BMJ Open Impact of depression on clinical outcomes following percutaneous coronary intervention: a systematic review and meta-analysis

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ABSTRACT

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Objectives The objective of this meta-analysis was to assess whether depression in percutaneous coronary intervention (PCI) patients is associated with higher risk of adverse outcomes.

Design Systematic review and meta-analysis. Methods EMBASE, PubMed, CINAHL and PsycINFO were searched as data sources. We selected prospective cohort studies evaluating the relationship between depression and any adverse medical outcome, including all-cause mortality, cardiac mortality and non-fatal events, from inception to 28 February 2019. Two reviewers independently extracted information and calculated the risk of cardiovascular events in patients with preoperative or postoperative depression compared with non-depressed patients.

Results Eight studies (n=3297) met our inclusion criteria. Most studies found a positive association between depression and adverse cardiovascular outcomes. Metaanalysis yielded an aggregate risk ratio of 1.57 (95% Cl 1.28 to 1.92, p<0.0001) for the magnitude of the relation between depression and adverse outcomes. Conclusions Our systematic review and meta-analysis suggests that depression is associated with an increased risk of worse clinical outcome or mortality in patients undergoing PCI. Assessment time and length of follow-up do not have a significant effect on this conclusion.

INTRODUCTION

Depression and coronary artery disease (CAD) are highly comorbid conditions with estimates of comorbidity from 20% to 50%.¹⁻³ Patients with a combination of depression and CAD are at increased risk for negative cardiac outcomes. Prior meta-analyses have demonstrated that depression is associated with a twofold to fourfold increase in the risk of future major adverse cardiovascular events in patients with postmyocardial infarction (MI), and this relationship has remained stable despite improvements in diagnosis and treatment.^{4 5} The adverse effects of depression are also observed in patients admitted with unstable angina.⁶

Strengths and limitations of this study

- This study emphasises the growing recognition that depression is a major risk factor of cardiovascular disease.
- Depression needs to be fully considered when as-sessing the prognosis of percutaneous coronary intervention patients.
- The quality of the included studies was relatively hiah.
- Further analyses were difficult to conduct due to the limited number of studies.

Protected by copyright, including for uses related to text Percutaneous coronary intervention (PCI) has become a common revascularisation procedure with demonstrated safety and efficacy. Successful PCI significantly reduces \mathbf{a} the rate of death or revascularisation, and \mathbf{a} improves quality of life.^{7 8} Nonetheless, major adverse cardiac events (MACE), such as mortality, non-fatal MI and repeat PCI, still remain a problem. According to several studies, about one-fifth of patients experi-ence depression before PCI, an even greater proportion of patients are depressed after the **g** procedure.^{9–11} Besides well-known factors, psychological factors such as depression have been demonstrated to predict adverse cardiac events after PCI by multiple studies.¹²⁻¹⁵ However, not all the studies have suggested that depression was associated with poor prognosis following PCI.¹⁶¹⁷ Meyer *et al*¹⁶ reported depressive symptoms were linked g to mortality during 2 years' follow-up, but the relationship disappeared 3 years later. Moreover, de Jager¹⁷ and colleagues found the predictive value of depression differs between angina pectoris (stable angina, SA) and acute coronary syndrome (ACS) cohorts. Furthermore, levels of depression tend to change over time and questions remain about when to assess depression. Considering these problems, we performed a systematic review and

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Box 1 Search strategy in PubMed

- 1. depression [Mesh]
- 2. depression*[Title/Abstract]
- 3. depressive disorder*[Title/Abstract]
- 4. depressive mood*[Title/Abstract]
- 5. dysthymia [Title/Abstract]
- 6. No 1 OR No 2 OR No 3 OR No 4 OR No 5
- 7. percutaneous coronary interventions [Mesh]
- 8. percutaneous coronary intervention*[Title/Abstract]
- 9. PCI [Title/Abstract]
- 10. Coronary Balloon Angioplasty [Title/Abstract]
- 11. angioplasty [Title/Abstract]
- 12. No 7 OR No 8 OR No 9 OR No 10 OR No 11
- 13. No 6 AND No 12

meta-analysis to determine the prospective relationship between depression and adverse clinical outcomes after PCI.

