 93 16 93 16 95 4 8 3 8 22 3 8 8 22 3 8 8 22 3 8 8 22 3 7 9 10 11 19 19 19 19 19 19 19 19 19	(P < 0.0. h <sup>2</sup> = 2.9 h <sup>2</sup> = 2.9 tic Total 1659 227 201 297 201 297 201 297 201 297 395 5051 159 141 5051 15051 15051 25051 25051 2603 3167 1240 281 282 263 392 456 263 392 456 263 392 456 263 392 456 263 394 456 263 394 456 263 394 456 263 394 456 263 271 297 201 201 201 201 201 201 201 207 201 207 201 207 201 207 201 207 207 207 207 207 207 207 207 207 207	0001) 2, df = 1 ( <b>Non-diala</b> <b>Events</b> 121 20 33 224 121 20 33 224 4 227 23 24 24 20 10 11 20 20 21 21 20 20 21 21 20 20 21 21 20 20 21 20 20 20 21 20 20 20 20 20 20 20 20 20 20	P = 0.09 betics Total 3559 664 4811 1355 1347 448 193 12742 2384 10772 2467 1072 2467 1033 2886 1034 288 1034 2955 1034 2155 1034 2155 1034 2158 1034 2158 21	), $P = 65.7$ <b>Weight</b> 4.5% 2.0% 2.4% 4.8% 4.8% 4.8% 6.0% 5.3% 0.5% 0.5% 0.5% 0.8% 0.5% 0.8% 0.5% 0.5% 0.8% 0.5%	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.35, 4.00]           1.44 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [0.91, 5.61]           2.25 [1.20, 4.21]           1.75 [1.61, 1.89]           1.89 [1.43, 2.60]           1.89 [1.43, 2.60]           1.89 [1.43, 2.60]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.01 [1.67, 2.42]           1.69 [1.62, 2.28]           0.52 [0.07, 1.42]           0.58 [0.19, 1.81]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.51 [1.89, 3.39]           1.52 [0.93, 2.47]           2.27 [1.42, 3.62]           1.66 [0.99, 1.36]           5.86 [3.41, 10.96]           5.86 [3.41, 10.96]           5.43 [3.41, 10.96]           5.43 [3.26, 9.40]           2.01 [1.30, 3.10]           1.90 [1.38, 2.60]           5.43 [3.26, 9.40]           2.51 [1.31, 2.07]           2.41 [1.32, 0.71]           1.53 [5.47]           1.40 [1.23, 1.60]           1.55 [1.66, 2.06]	Risk Ratio M-H, Random, 95% Cl
Test for overall effect: Z Test for subgroup diffect A Study or Subgroup 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fermandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2010 Jensen2010 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2014 Kuramitsu2013 Lee2012 Lima2013 Maeng2011 Marui2015 Muhlestein2003 Muramatsu2014 Norhammar2004 Onuma2011 Overgaard2013 Stone2011 Syed2010 Tad avents Heterogenetily: Tau'z = 0. Test for overall effect: Z	= 18.95 spances: C Diabe Events ity 93 16 19 954 8 8 8 23 101 101 61 19 954 8 8 8 23 3 79 101 61 2 2 3 79 101 61 2 4 4 37 70 101 61 2 2 4 4 4 0 2 3 3 2244 4 0 23 3 2244 22 3 29 9 2251 100 5 5 4 22 22 5 5 5 5 5 5 5 5 5 5 5 5 5 5	(P < 0.0, hi <sup>2</sup> = 2.9, ttic Total 16599 227 201 297 201 297 395 3167 390 3167 390 3167 390 3167 452 452 452 452 452 452 452 452 452 452	0001) 2, df = 1 ( <b>Non-dial</b> <b>Events</b> 121 20 33 224 4 227 24 8 4 422 24 24 24 24 24 24 24 24 24 24 24	P = 0.09 betics Total 3559 664 811 1355 811 1347 448 811 1347 448 1347 2384 3167 2384 1034 1034 2384 1034 1034 2384 1034 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2385 1034 2384 1034 2384 1034 2385 1034 2385 1034 2385 1034 2385 1034 2385 1034 2385 1034 2455 1034 2455 1037 2455 1047 1047	), P = 65.7 Weight 4.5% 2.0% 4.8% 4.8% 6.0	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.22 [1.35, 4.00]           1.41 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [0.91, 5.61]           2.25 [1.00, 4.21]           1.56 [1.27, 2.15]           2.25 [0.91, 5.61]           2.25 [0.94, 5.61]           2.25 [1.00, 4.21]           1.75 [1.61, 1.89]           1.89 [1.43, 2.50]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.21 [1.67, 2.42]           1.69 [0.14, 2.20]           1.40 [0.80, 2.45]           2.53 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.89, 3.39]           1.52 [0.93, 2.47]           2.27 [1.20, 3.21]           1.40 [0.80, 2.45]           5.53 [3.26, 9.40]           2.01 [1.7, 2.34]           2.07 [1.37, 3.13]           1.53 [1.13, 2.07]           2.40 [1.53, 5.17]           1.40 [1.23, 1.60]           1.55 [1.66, 2.06]	Risk Ratio H-H, Random, 95% Cl H-H, Rand
