



BMJ Open Psychological factors for the onset of depression: a meta-analysis of prospective studies

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ABSTRACT

Objectives A comprehensive overview of the evidence for factors derived from leading psychological theories of the onset of major depressive disorder (MDD) that underpin psychological interventions is scarce. We aimed to systematically investigate the prospective evidence for factors derived from the behavioural, cognitive, diathesis–stress, psychodynamic and personality-based theories for the first onset of MDD.

Design Systematic review and meta-analysis.

Methods Databases PubMed, PsycINFO, Cochrane and Embase and published articles were systematically searched from inception up to August 2019. Prospective, longitudinal studies that investigated theory-derived factors before the first onset of MDD, established by a clinical interview, were included. Screening, selection and data extraction of articles were conducted by two screeners. The Grading of Recommendations Assessment, Development and Evaluation criteria were used to estimate level of confidence and risk of bias. Meta-analysis was conducted using random-effects models and mixed-method subgroup analyses.

Primary and secondary outcome measures Effect size of a factor predicting the onset of MDD (OR, risk ratio or HR).

Results From 42 133 original records published to August 2019, 26 studies met the inclusion criteria. Data were only available for the cognitive (n=6585) and personality-based (n=14 394) theories. Factors derived from cognitive theories and personality-based theories were related to increased odds of MDD onset (pooled OR=2.12, 95% CI: 1.12 to 4.00; pooled OR=2.43, 95% CI: 1.41 to 4.19). Publication bias and considerable heterogeneity were observed.

Conclusion There is some evidence that factors derived from cognitive and personality-based theories indeed predict the onset of MDD (ie, dysfunctional attitudes and negative emotionality). There were no studies that prospectively studied factors derived from psychodynamic theories and not enough studies to examine the robust evidence for behavioural and diathesis–stress theories. Overall, the prospective evidence for psychological factors of MDD is limited, and more research on the leading psychological theories is needed.

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Major depressive disorder (MDD) is a prevalent and highly disabling mental health disorder that has been identified as one of

Strengths and limitations of this study

- This meta-analysis investigated the prospective evidence for factors derived from five psychological theories of major depressive disorder (MDD): behavioural, cognitive, psychodynamic, personality-based and diathesis–stress.
- Prospective, longitudinal studies that investigated theory-derived factors before the first onset of MDD, as established by a clinical interview, were included.
- This meta-analysis was an extensive broad review that included prospective, longitudinal studies that assessed the psychological factors before the first onset of MDD, and where MDD was established through clinical interviews.
- The limited number of eligible prospective studies with theory-derived factors on onset of MDD prevented us from drawing strong inferences on the evidence for the leading psychological theories.
- The influence of concurrent levels of baseline depressive symptoms on the prediction of MDD could not be ruled out, there was a potential publication bias and various ways to operationalise the theories across studies may have contributed to considerable heterogeneity.

the leading causes of disease burden.¹ There are several preventative interventions and treatment options available for MDD (antidepressants and psychological interventions).^{2,3} However, their effectiveness raises concerns, with high relapse rates and approximately 50% of patients showing a clinical meaningful reduction in symptoms, or attaining full remission.⁴ Moreover, there is no indication that the effectiveness of current treatments for MDD improved over the past years.⁴ A recent meta-analysis found a significant decline since 1960 of the effectiveness of psychological interventions compared with control groups (including active control, waitlist control, usual care, or placebo or antidepressants) for MDD for youth.⁵ In addition, reported treatment effects may be overestimated due to publication bias and other

biases (eg, bias due to treatment allocation, selective reporting of outcomes).^{3 6} The identification of factors that precede and increase the risk of the first onset of MDD might provide points to target with (preventive) interventions. Psychological factors believed to account for the onset of MDD generally originate from psychological models and theories.⁷ Up to now, a systematic review and meta-analysis of the empirical evidence for the leading psychological theories of the first onset of MDD is scarce.

Most current psychological interventions for prevention and treatment of MDD, for example, cognitive therapy (CT),^{8 9} behaviour activation (BA),¹⁰ psychoanalytic therapy¹¹ and interpersonal therapy (IPT),¹² are derived from five psychological theories, which guided our systematic search (see online supplemental appendix A): behavioural, cognitive, psychodynamic, personality-based and most theories include an overarching diathesis–stress perspective.¹³ The core principles of the five theories are briefly summarised below in reference to the corresponding psychological intervention.

Each theory postulates a hypothesis on specific factors that contribute to the aetiology of MDD. For example, cognitive theories emphasise the dominant role of cognitions in the development of MDD, and the way individuals view themselves, others and the world.^{8 9} Negative cognitive processing across these domains is proposed to lead to an increased risk of MDD. The factors for the onset of MDD include higher levels of dysfunctional attitudes and beliefs, negative attributional style, rumination and learnt helplessness.^{9 14–20} CT (often combined with behavioural interventions) is an example of a cognitive theory-based intervention.