METHODS

A systematic review and meta-analysis was performed following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines¹⁸ and an a priori study protocol.

Search strategy and selection criteria

Two authors (WYZ and NN) independently searched the literature in EMBASE, PubMed, CINAHL and PsycINFO databases without language restriction from inception to 28 February 2019. The search strategy contained keywords related to the population of interest (patients with CAD receiving PCI) and keywords related to depression. In PubMed, we used the combination of Medical Subject Headings (MeSH terms) and relevant free-text terms to identify the keywords for each topic. The set operator AND was used to form a complementary search strategy (see box 1).

The search terms from PubMed were adapted to the corresponding vocabulary of EMBASE, CINAHL and PsycINFO databases.

Selection and exclusion criteria

Studies investigating the association between depression and prognosis in patients receiving PCI were retrieved for review. Inclusion criteria were as follows: (1) prospective design, (2) patients diagnosed with CAD and receiving coronary stent implantation, (3) using established assessment instruments or structured clinical interviews to define major depression or depressive symptoms, and (4) reporting an endpoint of all-cause mortality, cardiac mortality, rehospitalisation or MACEs.

The exclusion criteria were as follows: (1) case report, animal research, review article or expert opinion, (2) depression not considered as a predictor, (3) unrelated to the search terms, (4) participants without PCI, and (5) data were not reported. For multiple publications from the same cohort,^{12 19–22} we chose the latest or most complete study for assessment.¹²

Data extraction

Two authors independently (JFT and XYY) read the abstract and title of every record identified by the search. Potentially eligible studies were reviewed in detail. Differences in opinion were resolved by consensus. Given that a variety of factors may influence outcome, the following data were extracted from the final eight studies by use of separate spreadsheets: first author's name, study design, ethnicity of the study population, diagnosis of CAD, g depression measurement, timing of assessment, outcome ş definition, length of follow-up, sample size and number of patients in the depressed and non-depressed groups. copyright,

Quality assessment

We used the Newcastle-Ottawa Scale²³ for guality assessment of included studies. The Newcastle-Ottawa Scale grades three domains: the selection of participants, comparability of the groups and assessment of outcome.²³ A study can be awarded a maximum of 9 stars for quality.

Each study can be awarded a maximum of 5 stars for quarty. Each study was assessed independently by two investiga-tors. The results are reported in table 1, online supple-mentary table S1. **Data synthesis and statistical analysis** Review Manager (RevMan) (V.5.3, The Cochrane Collab-oration, 2014) served as the statistical platform for data management and statistical analyses. Dichotomous frequency data were extracted from each study. Risk ratios (RR) were calculated from pooled data comparing depressed and non-depressed groups for the likelihood of adverse cardiovascular events. We calculated a pooled of adverse cardiovascular events. We calculated a pooled RR and 95% CI in the random effects model to account for possible methodological and clinical heterogeneity.

Heterogeneity analysis

ning, Al training, The statistical heterogeneity among studies was evaluated using the Cochran's Q test, I^2 statistic and df. The Q test was used to estimate test heterogeneity among trials. The Q value can be used to derive the I^2 value, which is the proportion (%) of variance in a pooled effect size due to heterogeneity rather than chance. Based on I², heteroge-

Publication bias Publication bias was assessed by means of Egger's regres-sion asymmetry test²⁵ and Begg's test.²⁶ We used the funnel plot to examine whether sample sizes influenced the results of the meta-analysis.

Sensitivity analysis and subgroup analysis

To further explore the sources of heterogeneity, we conducted a sensitivity analysis by omitting one study at a time and calculating the pooled effect size, 95% CI and heterogeneity of the remaining studies (table 2).