Test for overall effect: Z Test for subgroup diffect A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2010 Kirtane2008 Kirtane2008 Kirtane2009 Kuramitsu2013 Lee2012 Lima2013 Maeng2011 Marui2015 Muramatu2014 Norhammar2004 Onuma2011 Overgaard2013 Park2009 Silber2013 Stone2011 Sved2010 Tada2011 Sved2010 Tada2011 Subtotal (95% CI) Total (95% CI)	= 18.95 spances: C Diabe Events ity 93 16 19 95 4 8 8 262 6 00 23 79 101 61 2 4 4 7 3 262 20 23 244 24 23 224 24 44 40 20 223 224 24 24 23 29 265 100 20 5 10 20 20 20 20 20 20 20 20 20 20 20 20 20	(P < 0.0, h <sup>2</sup> = 2.9, tic Total 1659 227 201 297 1575 1575 1575 1575 1575 1575 1575 1575 1575 1575 141 1575 1575 1575 141 1575 1575 141 1575 141 1575 141 1575 141 1575 141 1575 141 1575 141 1575 141 1575 141 1575 141 1575 141 1575 1575 141 1575 1575 141 1575 1575 141 1575 1575 141 1575 1575 141 1575 1575 141 1575 1575 141 1575 1575 141 1575 1575 141 1575 1575 141 1575 1575 141 1575 1575 1575 141 1575 1575 141 1575 1575 1575 141 1575 1575 1575 141 1575	0001) 2, df = 1 ( <b>Non-diala</b> <b>Events</b> 121 20 33 224 89 10 11 124 20 33 224 49 20 33 224 49 20 32 24 42 22 23 328 81 11 4 126 217 7 7 7 8 7 8 9 9 29 9 29 20 60 10 11 12 12 12 20 33 32 24 49 29 20 20 33 22 4 20 33 22 4 20 33 22 4 20 33 22 4 20 33 22 4 20 33 22 4 20 33 22 4 20 33 22 4 4 20 33 22 4 4 20 33 22 4 4 20 33 22 4 4 20 33 22 4 4 20 33 22 4 4 20 33 22 4 4 20 33 22 4 4 20 33 22 4 4 20 33 22 4 4 20 33 22 4 4 20 33 22 4 4 20 33 22 4 4 20 33 22 4 4 22 20 33 22 4 4 22 22 22 22 22 22 22 22 22 22 22	P = 0.09 betics Total 3559 664 811 1355 4811 1347 448 312742 2384 3167 2384 3167 2384 3167 2384 3167 2384 3167 2384 3167 1347 2384 3168 31034 2384 31034 2384 31034 2384 31034 2384 31034 2384 31034 2384 31034 2384 31034 2384 31034 2384 31034 2384 31034 2384 31034 2384 31034 2384 31034 2384 31034 2385 31034 2455 2158 395 3957 3957 3957 3957 3957 3957 3957 3957 3957 3957 39777 39777 39777 39777 39777 3977 3977 3977 3977 3977 3977	), P = 65.7 Weight 4.5% 2.0% 4.8% 4.8% 4.4% 4.4% 5.3% 0.8% 2.3% 2.8% 2.8% 2.8% 2.8% 2.8% 2.9% 5.3% 2.8	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.25, 4.00]           1.41 [1.11, 1.78]           2.07 [1.50, 2.65]           2.25 [0.91, 5.61]           2.25 [1.20, 4.21]           1.69 [1.43, 2.60]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.01 [1.67, 2.42]           0.69 [1.69, 2.45]           2.05 [1.00, 12.22]           0.52 [0.07, 1.42]           0.59 [0.19, 1.81]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.40, 12.20]           1.40 [0.80, 2.45]           2.53 [1.40, 12.01]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.40, 0.21]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.40, 0.21]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.41, 0.96]           0.43 [0.02, 2.85]           5.53 [3.26, 9.40]           2.01 [1.30, 3.10]           1.90 [1.38, 2.60]           1.66 [1.77, 3.13]           1.53 [1.13, 2.07]	Risk Ratio H-H, Random, 95% CI H-H, Rand
Test for overall effect: Z Test for subgroup diffect A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2011 Kedhi2014 Kerelakes2010 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2009 Kurer2014 Kuramitsu2013 Maeng2011 Marui2015 Muhestein2003 Muramatsu2014 Norhammar2004 Onuma2011 Overgaard2013 Stone2011 Sybotal (95% CI) Total events	= 18.95 spances: C Diabe Events: C 93 16 93 16 93 16 93 49 94 8 8 23 379 95 4 8 8 23 379 91 55 4 8 23 379 91 55 4 4 4 4 00 23 24 4 4 4 00 23 24 24 4 4 00 23 24 24 55 10 55 50 22 51 10 10 10 10 10 10 10 10 10 10 10 10 10	$ \begin{array}{l} (P < 0.0, P <$	0001) 2, df = 1 ( <b>Non-diala</b> <b>Events</b> 121 20 33 3224 89 90 10 14 42 25 80 90 10 14 42 25 82 81 17 7 124 69 90 00 222 212 3 3 42 42 42 25 88 6 89 90 00 11 12 12 12 12 12 12 12 12 12 12 12 12	P = 0.09 Detics Total 3559 664 4811 1355 1347 448 193 12742 2384 10772 2384 10772 2467 1337 2686 1034 2884 1034 2884 1034 2884 1034 2884 1034 2884 1034 2884 1034 2885 1034 2885 1034 2885 1034 2955 1034 2158 8957 1123 1258 8957 2158 8957 2158 8957 2158 8957 2158 8957 2158 8957 2158 2159 2157 2158 2159 2157 2158 2159	), I <sup>2</sup> = 65.7 <b>Weight</b> 4.5% 2.0% 4.8% 4.8% 4.8% 4.8% 4.8% 4.8% 4.8% 4.8% 4.3% 6.0%	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.50, 2.65]           2.25 [1.50, 2.65]           2.25 [1.20, 4.21]           1.75 [1.61, 1.89]           1.89 [1.43, 2.50]           1.67 [1.07, 2.62]           1.68 [1.30, 2.73]           1.30 [0.69, 2.45]           2.20 [1.60, 7, 1.42]           0.59 [0.07, 1.42]           0.59 [0.07, 1.42]           0.59 [0.07, 1.42]           0.59 [0.07, 1.42]           0.58 [0.07, 1.42]           0.59 [0.09, 1.81]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.89, 3.39]           1.52 [0.30, 2.47]           2.27 [1.42, 3.62]           1.16 [0.90, 3.26]           5.86 [3.14, 10.96]           0.43 [0.02, 8.35]           5.33 [3.26, 9.40]           2.01 [1.30, 3.10]           1.90 [1.38, 2.60]           1.66 [1.17, 2.34]           2.07 [1.23, 1.60]           1.85 [1.66, 2.06]           69%	Risk Ratio M-H, Random, 95% Cl