Originating from a framework of the learning theory,²¹ behavioural theories, that underlie treatments like BA, emphasise the role of the environment and the interaction between individuals and their environment in the development of MDD (eg, references^{22–28}). It posited that decline of positive feedback prompts withdrawal behaviour (ie, low rate of response-contingent positive reinforcement) which further leads to depression.^{27 29} Examples of behavioural theory-derived factors are classical and operant conditioning, social skills or behaviours that lack potential reward-value such as withdrawal and inactivity.²⁹

The psychodynamic theories were among the earliest to explain mental disorders including MDD, and have been used by clinicians and researchers to develop successive, overlapping models.^{30–38} Vulnerability factors derived from these theories include the mother–child relationship, object relations, quality of attachment with caregivers^{35–38} and significant childhood experiences.^{30–35} Interventions derived from the psychodynamic theories (eg, psychoanalytic, psychodynamic and specific forms of IPT) often include a focus on attachment and interpersonal relationships.¹¹

Another longstanding perspective, personality-based theories of MDD, has become an umbrella of multiple

personality-based factors that may be related to the onset of MDD. The theories cover various taxonomies (traits/temperament)³⁹ and hierarchy ('Big Five',⁴⁰ 'Big Three').⁴¹ Among these, two major domains can be distilled: positive emotionality (PE) and negative emotionality (NE), with the assumption that depression-prone individuals experience heightened NE (eg, neuroticism) and reduced PE (eg, extraversion).⁴² Even though these four theories of MDD differ in the proposed vulnerability factors, the majority of these theories underscore the importance of stress in the development of MDD. Diathesis–stress theories underlying these theories propose that vulnerability factors (ie, the theory-derived vulnerability factors, 'diatheses') are activated by stress, or a combination of the vulnerability factor and stress, which leads to the development of MDD.⁴³

Over the past decades, numerous studies and reviews have been conducted to delineate putative factors leading to the onset of MDD (eg, references^{42 44–51}) indicating that cognitive processes such as rumination and a dysfunctional thinking style⁴⁸ and personality traits (eg, neuroticism)^{42 52} increase the risk to develop MDD. Nevertheless, these reviews have not culminated in definitive evidence that supports etiological theories for onset of MDD. Support for the theories is largely based on cross-sectional studies and/or studies that assessed MDD using self-reports instead of clinical interviews, or where relapse and onset were combined (eg, references^{48 49 53}). Clinical interviews are needed to reliably establish whether there is indeed a first onset of MDD, as opposed to (subthreshold and/or self-reported) depressive symptomatology alone since self-report measures are not sufficient. To overcome these limitations, a systematic review of prospective, longitudinal, studies is needed among individuals without a history of MDD, where theory-derived factors are measured before the onset of MDD. This systematic review and meta-analysis investigate and summarise the evidence for factors derived from five leading theories of MDD that underpin most used treatment options.

METHODS

The methodology adopted in this meta-analysis and review was in line with the guidelines of Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA, online supplemental appendix B).

Search strategies

The current study was embedded in a larger project ('My optimism wears heavy boots', Netherlands Institute for Advanced Study)⁵⁴ investigating the psychological and biological factors of MDD onset and relapse.^{55 56} Therefore, some searches were combined over topics (see online supplemental appendix A). PubMed, PsycINFO, Cochrane and Embase were searched for relevant articles published from inception up to August 2019. The search combined keywords and text words relate to: first onset and studies with a prospective longitudinal design; MDD

and five leading theories. Selection of the search terms indicative of the five psychological theories were guided by prior reviews, books and an extensive international expert panel (see acknowledgements for the expert panel). Snowballing was conducted by checking inclusions of previous published reviews and articles citing included studies.

Inclusion and exclusion criteria

Studies were eligible if the following criteria were fulfilled: (1) diagnostic status of MDD was indicated for all participants and was established through a clinical interview at follow-up (ie, Structured Clinical Interview for DSM (SCID), Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) from DSM, CIDI from International Classification of Diseases (ICD)); (2) at baseline, participants did not meet criteria for MDD (and did not have depressive symptoms above cut-off scores for MDD), and did not have prior history of MDD; (3) participants with first-onset MDD had no comorbidity with other types of depressive disorder, other mental disorders or physical disease; (4) the study

design was prospective/longitudinal; (5) the target variable(s) (theory-derived factors) were assessed before the first onset of MDD; participants needed to be assessed at least twice (baseline and follow-up) and (6) the study was original research, published in peer-reviewed journals in the English language. Studies with patients older than 65 years old were excluded because of the heterogeneity introduced by geriatric depression. When multiple publications with data from the same study cohort were available, we included the publication with longest period of follow-up length. When the follow-up period was equal, studies with largest number of total participants were included.

Selection process

The PRISMA flow diagram for all theories is depicted in figure 1. All records were screened by two screeners in an independent, but not fully blind way; the second screeners could see the decisions from the first screener. All eligible records that met the inclusion criteria during initial screening of the titles and abstracts were further assessed for eligibility by two screeners based on full