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Table 1 Chai	racteristics of	studies include	Characteristics of studies included in the meta-analysis						
Study	Ethnic	CAD type	Assessment timing	Measurement of depression	Number of patients (depressed/non- depressed)	Outcome	Number of events (depressed/non- depressed)	Follow- up time (years)	SON
de Jager <i>et al</i> ¹⁷	Netherlands	SA and ACS	1 month after PCI	HADS	528 (104/424)	All-cause mortality	35/98	10	6
Wang <i>et al</i> ¹¹	China	SA and ACS	2 weeks after PCI	HADS MINI	400 (154/246)	MACE (all-cause mortality, non- fatal MI and revascularisation)	42/32	З	6
Yu <i>et al</i> ¹³	Korea	CAD	Baseline during hospitalisation 1 month after discharge	PHQ-9	211 (64/157)	MACE (rehospitalisation, reinfarction, revascularisation or cardiac death)	13/21 11/23		~
Park <i>et al</i> ¹⁵	Korea	CAD	1-4 days after PCI	HADS	133 (44/89)	Recurrent cardiac events (MI, ISR, revascularisation)	11/7	-	9
van Dijk <i>et al</i> ¹²	Netherlands	SA and ACS	6 months after PCI	HADS	1112 (276/836)	All-cause mortality	122/262	10	o
Schmidt <i>et al</i> ¹⁴	Brazil	SA and ACS	Baseline	BDI	125 (31/94)	MACE (death, MI or TVR)	6/13	-	7
Meyer <i>et al</i> ¹⁶	Germany	Stable coronary heart disease	Before PCI	HADS	470 (101/369)	All-cause mortality MACE (NR)	11/33 16/57	2 and 5	6
Li et a/ ¹⁰	China	CAD	Baseline during hospitalisation	SDS	308 (112/196)	MACE (all-cause mortality, non- fatal MI and revascularisation)	9/4	.	7
ACS, acute coro events (the defin not reported info	rary syndrome; E itions differ acco rmation; PCI, pe	3DI, Beck Depress rding to the study rcutaneous corona	ACS, acute coronary syndrome; BDI, Beck Depression Inventory; CAD, coron events (the definitions differ according to the study and have been shown in t not reported information; PCI, percutaneous coronary intervention; PHQ-9, P.	nary artery disease; the table); MI, myoo atient Health Ques	HADS, Hospital Anxiet cardial infarction; MINI, tionnaire-9;SA, stable a	ACS, acute coronary syndrome; BDI, Beck Depression Inventory; CAD, coronary artery disease; HADS, Hospital Anxiety and Depression Scale; ISR, in-stent restenosis; MACE, major adverse cardiac events (the definitions differ according to the study and have been shown in the table); MI, myocardial infarction; MINI, Mini-International Neuropsychiatric Interview; NOS, Newcastle-Ottawa Scale; NR, not reported information; PCI, percutaneous coronary intervention; PHQ-9, Patient Heatth Questionnaire-9;SA, stable angina; SDS, Self-Rating Depression Scale; TVR, target vessel revascularisation.	restenosis; MACE, maji tterview; NOS, Newcastl scale; TVR, target vessel	or adverse ca e-Ottawa Sca revascularisa	diac Ile; NR, tion.

Study omitted	Risk ratio (95% CI)	Heterogeneity (I ²)	P value
de Jager <i>et al</i> ¹⁷	1.63 (1.25 to 2.13)	44%	<0.001
Wang et al ¹¹	1.47 (1.21 to 1.79)	24%	<0.001
Yu et al ¹³	1.59 (1.26 to 2.00)	45%	<0.001
Park et al ¹⁵	1.50 (1.25 to 1.79)	24%	<0.001
van Dijk et al ¹²	1.67 (1.26 to 2.21)	38%	<0.001
Schmidt <i>et al</i> ¹⁴	1.59 (1.27 to 1.99)	44%	<0.001
Meyer <i>et al</i> ¹⁶	1.64 (1.34 to 2.02)	31%	<0.001
Li et al ¹⁰	1.51 (1.26 to 1.81)	25%	<0.001
We conducted subgroup a	ssociation of depression with	RESULTS Study selection and description	



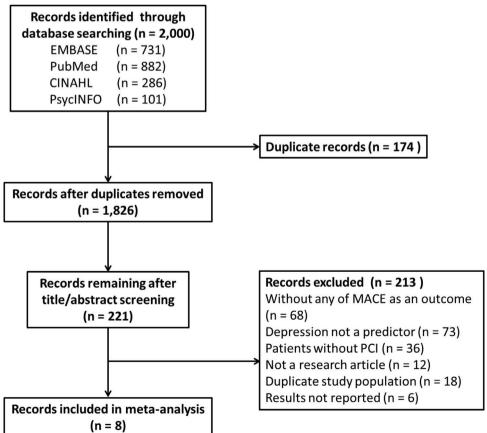


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart for systematic review of depression and cardiovascular events following percutaneous coronary intervention (PCI). MACE, major adverse cardiac event.

a total of 3297 participants from the Netherlands, China, Korea, Brazil and Germany. The quality of the studies was good, with 4 of 8 (50%) studies rated 9 stars on the Newcastle-Ottawa Scale.