Test for overall effect: Z Test for subgroup diffect A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fermandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2010 Jensen2010 Jensen2010 Kirtane2008 Kirtane2009 Kufner2014 Kuramitsu2013 Lee2006 Lee2012 Lima2013 Maeng2011 Marni2015 Muhlestein2003 Muramatsu2014 Norhammar2004 Onuma2011 Overgaard2013 Stone2011 Syed2010 Tada2011 Systemethy Symbol Symbol Symbo	= 18.95 spances: C Diabe Events ity 93 16 19 95 4 8 8 22 3 79 95 4 8 8 22 3 79 101 61 19 95 4 8 8 22 3 79 101 61 9 54 8 8 22 3 79 101 101 101 102 103 101 101 101 102 103 101 101 101 101 102 103 101 101 101 101 101 101 101	(P < 0.0, hi <sup>2</sup> = 2.9, tic Total 16599 2277 201 2977 395 1599 247 395 159 394 11575 395 394 11575 395 394 287 1065 394 452 263 394 452 263 394 452 263 394 452 263 394 452 263 277 1065 878 81869 155 4400 271 28700 = 101.4 (P < 0.0 28700 = 101.4	0001) 2, df = 1 ( <b>Non-dial</b> <b>Events</b> 121 20 33 224 829 10 112 121 20 33 3224 84 422 225 3288 117 14 1246 6217 84 422 2328 300 229 290 60 2222 12 12 3 30 00 222 12 12 3 846 6 8, df = 31	P = 0.09 betics Total 3559 664 811 1355 811 1347 448 811 1347 448 11347 2384 3167 2384 1072 2384 1072 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 2384 1034 1034 2384 1034 1034 2384 1034 1034 2384 1034 1034 2384 1034 1034 2384 1034 1034 2056 1137 1123 2056 1123 2056 1123 2057	), P = 65.7 Weight 4.5% 2.0% 4.4% 4.4% 6.0% 4.4% 6.0% 4.4% 6.0	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.25 [1.35, 4.00]           1.41 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [0.91, 6.61]           2.25 [0.91, 6.61]           2.25 [1.00, 4.21]           1.75 [1.61, 1.89]           1.89 [1.43, 2.50]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.21 [1.67, 2.42]           1.69 [1.42, 2.80]           0.59 [0.19, 1.81]           3.82 [1.20, 1.2.20]           1.40 [0.80, 2.45]           2.53 [1.89, 3.39]           1.52 [0.93, 2.47]           2.27 [1.32, 2.47]           2.27 [1.32, 3.26]           0.40 [0.80, 2.45]           2.53 [1.40, 1.20]           1.40 [0.80, 2.45]           2.53 [1.40, 1.30]           5.86 [3.14, 10.96]           0.43 (0.02, 3.35]           5.53 [3.26, 9.40]           2.01 [1.7, 3.31]           1.53 [1.13, 2.07]           1.40 [1.23, 1.60]           1.53 [1.53, 5.17]           1.40 [1.23, 1.60]           1.55 [1.66, 2.06]           69%	Risk Ratio H-H, Random, 95% Cl H-H, Rand
Test for overall effect: Z Test for subgroup diffect A <u>Study or Subgroup</u> 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fermandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2010 Kirtane2008 Kirtane2008 Kirtane2009 Kurantisu2013 Lee2006 Lee2012 Lima2013 Macrigueta Marri2014 Norhammar2004 Onuma2011 Overgaard2013 Park2009 Silber2013 Stone2011 Syed2010 Tada2011 Syed2010 Tada2011 Subtotal (95% CI) Total events Heterogeneily: Tau² = 0. Test for overall effect: Z Total (95% CI) Total effect: Z	= 18.95 spances: C Diabe Events: lity 93 16 19 954 882 862 862 862 862 862 862 862 862 862	(P < 0.0, hi <sup>2</sup> = 2.9, tic Total 1659 227 201 297 201 297 395 559 159 395 159 390 3167 15051 1575 551 1575 390 2870 3141 2877 456 452 452 452 453 456 452 453 457 457 457 457 457 457 457 457 457 457	0001) 2, df = 1 ( <b>Non-dial</b> <b>Events</b> 121 20 33 3224 49 90 0 33 224 49 20 33 224 49 225 3228 112 4 225 3228 114 126 217 84 425 227 23 224 24 29 90 00 2022 122 33 30 00 2022 123 33 204 44 121 20 33 224 40 217 124 20 32 224 20 20 33 224 40 20 33 224 40 227 20 33 224 40 227 20 33 224 40 227 20 33 224 40 227 20 33 224 40 227 20 33 224 40 227 20 33 224 40 227 20 33 224 40 227 20 33 224 40 227 20 33 224 40 227 20 33 224 40 