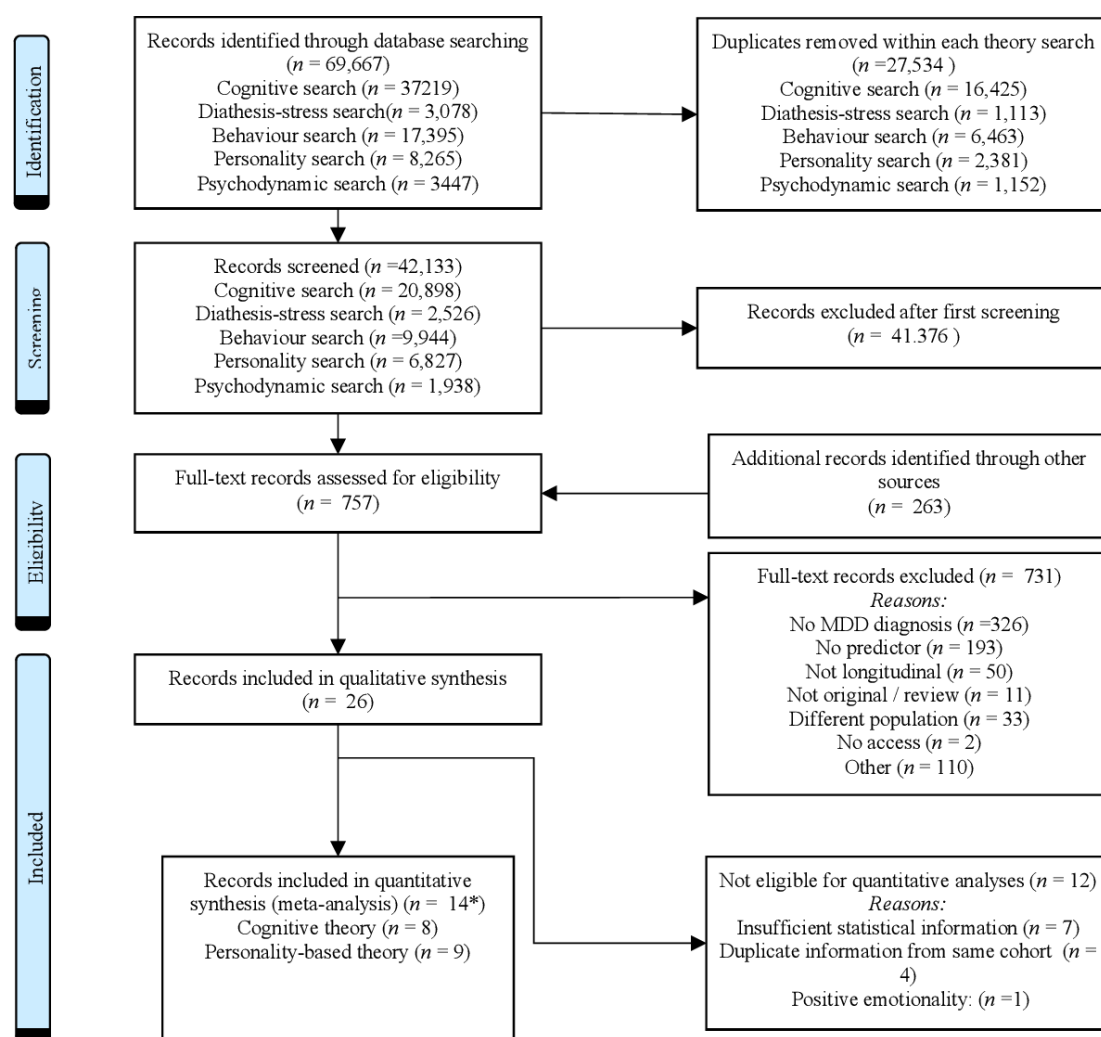


Figure 1 PRISMA flow diagram for the systematic review. *Studies can be included in both theories at same time. PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses; MDD, major depressive disorder

texts. Any disagreement was resolved by discussion and consulting a senior author. Multiple screeners were included and assigned pairwise during this process, see author contributions and acknowledgements for the full list.

Quality assessment and data extraction

Two researchers assessed the risk of bias and level of confidence for the overall evidence for the psychological theories, using the criteria of the Grading of Recommendations Assessment, Development and Evaluation.⁵⁷ Risk of bias was indicated in '+' (low risk of bias=0), '?' (unclear risk of bias=1) and '-' (high risk of bias=2). Score 0–6, 6–12 and 12–18, indicated low, moderate and high risk of bias, respectively. We extracted demographic information, baseline depressive symptoms and its measurement scales, method of MDD diagnosis, psychological factors and statistical information to calculate the effect sizes. Authors were contacted when a study met the inclusion criteria, but reported insufficient data to calculate effect sizes. These authors were inquired via emails (a reminder was sent 2 weeks after if no response) on the possibility to provide the relevant statistics within 2 months. Studies were excluded in the meta-analysis if the necessary data were not provided within this timeframe.

Primary outcome

Primary outcome was the onset of MDD at study follow-up, as established by a clinical interview (eg, ICD, SCID) or expert opinion (eg, trained psychiatrist or clinical psychologist).

Statistical analysis

The programme Comprehensive Meta-Analysis (CMA V.3.3)⁵⁸ was used to enter data of each study and each identified factor, and to calculate pooled effect sizes, forest plots, funnel plots and heterogeneity. The effect size of each factor reported in the article had to be expressed as an OR, risk ratio (RR) or HR, with 95% CIs, to indicate the relationship between the factor and time to, or odds or risk of having an onset of MDD at study follow-up. Alternatively, we calculated the OR, RR or HR by using reported statistics from each study and each factor. For example, the article needed to report means, SD, number of participants or beta coefficient with SE. These data were entered and OR, RR or HR with 95% CIs were then calculated using CMA.⁵⁸ If more than one measure from the same main psychological theory was reported in the same study, a combined effect size was calculated in CMA.⁵⁸ If a study reported multiple factors derived from different theories, the effect sizes of these factors were allocated to the corresponding theory or theories.