Of the identified studies five measured depression only once, varying from before the procedure during hospitalisation to 6 months after PCI. Three of the studies assessed depression twice. The research by Yu et al [13] measured depression at baseline during hospitalisation and 1 month after discharge. Wang et al [11] and Li et al [10] assessed depression both before and after the PCI. These two studies suggested depression was present in nearly 40% of the postoperative patients, increasing more than 10 percentage points than that before the operation.

Four of the eight studies defined depression according to the Hospital Anxiety and Depression Scale (HADS).² The level of depression was considered clinically relevant at a cut-off HADS score of 8. Wang et al [11] used a combination of HADS and the Mini-International Neuropsychiatric Interview to identify patients with depression. Yu et al [13] used the 9-Question Primary Care Evaluation of Mental Disorders Brief Patient Health Questionnaire-9 to define depression (non-depressed ≤ 4 , depressed 5–27). Schmidt et al [14] identified patients with depression using the Beck Depression Inventory with 20 points as the cut-off value. The study by Li et al [10] defined depression according to the Zung Self-Rating Depression Scale.

Two studies reported all-cause mortality, four studies reported adverse cardiac events as an outcome and two studies reported both all-cause mortality and adverse cardiac events separately. MACE was defined according to the individual study criteria and included all-cause mortality, non-fatal MI, revascularisation (as evidenced by repeated PCI, target vessel revascularisation, target lesion revascularisation or coronary artery bypass graft (CABG)) and rehospitalisation with cardiac death. Specific characteristics of the included studies are summarised in table 1.

Meta-analysis results

Effect of depression assessed at any time on composite outcome

For the pooled sample (eight studies), depression assessed at any time period resulted in a significant increase in the incidence of cardiac events (RR=1.57, 95% CI 1.28 **Open access**

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to 1.92) in the random effects model, indicating that depressed individuals have a 57% greater risk of poor outcome than non-depressed patients. The overall results are displayed in figure 2.

Depression and all-cause mortality as an outcome

As shown in figure 3, in the subanalysis of four studies that included all-cause mortality as an outcome, depression was associated with a significantly higher risk of death after PCI (RR=1.43, 95% CI 1.24 to 1.65).

Sensitivity analysis

Protected To determine the reliability of the results, sensitivity analyses were performed by omitting one study at a time. No by copyright individual study had a substantial impact on the pooled effect size and heterogeneity. The RR changed slightly only when excluding the study by van Dijk *et al*¹² with the largest number of participants (RR=1.67, 95% CI 1.26 to 2.21) (see table 2). including

Publication bias

The funnel plot demonstrated slight asymmetry (figure 4), suggesting that there may be unpublished studies which ₫ have found no relationship between depression and uses clinical outcomes. However, neither Egger's test nor Begg's test revealed evidence of publication bias (p>0.1), ē although these results should be interpreted with caution ated to text due to the limited number of included studies.

Subgroup analysis

Subgroup analysis by depression assessment time

The pooled RR was also calculated for studies assessing depression during hospitalisation and for those measuring depression 2 weeks or more after PCI. For studies with depression assessed in hospital, RR=1.71 (95% CI 1.06 to 2.73) and for those with depression evaluated 2 weeks or more after PCI, RR=1.65 (95% CI 1.30 to 2.08) (figure 5).