227 22 22 22 22 22 22 22 23 30 224 40 227 22 22 22 22 23 30 30 31 224 40 227 22 22 22 22 23 30 30 31 224 40 227 22 22 22 22 23 30 30 224 40 227 22 22 22 22 22 23 30 30 224 40 227 22 24 40 227 22 24 40 227 22 24 40 227 22 24 40 227 22 24 40 227 22 24 40 227 22 24 40 227 22 24 40 227 22 24 40 227 22 24 40 227 22 24 40 227 22 24 40 227 22 24 40 227 22 24 40 227 22 24 40 227 33 30 00 20 22 2 22 22 23 30 00 20 22 2 23 30 30 20 24 20 22 2 2 2 2 2 2 2 2 2 2 2 2 2	P = 0.09 betics Total 3559 664 811 1355 448 11347 448 11347 448 1347 448 1347 448 1347	), P = 65.7 Weight 4.5% 2.0% 4.8% 4.8% 4.4% 2.4% 4.8% 4.4% 5.3% 2.8% 2.7% 2.8% 2.8% 2.8% 2.8% 2.8% 2.8% 2.7	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.35, 4.00]           1.41 [1.11, 1.78]           2.07 [1.50, 2.85]           2.25 [0.91, 5.61]           2.25 [0.91, 5.61]           2.25 [0.94, 5.61]           2.25 [0.94, 5.61]           2.25 [0.94, 5.61]           2.25 [0.94, 5.61]           2.25 [0.94, 5.61]           2.25 [0.94, 5.61]           2.25 [1.64, 1.89]           1.89 [1.43, 2.00]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.01 [1.67, 2.42]           0.69 [0.19, 1.81]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.40, 10.20]           2.41 [1.09, 1.30]           5.85 [3.41, 10.66]           0.43 [0.02, 3.53]           5.53 [3.26, 9.40]           2.01 [1.67, 2.34]           1.60 [1.72, 3.13]           1.53 [1.13, 2.07]           2.81 [1.53, 5.17]           1.40 [1.23, 1.60]           1.85 [1.66, 2.06]           69%	Favours (diabetics) Favours (non-diabetics)
Test for overall effect: Z Test for subgroup diffect A Study or Subgroup 1.6.3 Long-term Mortal Akin2012 Banning2010 Billinger2008 Biondal2012 Claessen2011 Daemen2008 Fernandez2011 Garg2008 Jensen2010 Jensen2010 Jensen2010 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2008 Kirtane2009 Kirtane2009 Kirtane2009 Kuramitsu2013 Maeng2011 Maviz015 Muramatsu2014 Norhammar2004 Onuma2011 Overgaard2013 Stone2011 Subtotal (95% CI) Total events Heterogeneity: Tau <sup>2</sup> = 0. Test for overall effect: Z Total (95% CI)	= 18.95 spances: C Diabe Events Ity 93 166 19 954 8 3 262 101 101 6 102 23 3 79 101 6 101 6 102 23 23 244 4 4 0 23 29 244 4 4 0 23 23 29 244 4 40 23 23 29 244 40 0 23 399 2651 106 5 5 0 5 0 5 0 5 0 5 0 5 0 5 0 5 0 5 0	$ \begin{array}{l} ({\bf p} < 0.0, {\bf h}^2 = 2.9 \\ {\bf h}^2 = 2.9 \\ {\bf tic} \\ \hline {\bf Total} \\ 1659 \\ 227 \\ 201 \\ 297 \\ 201 \\ 297 \\ 395 \\ 5051 \\ 1575 \\ 5051 \\ 1575 \\ 390 \\ 3167 \\ 11575 \\ 390 \\ 3167 \\ 1140 \\ 287 \\ 390 \\ 3167 \\ 1140 \\ 287 \\ 390 \\ 281 \\ 106 \\ 287 \\ 106 \\ 287 \\ 106 \\ 287 \\ 00 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 1$	0001) 2, df = 1 ( <b>Non-dial</b> <b>Events</b> 121 20 33 3224 89 10 124 233 3224 49 10 1246 217 87 88 60 910 1246 217 87 87 80 80 80 10 1246 217 1246 212 22 22 22 22 22 22 22 22 22 22 22 22	P = 0.09 betics Total 3559 664 811 1355 1347 481 1347 2384 3167 2477 2384 3167 2477 2384 3167 2477 2384 3167 2477 2384 3167 24777 24777 24777 2477 2477	), P = 65.7 Weight 4.5% 2.0% 4.8% 4.8% 4.8% 4.8% 4.8% 4.8% 4.8% 4.2% 0.8% 0.8% 0.8% 0.8% 0.8% 0.8% 0.8% 0.5% 0.8% 0.5% 0.8% 0.5% 0.	Risk Ratio           M-H, Random, 95% CI           1.65 [1.27, 2.15]           2.34 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.23, 4.44]           2.32 [1.50, 2.65]           2.25 [1.50, 2.65]           2.25 [1.50, 2.65]           2.25 [1.00, 2.65]           2.25 [1.00, 2.65]           2.25 [1.00, 2.61]           2.55 [1.00, 2.42]           1.69 [1.43, 2.60]           1.67 [1.07, 2.62]           1.88 [1.30, 2.73]           1.30 [0.69, 2.45]           2.01 [1.67, 2.42]           1.69 [1.26, 2.28]           0.52 [0.07, 1.42]           0.59 [0.19, 1.81]           3.82 [1.20, 12.20]           1.40 [0.80, 2.45]           2.53 [1.89, 3.39]           1.52 [0.93, 2.47]           2.27 [1.42, 3.62]           1.16 [0.99, 1.36]           5.53 [3.26, 9.40]           2.01 [1.30, 3.10]           1.90 [1.38, 2.60]           1.66 [1.77, 3.31]           1.53 [1.13, 2.07]           2.81 [1.53, 5.17]           1.40 [1.23, 1.60]           1.53 [1.13, 2.07]           2.81 [1.53, 5.17]           1.66 [1.77, 3.33] </td <td>Risk Ratio M-H, Random, 95% CI</td>	Risk Ratio M-H, Random, 95% CI