We then calculated pooled effect sizes (HR, RR and OR) and its 95% CI of each main theory separately using all (combined) factors assigned to that main theory. For example, the pooled effect size was calculated for all factors combined related to the cognitive theory

(eg, dysfunctional attitudes, rumination, automatic thoughts). Since we expected considerable heterogeneity among studies and measures, a random effects model was employed to calculate pooled effect sizes. Second, separate subgroup analyses were conducted for each factor alone, if there were enough studies reporting that factor. To conduct these subgroup analyses, pooled effect sizes of each (theory-derived) factor were calculated using a mixed-effects model, with a random effects model to summarise the studies within each subgroup and a fixed effects model to test for differences between subgroups.

The I^2 was calculated to assess heterogeneity between studies for each analysis. In general, heterogeneity is categorised at 0%–40% (low), 30%–60% (moderate), 50%–90% (substantial) and 75%–100% (considerable).⁵⁹ The 95% CIs around I^2 were calculated using the non-central χ^2 -based approach within the Heterogi module for Stata.⁶⁰ Funnel plots were visually inspected for publication bias, and investigated with Egger's test and Duval and Tweedie's trim and fill procedure. Trim-and-fill procedure was used to adjust potential publication bias. In this procedure, the asymmetric outlying studies in the funnel plot were first trimmed off and the true centre of the funnel was estimated with the symmetric remainders. Then, the funnel plot was filled with replacement of the trimmed studies and their missing counterparts around the centre. A newly pooled overall effect size based on this filled funnel plot indicated the OR after statistically adjusting the publication bias.

A priori, we aimed to conduct a meta-regression if the number of studies was sufficient, including investigating several potential continuous moderators of interest such as age, percentage female and baseline depressive symptoms were investigated. These variables were considered clinically relevant to major depression.^{61–63} Sensitivity analyses were conducted to examine if potential outliers, research designs and low-quality studies, affected the pooled effect sizes. The minimum number of studies was set at three studies for the main and subgroup analyses, and 10 for meta-regression.

Patient and Public Involvement

No patient involved.

RESULTS

Out of 69 667 identified records (see [figure 1](#)), 42 133 records were inspected on title/abstract after removal of duplicates, of which 52 articles met initial inclusion criteria across the psychological theories. For 26 of these articles (see online supplemental appendix C), participants with prior MDD episodes were included and therefore those articles were excluded. In total, 26 articles were included in the final review. There were no eligible articles detected for the psychodynamic theories. A quantitative meta-analysis was only possible for the cognitive and personality-based theories. See [table 1](#) for the characteristics of the included studies.

Table 1 Selected characteristics of included studies

Source (author, year)	Vulnerability measure	N	age/ range	SD of age	Sex (% female)	follow-up (months)	Diagnostic tool	depression severity	1	2	3	4	5	6	7	8	9	Country
Cognitive theories																		
Alloy <i>et al</i> , 2006 ⁶⁷ * †	CSQ, DAS	347	18.89	Nr	67.1	30	K-SADS	Nr	+	+	+	+	+	+	?	?	+	USA
Goodyer <i>et al</i> , 2000 ⁷³ †	RSQ	172	13.75	Nr	60.4	12	K-SADS	Low	+	+	+	?	+	+	+	?	–	UK
Girolabhui <i>et al</i> , 2018 ⁷⁴ †	HSC, ACSQ-M	173	12–13	Nr	56	18	K-SADS-E	Low	+	+	+	+	+	+	+	+	+	USA
Kruijt <i>et al</i> , 2013 ⁷⁵ * †	LEIDS	834	41.5	11.5	63.8	24	CIDI	Low	–	+	+	+	+	?	+	?	?	NL
Mathew <i>et al</i> ., 2011 ⁷⁶	DAS	1222	16.6	1.2	49.2	144	K-SAD/ SCID;	Nr	+	+	+	–	+	?	+	?	–	USA
Nusslock <i>et al</i> , 2011 ⁶⁸ †	CSQ, DAS, RSQ	40	20.32	1.25	42.5	36	SADS-C; SADS-L	Low	+	+	+	+	+	+	?	?	–	USA
Ormel <i>et al</i> , 2004 ⁶⁹ * †	UCS	3998	40	11.4	49.7	36	CIDI	Nr	+	+	+	–	+	?	?	?	–	NL
Otto <i>et al</i> , 2007 ⁶⁶ * †	DAS	500	40.9	2.5	100	36	SCID	Low	+	+	+	?	+	+	+	?	–	USA
Stange <i>et al</i> , 2016 ⁷⁷	CRSQ	341	12.41	0.63	53.2	34.13	K-SADS	Low	+	+	+	+	+	?	–	?	?	USA
Stone <i>et al</i> ., 2011 ⁷⁸ †	CRSQ	95	11–15	Nr	62	24	K-SADS	Nr	+	+	+	+	+	+	+	?	–	USA
Wilkinson <i>et al</i> ., 2013 ⁷⁹ †	RDQ	598	13.7	1.2	43	12	K-SADS-L	Low	+	+	+	+	+	+	+	?	+	UK
Personality-based theories																		
Elidesouky <i>et al</i> ., 2018 ⁸⁰ †	NEO-PI-R, MAPP, SIDP-IV	758	59.60	2.7	55	60	C-DIS-IV	Nr	+	+	+	+	+	?	+	+	+	USA
Bijl <i>et al</i> , 2002 ⁸¹ ¶	GNQ	4455	18–64	Nr	50.3	12	CIDI	Nr	+	+	+	+	+	+	+	?	+	NL
Fanous <i>et al</i> , 2007 ⁸² *, †	EPQ	1862	36.8	9.1	0	12	SCID	Nr	+	+	+	+	+	+	+	?	–	USA
Goldstein <i>et al</i> , 2017 ⁸³ †	BFI	463	14.4	0.63	100	18	K-SADS-PL	Nr	+	+	+	+	+	+	+	+	–	USA
Kendler <i>et al</i> , 1993 ⁸⁴ **	EPQ-FormB	1477	30.1	7.6	100	12	DSM-III	Nr	+	+	+	?	+	+	?	?	–	USA
Kendler <i>et al</i> , 2006 ⁸⁵	EPQ-FormB	20 081	29.2	8.9	Nr	17.4	CIDI	Nr	+	+	+	+	+	?	+	?	–	SE
Kessler <i>et al</i> , 2008*, 86 †	GPS, ABI	4470	18–54	Nr	Nr	120	CIDI	Nr	+	+	+	+	+	+	+	?	+	USA
Kopala-Sibley <i>et al</i> , 2017 ⁸⁷ †	BFI	504	14.4	0.6	100	12	K-SADS-PL	Nr	+	+	+	+	+	+	+	?	–	USA