Subgroup analysis by follow-up time

We used 1 year as the cut-off for distinguishing shortterm from long-term follow-up to evaluate whether the prognostic value of depression for predicting adverse and similar technologies outcomes was temporally limited. The pooled RR for studies with follow-up time less than or equal to 1 year

	Depress	sion	Non-depre	ssion		Risk Ratio		Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C		M-H, Rand	lom, 95% Cl	
De Jager et al. 2018	35	104	98	424	20.3%	1.46 [1.06, 2.01]				
Wang et al. 2013	42	154	32	246	15.2%	2.10 [1.39, 3.17]				
Yu et al. 2015	13	64	21	157	8.4%	1.52 [0.81, 2.84]		-		
Park et al. 2015	11	44	7	89	4.8%	3.18 [1.32, 7.63]				
Dijk et al. 2015	122	276	262	836	32.2%	1.41 [1.19, 1.67]			*	
Schmidt et al. 2011	6	31	13	94	4.8%	1.40 [0.58, 3.37]				
Meyer et al. 2014	16	101	57	369	11.5%	1.03 [0.62, 1.71]		_	•	
Li et al. 2012	9	112	4	196	2.9%	3.94 [1.24, 12.49]				
Total (95% CI)		886		2411	100.0%	1.57 [1.28, 1.92]			•	
Total events	254		494							
Heterogeneity: Tau ² = Test for overall effect:	,		, (0.15); l²	= 35%		⊢ 0.01	0.1 Favours depression	1 10 Favours non-depress	100

Figure 2 Forest plot of depression and a composite outcome following percutaneous coronary intervention (PCI).

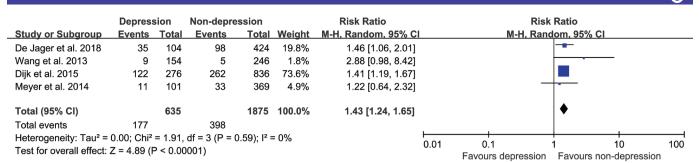


Figure 3 Forest plot of depression and all-cause mortality as an outcome following percutaneous coronary intervention (PCI).

was 2.04 (95% CI 1.27 to 3.28), whereas the increase in risk became less pronounced when examining composite outcomes with longer follow-up times (RR=1.46, 95% CI 1.19 to 1.80) (figure 6).

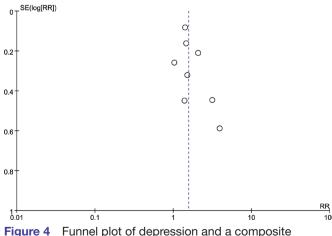
Heterogeneity

Heterogeneity across studies was determined to test the appropriateness of combining studies. Slight heterogeneity was apparent among all included studies ($I^2=35\%$, p for heterogeneity=0.15). However, heterogeneity remained low ($I^2=0\%-49\%$) in all subgroups, indicating relative consistency across studies.

DISCUSSION

By combining the results from eight prospective observational cohort studies with 3297 participants, this meta-analysis presents evidence that symptoms of depression are associated with a 57% higher risk of adverse clinical outcome and a 43% higher risk of mortality in patients undergoing PCI. Sensitivity and subgroup analyses suggested that this relationship was not markedly affected by the timing of depression assessment, length of patient follow-up or type of outcome. Ultimately, the results of this study emphasise the growing recognition that depression is a major risk factor for poor outcomes in patients with coronary heart disease (CHD).

The relationship between CHD and depression has been widely examined. Meta-analyses have demonstrated



outcome following percutaneous coronary intervention (PCI). RR, risk ratio. outcome following percutaneous coronary intervention (PCI). that depressive symptoms have an unfavourable impact on mortality and cardiovascular events in CHD or patients with post-MI.^{5 28} However, little is known about the impact of depression on prognosis in PCI patients. We found that patients with depression exhibited a significantly increased risk for the primary endpoint of MACE and for the secondary endpoint of death. The results of this meta-analysis are in concordance with prior findings focusing on other CHD populations.

While a positive correlation between depression d symptoms and adverse cardiac outcomes was found in Q our research, careful consideration should be given es to different methods of depression assessment. In the majority of included articles, depression was defined based on scores of a self-report screening instrument, for example, the HADS, rather than structured or semistructured diagnostic interviews. Although several screening instruments have shown high sensitivity or specificity for patients with CAD and were used more often by physicians in general hospitals to assess depression,^{29–31} no consensus has yet been reached on the optimal screening tool for use in identifying depression in patients with CHD.³² Since the word 'depression' may include different meanings ranging from transient negative emotions through d to serious clinical symptoms, more caution needs to be \triangleright taken when investigating the prognostic value of deprestra sion in further studies.