FIGURE 4. (A) Forest plot showing the in-hospital and short-term mortality in diabetic patients. (B) Forest plot showing the long-term mortality in diabetic patients.

	Metabolic syn	ndrome	Non-metabolic syn	drome		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I M-H, Fixed, 95% Cl	
1.4.2 Short-term Mor	rtality							
Butler2006	170	1169	265	1866	43.4%	1.02 [0.86, 1.22]	•	
Kim2010	3	170	2	168	0.4%	1.48 [0.25, 8.76]		
Rana2005	11	448	7	453	1.5%	1.59 [0.62, 4.06]	- <u>+</u>	
Subtotal (95% CI)		1787		2487	45.3%	1.05 [0.88, 1.25]	•	
Total events	184		274					
Heterogeneity: Chi <sup>2</sup> =	0.97, df = 2 (P =	0.62); I <sup>2</sup> =	0%					
Test for overall effect:	: Z = 0.51 (P = 0.6	61)						
1.4.3 Long-term Mor	tality							
Kasai2006	43	318	45	430	8.1%	1.29 [0.87, 1.91]	T=	
Kasai2008	43	318	45	430	8.1%	1.29 [0.87, 1.91]	T	
Kim2010	5	170	2	168	0.4%	2.47 [0.49, 12.56]		
Lee2015	5	570	5	333	1.3%	0.58 [0.17, 2.00]		
Maron2011	278	1362	129	886	33.2%	1.40 [1.16, 1.70]		
Marso2012	3	239	19	434	2.9%	0.29 [0.09, 0.96]		
Patsa2013	2	147	5	364	0.6%	0.99 [0.19, 5.05]		
Subtotal (95% CI)		3124		3045	54.7%	1.29 [1.11, 1.51]	▼	
Total events	379		250					
Heterogeneity: Chi <sup>2</sup> =	8.97, df = 6 (P =	0.18); l <sup>2</sup> =	33%					
Test for overall effect:	: Z = 3.32 (P = 0.0	0009)						
Total (95% CI)		4911		5532	100.0%	1.18 [1.05, 1.33]	•	
Total events	563		524					
Heterogeneity: Chi <sup>2</sup> =	13.78. df = 9 (P =	= 0.13); l <sup>2</sup>	= 35%					-
Test for overall effect:	Z = 2.87 (P = 0.0	004)					0.01 0.1 1 10 10	)0
Test for subaroup diff	erences: Chi <sup>2</sup> = 3	.24. df = 1	(P = 0.07), l <sup>2</sup> = 69.1%	6			Favours [IVIS] Favours [non-MS]	