Continued

Table 1 Continued

Source (author, year)	Vulnerability measure	N	Mean age/range	SD of age	Sex (% female)	Length of follow-up (months)	Diagnostic tool	Baseline depression severity	Risk of bias					Country
Kruijt <i>et al</i> , 2013 ⁷⁵ §†	NEO-FFI	834	41.5	11.5	63.8	24	CIDI	Low	-	+	+	+	?	NL
Mathew <i>et al</i> , 2011 ⁷⁶	MMPI	1222	16.6	1.2	49.2	144	K-SADS /SCID	Nr	+	+	-	+	?	USA
Noteboom <i>et al</i> , 2016 ⁸⁸ §†	NEO-FFI	648	41.4	14.7	61.1	24	CIDI	Nr	+	+	+	+	?	NL
Nusslock <i>et al</i> , 2011 ^{68,*†}	BAS/BIS	40	20.32	1.25	42.5	36	SADS-C; SADS-L	Low	+	+	+	+	?	USA
Ormel <i>et al</i> , 2004 ^{69,*††}	ABI	3998	40	11.4	49.7	36	CIDI	Nr	+	+	+	-	?	NL
Roberts and Kendler, 1999 ⁸⁹ **	EPQ	1128	30.1	7.6	100	17	SCID	Nr	+	+	+	-	?	USA
Tokuyama <i>et al</i> , 2003 ⁷⁰ *†	FFI	1365	34.2	10.3	52.6	12	DSM-IV	Nr	+	?	+	-	?	JP
Behavioural theories														
Stavrakakis <i>et al</i> , 2013 ⁶⁵	Physical activity	2149	13.02	0.61	52.9	30	CIDI	Nr	+	+	+	?	?	NL
Østergaard <i>et al</i> , 2012 ⁶⁴	Time of sitting	11 862	43	Nr	60.6	144	ICD	Nr	+	+	+	+	?	DK
Diathesis-stress theories														
Coventry <i>et al</i> , 2009 ⁷²	KPSS x SLE	6755	Nr	Nr	62.7	12	SSAGA	Nr	+	+	+	?	?	AU
Carter and Garber, 2011 ⁷¹	CASQ x x LEDS-A	207	11.86	0.57	54.2	72	K-SADS-PL	Low	+	+	+	+	?	USA

Continued

Table 1 Continued

Source (author, year)	Vulnerability measure	N	Mean age/range	SD of age	Sex (% female)	Length of follow-up (months)	Diagnostic tool	Baseline depression severity	Risk of bias	Country
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Risk of bias: 1, selection of participants; 2, diagnosis of MDD; 3, without prior history of depression; 4, covariates controlled; 5, assessment of vulnerabilities; 6, quality of assessment; 7, adequate follow-up; 8, similar treatment between onset and non-onset group; 9, other sources of bias; '+', low risk of bias; '-', high risk of bias; '?', unclear risk of bias.