Considering that several previous studies failed to **G** demonstrate a negative impact of depression on outcome during long-term follow-up,¹⁶¹⁷ we conducted a subgroup analysis according to follow-up time. The predictive value of depression was significant in both groups but less pronounced in the long-time follow-up group (RR=1.46 vs RR=2.04 for short-term follow-up). Whether depression still has a marked effect on the long-term prognosis of PCI requires further study.

Although the prevalence of depression after PCI is approximately 20%–30%, the symptoms are likely to abate during recovery. Previous studies have found that PCI contributes to a higher risk of developing depressive symptoms in patients with CHD during hospitalisation.^{9 33} Therefore, depression measured too close to the point of interventional treatment may reflect a transient stress response and (or) worsening of physical symptoms. A meta-analysis by Ravven *et al*^{β4} showed that the risk of depression decreased throughout the long-term

Group A: Depression assessed baseline during hospitalisation

	Depres	sion	Non-depre	ession		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Yu et al. 2015	13	64	21	157	24.5%	1.52 [0.81, 2.84]	+
Park et al. 2015	11	44	7	89	17.4%	3.18 [1.32, 7.63]	
Schmidt et al. 2011	6	31	13	94	17.3%	1.40 [0.58, 3.37]	
Meyer et al. 2014	16	101	57	369	28.8%	1.03 [0.62, 1.71]	
Li et al. 2012	9	112	4	196	12.0%	3.94 [1.24, 12.49]	
Total (95% CI)		352		905	100.0%	1.71 [1.06, 2.73]	◆
Total events	55		102				
Heterogeneity: Tau ² =	0.13; Chi ²	= 7.68,	df = 4 (P =	0.10); l² :	= 48%		
Test for overall effect:	Z = 2.22 (I	P = 0.03	3)				0.01 0.1 1 10 100 Favours depression Favours non-depression

Group B: Depression assessed two weeks or more after PCI

Group B: Depre	Depress		Non-depre			Risk Ratio		R	isk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		<u>M-H, R</u>	andom, 95% C	:	
De Jager et al. 2018	35	104	98	424	26.7%	1.46 [1.06, 2.01]					
Wang et al. 2013	42	154	32	246	20.0%	2.10 [1.39, 3.17]					
Yu et al. 2015	11	35	23	186	11.2%	2.54 [1.37, 4.73]					
Dijk et al. 2015	122	276	262	836	42.1%	1.41 [1.19, 1.67]			-		
Total (95% Cl)		569		1692	100.0%	1.65 [1.30, 2.08]			•		
Total events	210		415								
Heterogeneity: Tau ² =	0.03; Chi ²	= 5.85,	df = 3 (P = 0	0.12); l² =	= 49%		0.01	0.1	1	10	اــــــــــــــــــــــــــــــــــــ
Test for overall effect:	Z = 4.17 (F	> < 0.00	01)					Favours depression	on Favours n		
iqure 5 (A B) Th	e influen	ice of	different e	valuati	ion time	of depression on th	e risk of	adverse card	ac events	PCI	
	·		different e	evaluati	ion time	of depression on th					on

post-CABG period and that measurements taken in the 2weeks after the operation may reflect the known consequences of surgery rather than a mood disorder. For these reasons, we also performed a subanalysis to determine the potential impact of evaluation time on the relationship between depression and prognosis. In this case, depression increased the risk of poor outcome whether

õ to 2.73) or >2 weeks after PCI (RR=1.65, 95% CI 1.30 to 2.08), indicating that the evaluation time has little influtext ence on the adverse effects of depression. This result is in ence on the adverse effects of depression. This result is in line with another recent finding that depression diagnosis