FIGURE 5. Forest plot showing the mortality in patients with metabolic syndrome.

	Smokers		Non-smokers		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	M-H, Fix	ed, 95% Cl	
1.3.2 Short-term Mort	ality									
Arbel2014	152	3201	125	1363	47.4%	0.52 [0.41, 0.65]				
Goto2011	20	1563	58	1765	14.7%	0.39 [0.24, 0.64]				
Mohamedali2013	7	258	28	501	5.1%	0.49 [0.21, 1.10]			+	
Robertson2014	21	2362	60	5279	10.0%	0.78 [0.48, 1.28]			+	
Tan2014	31	448	68	603	15.7%	0.61 [0.41, 0.92]				
Weisz2015	12	898	22	638	7.0%	0.39 [0.19, 0.78]				
Subtotal (95% CI)		8730		10149	100.0%	0.53 [0.45, 0.62]		•		
Total events	243		361							
Heterogeneity: Chi <sup>2</sup> = 5.18, df = 5 (P = 0.39); l <sup>2</sup> = 3%										
Test for overall effect: Z = 7.56 (P < 0.00001)										
Total (95% CI)		8730		10149	100.0%	0.53 [0.45, 0.62]		•		
Total events	243		361							
Heterogeneity: Chi <sup>2</sup> = 5.18, df = 5 (P = 0.39); l <sup>2</sup> = 3%										400
Test for overall effect: Z = 7.56 (P < 0.00001)							0.01	0.1 Eavours [emokors]	1 10 Fovours Inon smoko	100
Test for subgroup differences: Not applicable						Favours [sinokers]	ravours [non-smoke	5]		