*Data derived from the Cognitive Vulnerability of Depression project

†Studies included in the meta-analysis

‡Cambridge secondary students

\$Data derived from the Netherlands Study of Depression and Anxiety project; both studies were included in the meta-analysis since they measured different personality factors

¶Data derived from the Netherlands Mental Health Survey and Incidence Study (NEMESIS); data with the longest follow-up were retained in the meta-analysis

**Data derived from the Virginia Twin Study; data with longest follow-up were retained in the meta-analysis

ABI, Amsterdam Biographic Inventory; ACSQ, Adolescent Cognitive Style Questionnaire-Modified; ALEQ, Adolescent Life Events Questionnaire; ASI, Attachment Style Interview; BFI, Big Five Inventory; CAS, Child Assessment Scale (for structured interview); CASQ, Children's Attributional Style Questionnaire; CIDI, Composite International Diagnostic Interview; CRSQ, Children's Response Styles Questionnaire; CSQ, Cognitive Style Questionnaire; DAS, Dysfunctional Attitudes Scale; DIA-X/M-CIDI, Munich-Composite International Diagnostic Interview; DIS, Diagnostic Interview Schedule; DSM-III, Diagnostic and Statistical Manual of Mental Disorders-III; EPQ, Eysenck Personality Questionnaire; FPI, Freiburg Personality Inventory; GNQ, Groningse Neuroticisme Questionnaire; HSC, Hopelessness Scale for Children; ICD, International Classification of Diseases; IPPA, Inventory of Parent and Peer Attachment; KASQ-C, Kasstan Attributional Style Questionnaire for Children; KPSS, Kessler Perceived Social Support; K-SADS, Schedule for Affective Disorders and Schizophrenia for School-Age Children; K-SADS-L, Kiddie Schedule for the Affective Disorders Lifetime version; K-SADS-PL, Kiddie Schedule for the Affective Disorders Past and Lifetime version; LEDS, Life Events and Difficulties (LEDS) interview; LEDS-A, Life Events and Difficulties (LEDS) interview for adolescents; LEDS-r, Leiden Index of Depression Sensitivity-revised; MAPP, Multisource Assessment of Personality Pathology; MLES, Major Life Events Scale; MMPI, Minnesota Multiphasic Personality Inventory; MPQ, Multidimensional Personality Questionnaire; NEO-FFI, Neuroticism-Extraversion-Openness Five Factor Inventory; NEO-PI-R, Neuroticism-Extraversion-Openness Personality Inventory-Revised; NR, not reported; NRI, Network of Relationships Inventory; PSE, Present Extraversion-Openness Five Factor Inventory; NEO-PI-R, Neuroticism-Extraversion-Openness Personality Inventory-Revised; NR, not reported; NRI, Network of Relationships Inventory; PSE, Present State Examination; RDQ, Responses to Depression Questionnaire; RRS, Ruminative Response Scale; RSQ, Response Style Questionnaire; SADS-C, Schedule for Affective Disorders and Schizophrenia-Change version; SADS-L, Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiological version-Present and Lifetime; SCID, Structured Clinical Interview for DSM; SCID-NP, Structured Clinical Interview for DSM; Non-patient Lifetime; SIDP-IV, Semi-Structured Interview for DSM-IV Personality; SLE, Stressful Life Events; SPIKE, Structured Psychopathological Interview and Rating of the Social Consequences of Epidemiology; SSAGA, Semi-Structured Assessment for the Genetics of Alcoholism; UCS, Utrecht Coping Scale.

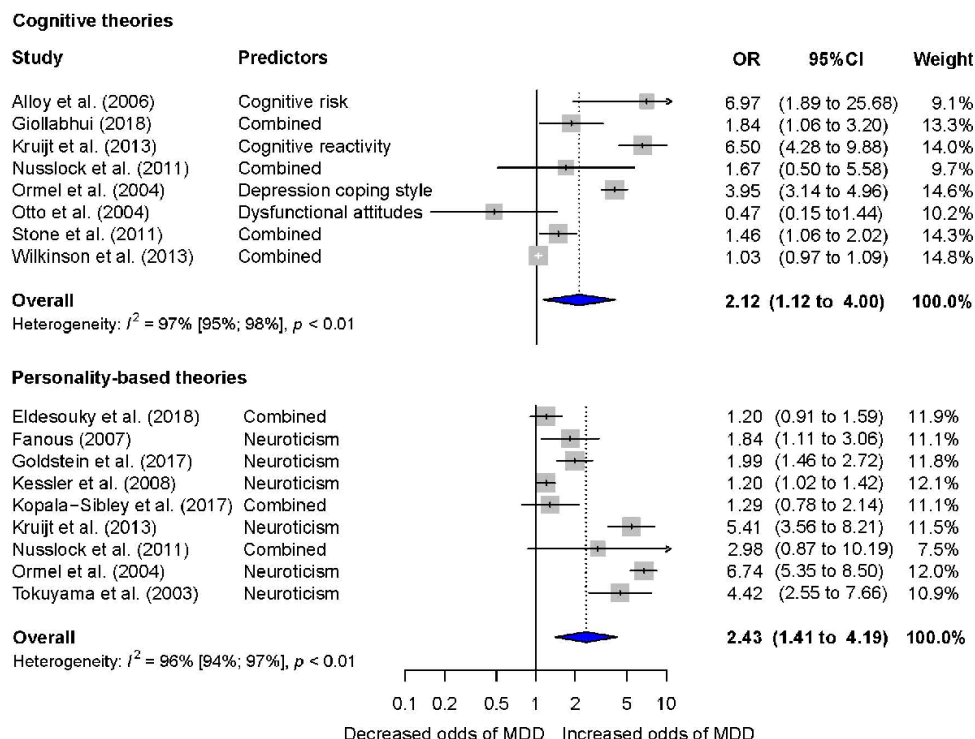


Figure 2 Forest plot of cognitive and personality-based theories to predict first onset of MDD. MDD, major depressive disorder.