Group A: Forest plot of studies with average follow-up period less than or equal to 1 year

mine the potentia tionship between depression increa	l impac depress	t of e sion a	valuation nd progr	time o nosis. I	on the 1 n this c	rela- line with a ase, at any tim	nothe e foll	er recent find owing CAD	diagnosis w ³⁵ The timi	pression d as associat	iagnosis ted with	
Group A: Fores	-				age fol	low-up period les	ss tha	an or equal	-			ining,
01	Depres		Non-depre			Risk Ratio			Risk Ratio			≥
Study or Subgroup	Events				Weight			M-I	<u>I, Random, 95%</u>			- 5
Yu et al. 2015	13	64	21	157	38.4%	1.52 [0.81, 2.84]						raining,
Park et al. 2015	11	44	7	89	23.5%	3.18 [1.32, 7.63]						ī
Schmidt et al. 2011	6	31	13	94	23.4%	1.40 [0.58, 3.37]						Ģ,
Li et al. 2012	9	112	4	196	14.8%	3.94 [1.24, 12.49]				•		and
Total (95% CI)		251		536	100.0%	2.04 [1.27, 3.28]			•			d s
Total events	39		45									З
Heterogeneity: Tau ² =	0.05; Chi ²	= 3.80,	df = 3 (P = 0	0.28); I ² :	= 21%			0.1	1	10	400	milar
Test for overall effect:	Z = 2.94 (F	P = 0.00	03)				0.01	••••	ession Favour		100	
								Favours depre	ESSION FAVOUR	s non-depress		fec
Group B. Fores	t plot d	of stu	dies wit	h aver	age fo	low-up period m	ore th	nan 1 vear				hr
0.00p D. 1 0100	Depress		Non-depre		-90.0	Risk Ratio		ian'i you	Risk Ratio			nologies.
Study or Subgroup	Events		•		Weight	M-H. Random, 95% Cl		M-H	I. Random, 95%	CI		ğ
De Jager et al. 2018	35	104	98	424	24.8%	1.46 [1.06, 2.01]		101-1				- es
•	42	154	32	424 246	24.8% 17.7%	• • •						•
Wang et al. 2013	42	154	32	240	17.7%	2.10 [1.39, 3.17]						

Group B: Forest plot of studies with average follow-up period more than 1 year

	Depression Non-depression Risk Ratio		Risk Ratio		Risk	Ratio					
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C		M-H, Ran	<u>dom, 95% Cl</u>		
De Jager et al. 2018	35	104	98	424	24.8%	1.46 [1.06, 2.01]					
Wang et al. 2013	42	154	32	246	17.7%	2.10 [1.39, 3.17]					
Dijk et al. 2015	122	276	262	836	44.7%	1.41 [1.19, 1.67]			-		
Meyer et al. 2014	16	101	57	369	12.9%	1.03 [0.62, 1.71]			<u></u>		
Total (95% CI)		635		1875	100.0%	1.46 [1.19, 1.80]			•		
Total events	215		449								
Heterogeneity: Tau ² =	0.02; Chi ²	= 4.94	, df = 3 (P = 0	0.18); l² :	= 39%				1	+	400
Test for overall effect:	Z = 3.65 (I	P = 0.00	003)	,.			0.01	0.1 Favours depression	1 Favours non-	10 depressio	100 n

Figure 6 Relationship between depression and (A) short-term or (B) long-term prognosis after percutaneous coronary intervention (PCI).

measures and the clinical significance of tests conducted at different times before or after PCI should be carefully considered in future studies.

The results of this meta-analysis have some limitations. Few studies have examined the relationship between depression and adverse clinical outcomes following PCI; thus, only eight studies were suitable for inclusion. Studies included in the meta-analysis were observational and were subject to patient selection bias, lack of independent events adjudication and heterogeneity in exposure definitions. Depression was analysed as a dichotomous variable, limiting examination of relationships between depressive symptom severity and clinical outcomes in patients treated by PCI. In addition, although some studies investigated the prognostic value of depression in different indication groups (SA and ACS), most did not report the results separately; therefore, we were unable to analyse depression risk by patient indications for PCI. Finally, because of the small number of studies in this field, we could not conduct further subgroup analyses, and this may have certain impact on the accuracy of our research.

CONCLUSIONS

This meta-analysis suggests that depression is associated with increased mortality and a greater risk of adverse clinical outcome after PCI. The risk appears to be stable whether depressive symptoms are measured in hospital or following treatment. The identification of depression in PCI patients is critical in view of its negative effect on postoperative recovery, morbidity and mortality.

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