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FIGURE 6. (A) Forest plot showing the short-term mortality in smokers. (B) Forest plot showing the long-term mortality in smokers.

	High BMI		Low and normal BMI		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I M-H, Fixed, 95% CI		
1.5.1 In-hospital Mort	ality								
Akin2012	19	4370	11	1436	0.4%	0.57 [0.27, 1.19]	——————————————————————————————————————		
Ellis1996	33	2841	17	614	0.7%	0.42 [0.24, 0.75]	— <del>—</del>		
Gruberg2002	416	7710	204	1923	8.4%	0.51 [0.43, 0.60]	-		
He2015	2	528	5	549	0.1%	0.42 [0.08, 2.13]			
Kang2009	67	2442	65	1382	2.1%	0.58 [0.42, 0.82]			
Kosuge2008	24	980	108	2096	1.8%	0.48 [0.31, 0.73]			
Lancefield2010	26	3442	17	1320	0.6%	0.59 [0.32, 1.08]			
Mehta2007	39	1622	31	703	1.1%	0.55 [0.34, 0.87]			
Minutello2004	549	69501	321	25934	12.0%	0.64 [0.56, 0.73]	-		
Numasawa2015	55	3735	154	6407	2.9%	0.61 [0.45, 0.83]			
Payvar2013	1014	83861	4297	217616	61.2%	0.61 [0.57, 0.66]			
poludasu2008	0	631	0	146		Not estimable			
Powell2003	84	4763	41	1269	1.7%	0.55 [0.38, 0.79]			
Shubair2006	50	3645	17	986	0.7%	0.80 [0.46, 1.37]			
Witassek2014	131	4577	86	2361	2.9%	0.79 [0.60, 1.03]			
Subtotal (95% CI)		194648		264742	96.5%	0.61 [0.58, 0.64]	•		
Total events	2509		5374						
Heterogeneity: Chi <sup>2</sup> = 13.38, df = 13 (P = 0.42); l <sup>2</sup> = 3%									
Test for overall effect: 2	Z = 18.78	(P < 0.00	001)						
1.5.2 Short-term Mort	ality								
Akin2012	105	4370	47	1436	1.8%	0 73 [0 52 1 03]			
Kang2009	25	1685	26	951	0.9%	0.54 [0.32, 0.93]			
Lancefield2010	38	3442	22	1320	0.8%	0.66 [0.39, 1.12]			
Subtotal (95% CI)	00	9497	22	3707	3.5%	0.67 [0.52, 0.86]	$\bullet$		
Total events	168		95				·		
Heterogeneity: $Chi^2 = 0.86$ . $df = 2 (P = 0.65)$ ; $l^2 = 0\%$									
Test for overall effect: Z = 3.12 (P = 0.002)									
Total (95% CI)		204145		268449	100.0%	0.61 [0.58, 0.64]	•		
Total events	2677		5469						
Heterogeneity: Chi <sup>2</sup> = 1	14.90. df =	= 16 (P = )	$(0.53):  ^2 = 0\%$				· · · · · · · · · · · · · · · · · · ·		
Test for overall effect: $Z = 19.04$ (P < 0.0001) 0.01 0.1 1 10 100									
Test for subgroup differences: Chi <sup>2</sup> = 0.60, df = 1 (P = 0.44), l <sup>2</sup> = 0%									
Test for subgroup differences: Chi <sup>2</sup> = 0.60, df = 1 (P = 0.44), l <sup>2</sup> = 0%									

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	High BMI		Low and normal BMI			Risk Ratio	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI		
1.5.3 Long-term Mortality									
Gruberg2002	416	7710	204	1923	13.4%	0.51 [0.43, 0.60]	+		
Gruberg2005	16	431	6	168	2.4%	1.04 [0.41, 2.61]			
Gurm2002	251	2703	107	931	12.1%	0.81 [0.65, 1.00]			
He2015	8	528	11	549	2.5%	0.76 [0.31, 1.87]			
Kaneko2013	11	473	46	731	4.3%	0.37 [0.19, 0.71]			
Kang2009	30	1296	32	717	6.2%	0.52 [0.32, 0.85]			
Lancefield2010	88	3442	58	1320	9.3%	0.58 [0.42, 0.81]			
Mehta2007	265	1622	239	703	13.6%	0.48 [0.41, 0.56]	<b>T</b>		
Nikolsky2005	21	1074	4	233	1.9%	1.14 [0.39, 3.29]			
Park2013	346	10749	658	12432	14.2%	0.61 [0.54, 0.69]	*		
Poston2004	50	1211	26	391	6.7%	0.62 [0.39, 0.98]			
Sarno2010	40	1204	15	497	4.9%	1.10 [0.61, 1.97]			
Wang2012	108	4491	38	1592	8.4%	1.01 [0.70, 1.45]	.+-		
Subtotal (95% CI)		36934		22187	100.0%	0.64 [0.54, 0.75]	◆		
Total events	1650		1444						
Heterogeneity: Tau <sup>2</sup> = 0.04; Chi <sup>2</sup> = 37.34, df = 12 (P = 0.0002); l <sup>2</sup> = 68%									
Test for overall effect: Z = 5.64 (P < 0.00001)									
Total (95% CI)		36934		22187	100.0%	0.64 [0.54, 0.75]	•		
Total events	1650		1444						
Heterogeneity: Tau <sup>2</sup> = 0.04; Chi <sup>2</sup> = 37.34, df = 12 (P = 0.0002); l <sup>2</sup> = 68%									
Test for overall effect: Z = 5.64 (P < 0.00001)									
Test for subgroup differences: Not applicable									

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FIGURE 7. (A) Forest plot showing the in-hospital and short-term mortality in overweight and obese patients. (B) Forest plot showing the long-term mortality in overweight and obese patients.

Obesity is another modifiable risk factor for cardiovascular diseases. Surprizingly, our study showed an unexpectedly, significantly decreased mortality in these high BMI patients in all the follow-up categories after PCI. A significant 1.79%

overall death has been observed in the overweight and obese patients whereas a higher overall mortality of 2.38% was observed among the combined normal weight/underweight patients. Several studies have shown the existence of an



FIGURE 8. Funnel plots for the subgroup analysis.