Behavioural theories

Two studies were eligible for the behavioural theories^{64 65} and could not be meta-analysed. Both studies investigated the association between physical activities and onset of MDD, involving 14 011 adolescents and adults. Low levels of physical activities were not associated with an increased risk of developing MDD.

Cognitive theories

Eleven studies were included (8320 participants), of which eight studies were eligible for the quantitative synthesis (6585 participants; M_{age} range=13–41; see figure 1). Follow-up time ranged from 1 to 12 years. The result of the overall analysis is shown in figure 2. The pooled OR for the cognitive theory was 2.12 (95% CI: 1.12 to 4.00), which indicates that the combination of cognitive theory-derived factors predicted the first onset of MDD. Heterogeneity was considerable ($I^2=97\%$, 95% CI: 95% to 98%). Inspection of the funnel plot and Egger's test ($p=0.12$) did not indicate asymmetry; while Duval and Tweedie's trim and fill procedure (three studies trimmed) suggest potential publication bias. After statistically adjusting for publication bias, the overall OR decreased to 1.11 with 95% CI as 0.60 to 2.06. The level of confidence was moderate. Given the low number of studies (<10), no meta-regression analysis or subgroup analyses were conducted. Therefore, we were unable to examine potential moderators. The results remained comparable after removing one study with a moderate risk of bias⁶⁶ ($OR=1.90$, 95% CI: 1.02 to 3.55), however, were non-significant after conducting sensitivity analyses where one study with a different research design was

removed (behaviour risk design;⁶⁷ $OR=1.88$, 95% CI: 0.97 to 3.94). Two studies reported predictive value with one study controlling for baseline depressive symptom exclusively, and the other study controlling for other covariates concurrently.^{66 68} We could therefore not investigate the impact of depressive symptoms on the meta-analysis.

Personality-based theories

Negative emotionality

In total, 15 studies that investigated NE could be included in the qualitative synthesis (43 305 participants), of which nine studies were included in the quantitative analysis (14 394 participants, M_{age} range=14–64). Follow-up length varied from 1 to 12 years. Eight of these nine studies investigated the role of neuroticism as a vulnerability factor; other factors were borderline personality and behaviour inhibition system. The pooled OR for the NE was 2.43 (95% CI: 1.41 to 4.19), indicating that NE was related to the first onset of MDD. See figure 2 for the overall results. Heterogeneity between studies was considerable ($I^2=96\%$; 95% CI: 94% to 97%), with a wide CI. The confidence of evidence was of high certainty. Inspection of the funnel plot and Egger's test ($p=0.52$) did not indicate asymmetry, while trim and fill procedure indicated risk for publication bias with four trimmed studies resulted in an adjusted OR as 1.39 (95% CI: 0.74 to 2.59). Sensitivity analysis revealed similar decline after removal of two studies^{69 70} with moderate risk of bias ($OR=1.86$; 95% CI: 1.25 to 2.78). The limited number of studies prohibited subgroup analyses and metaregression to investigate the effects of baseline depressive symptoms on the results.

Positive emotionality

Six studies (8848 participants) focused on PE. The pooled *OR* was 0.93 (95% CI: 0.84 to 1.03), which indicates that positive personality traits did not decrease the odds of MDD onset. After removing one study with a high risk of bias, the effect remained non-significant (*OR*=0.94; 95% CI: 0.85 to 1.05). Heterogeneity between studies was low ($I^2=37\%$; 95% CI: 0% to 75%). A publication bias was not indicated (Egger's test $p=0.63$; number of trimmed studies=0).

Diathesis–stress theories

Two studies were identified that prospectively examined the interaction between theory-derived factors with stress on first onset of MDD, that is, diathesis–stress theories.^{71 72} Therefore, quantitative analyses were prohibited. The studies indicated non-significant results of social support⁶⁹ and negative attributional style⁶⁸ separately in interaction with stress, as predictors of MDD. No other studies included in the other theories combined the factors with measures of stress.

DISCUSSION

The aim was to systematically examine the evidence for psychological factors derived from five leading psychological theories that explain onset of MDD: behavioural, cognitive, personality-based, psychodynamic theories, including the diathesis–stress theory. Out of 42 133 identified records, 26 studies examined theory-derived factors prospectively in participants without a history of MDD, of which 14 studies could be meta-analysed for the cognitive and personality-based theories. We identified no prospective studies on psychological factors such as attachment, object relations and identification, as mentioned in psychodynamic theories, and there were not enough studies for quantitative analyses of factors derived from the behavioural theory or diathesis–stress theory. Consistent with previous reviews,^{42 48} individuals with higher levels of dysfunctional attitudes, rumination, and greater cognitive reactivity, as well as higher levels of the personality trait 'NE', had an increased odd to develop MDD. Therefore, there was some prospective evidence for the cognitive and personality-based theories of MDD.