"obesity paradox" in such patients after cardiovascular inter-vention.<sup>44</sup> The baseline features in this study showed a higher rate of diabetes, dyslipidemia, and hypertension among the overweight and obese patients. Intensive medications and aggressive medical therapies, regular counselling about health benefits, younger age, and having a good storage for nutrients after PCI could all be responsible for such a phenomenon. Size of the coronary blood vessels could also be considered as one of the reasons for this "obesity paradox."44 However, a few studies also showed different results. The study by Akin et al<sup>35</sup> in 2012 revealed no evidence of such a phenomenon. In his study, normal body weight patients and obese patients had similar rates of all-cause mortality. Such a different result in his study could be due to the fact that his study dealt with the comparison of different types of drug eluting stents and their corresponding adverse clinical outcomes after PCI. However, it is not clear whether or not this increased mortality risk could also have been more prominent among the underweight which could not be compensated by the normal weight population.

Smoking, which is another modifiable cardiovascular risk factor, has proved to be associated with cardiovascular disorders. Unexpectedly, results from our study showed a significantly decreased risk of overall mortality in these smokers (3.37%) compared to nonsmokers (5.13%) after PCI. According to the baseline features in this study, most of the nonsmokers were diabetics and suffered from high blood pressure. The existence of a "smoking paradox" has also been observed in other studies. For example, the study by Hasdai and Holmes found lower adverse outcomes in smokers compared to nonsmokers after PCI.<sup>111</sup> The question about why smokers have a lower mortality rate compared to nonsmokers after PCI is more interesting than its answer. Reasons suggested for this smoking paradox could be younger age, a more favorable clinical and angiographic profile among these smokers, and less damage to microvascular function in these patients after PCI. However, many other studies had different results compared to our metaanalysis. The study Jang et al<sup>112</sup> showed that individuals who continue smoking after PCI experienced significantly poorer outcomes compared to patients who have never smoked. Another study by Castela et al showed a higher rate of vascular complications, but a similar mortality rate between smokers and nonsmokers at 1 year. However, a smaller population size and a different definition of smoker could be responsible for this different result in his study.

Apart from these cardiovascular risk factors, an increased mortality in these patients after PCI could also have been due to factors such as drug eluting stents, which are associated with a higher long-term risk of stent thrombosis. Also, glucose-lowering drugs in DM patients have been associated with an increased risk of mortality in this modifiable cardiovascular risk group.<sup>113,114</sup> Moreover, a study by Yusuf et al<sup>115</sup> showed no difference in cardiovascular mortality even with intensive lifestyle intervention in DM patients indicating that there may be other factors such as socio-economic status which contribute to this increase in mortality in these high risk patients.

This meta-analysis with a large number of patients is the one and only meta-analysis comparing mortality between patients with low and high modifiable cardiovascular risk factors after PCI. Including 100 studies consisting of 844,190 patients with several modifiable cardiovascular risk factors such as DM, high BMI, hypertension, dyslipidemia, smoking and MS, and their impact on mortality after PCI makes this metaanalysis a completely new research in the field of interventional cardiology.

Several limitations in this meta-analysis were as follows: in a few studies, all-cause mortality was not among the clinical endpoints, however, being part of it, data concerning cardiac death has been considered. One study included mortality and myocardial infarction together. Because these data could not be separated, we have included them together in our meta-analysis. One study about smokers and PCI included data for the smokers undergoing fibrinolysis and PCI together. This may affect the result of our study to a certain extent. Moreover, in 1 study, overweight patients and obese patients were classified as a BMI >23.5 and 27.5 kg/m<sup>2</sup> instead of 25 and 30 kg/m<sup>2</sup>, respectively. Another study classified a BMI of  $25-35 \text{ kg/m}^2$  to be considered as overweight and  $>35 \text{ kg/m}^2$  to be considered as obese patients. Data for the baseline characteristics in several studies were not provided in the original article or could not be converted to dichotomous variables. Therefore, these data have been omitted in our meta-analysis. The baseline features of all the 100 studies have been analyzed and, the data concerning the number of patients with their corresponding risk factor in the whole study were obtained from the baseline features of each study. However, studies without dichotomous data at baseline, or if corresponding data were not available, have been omitted from this count. Therefore, except for the data being analyzed, the count for "modifiable cardiovascular risk factors for the whole study" is just an approximation for this study. However, despite these limitations, our data point to the urgent need for comprehensive comparison between these 2 groups of patients.

#### CONCLUSION

Certain modifiable cardiovascular risk subgroups had a significantly higher impact on mortality after PCI. However, mortality among the obese patients and the smokers showed an unexpected paradox after coronary intervention.

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