This extensive systematic search enabled us to investigate prospectively assessed factors derived from five theories in clinically established MDD, while the lack of evidence overall remains noteworthy. Despite the strengths of this meta-analysis, that is, the inclusion of prospective, longitudinal studies that assessed the psychological factors before the first onset of MDD, and where MDD was established through clinical interviews, some limitations should be noted. The influence of concurrent levels of baseline depressive symptoms on the prediction of MDD cannot be ruled out due to the low number of studies reporting baseline symptomatology (4/14). The marked heterogeneity that was observed may be attributed to low levels of consensus on operationalization of the theories, after

consultation of lead experts in clinical psychology and psychiatry (see acknowledgements for details) to determine which factors belonged to which theories. Together with the potential publication bias, this can diminish the reliance of our result.

Despite these limitations, the present review takes an important first step to demonstrate the overall empirical status of five leading psychological theories that underpin widely used psychological interventions for MDD. The prospective evidence for the cognitive and personality-based theories in relation to onset of MDD could assist researchers and clinicians to identify potential treatment targets and/or defined high-risk groups. As mentioned, cognitive theories⁹ and personality theories⁴² as well as psychodynamic theories have an overlap with the diathesis–stress theory, yet there were not enough studies prospectively measuring stress or life events to investigate diathesis–stress theories. This precluded further examination of the influence of theory-derived factors under certain stressful situation. Overall, the limited number of eligible prospective studies on onset of MDD prevented us from drawing strong inferences.

The results highlight the lack of evidence of the factors derived from each theory in the onset of MDD. A research agenda should be formulated to systematically address these identified issues, including improved operationalization of leading theories, improved assessment of their factors and the use of prospective designs. All to ensure that interventions for depression are grounded in a solid foundation of clinical research. A framework that incorporates psychological, biological, environmental and social risk factors would provide a more integrative, holistic approach to unravel the underlying mechanisms of MDD.

CONCLUSION

There is some evidence that factors derived from cognitive and personality-based theories indeed predict the onset of MDD (ie, dysfunctional attitudes, cognitive styles, cognitive reactivity and NE). However, there were no studies that prospectively studied factors derived from psychodynamic theories and not enough studies to be able to examine the robust evidence for behavioural and diathesis–stress theories. More prospective and unified research is required to enable future systematic reviews. Overall, the prospective evidence for theory-derived psychological factors of MDD is limited.

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Appendix A: Search terms overview for all theories

Note: The searches for psychodynamic, personality and part of cognitive theories were combined for onset and relapse/recurrence; the search for diathesis-stress theory combined psychological and biological risk factors for MDD. We then re-ran each search using only the specific terms for depression onset to calculate the number of hits, exclusions, and inclusions for the current overview. Snowballing procedures including checking inclusions of previous relative reviews and articles cited each inclusion were also conducted to identify any studies undetected in the original search.

Search terms Behavioral theories

Database	Search strategy
Pubmed	1. ("depressive disorder"[MeSH Terms] OR "depression"[MeSH Terms] OR depression[Title/Abstract] OR depressive[Title/Abstract] OR depressed [Title/Abstract] OR affective[Title/Abstract])
	2. ("behavior* theory"[Title/Abstract] OR "behaviour* theory" [Title/Abstract] OR "behavioral model" [Title/Abstract] OR "behavioural model" [Title/Abstract] OR "behavioral intervention" [Title/Abstract] OR "behavioural intervention" [Title/Abstract] OR "behaviour* therapy"[Title/Abstract] OR "behaviour* therapy"[Title/Abstract] OR "social learning"[Title/Abstract] OR "self-efficacy" [Title/Abstract] OR "observational learning" [Title/Abstract] OR "self-regulation" [Title/Abstract] OR conditioning [Title/Abstract] OR conditioned [Title/Abstract] OR "classical condition*" [Title/Abstract] OR "operant condition*" [Title/Abstract] OR reinforcement [Title/Abstract] OR "learning theory" [Title/Abstract] OR "behavior* activation" [Title/Abstract] OR "behaviour* activation" [Title/Abstract] OR "functional analysis" [Title/Abstract] OR "problem solving" [Title/Abstract] OR "social skills" [Title/Abstract])
	3. (onset [Title/Abstract] OR first-ever [Title/Abstract] OR predictor [Title/Abstract] OR preventi* [Title/Abstract] OR prospective [Title/Abstract] OR risk [Title/Abstract] OR vulnerability[Title/Abstract] OR longitud*[Title/Abstract] OR precipitating [Title/Abstract] OR protective [Title/Abstract] OR resilience[Title/Abstract] OR susceptibility[Title/Abstract] OR epidemiology[Title/Abstract])
	4. 1 AND 2 AND 3 [Filter: human, English, not review]
PsychInfo	1. (depression/ or depressive/ or depressed/ or affective).ab,ti.
	2. (onset/ or first-ever /or predictor/ or prevention/or preventive/or prospective/or risk/or vulnerability/or longitud*/or precipitating/or protective/or resilience/or susceptibility/or epidemiology)).ab,ti.
	3. (*behavioral theory/ or *behavioural theory/ or *behavioral model/ or *behavioural model/ or *behavioral intervention/ or *behavioural intervention/ or *behavioral therapy/ or *behavioural therapy/ or *social learning/ or *self-efficacy/ or *observational learning/ or *self-regulation/ or conditioning/ or conditioned/ or *classical conditioning/ or *classical conditioned/ or *operant conditioning/ or *operant conditioned/ or reinforcement/ or *learning theory/ or *behavioral activation/ or *behavioural activation/ or *functional analysis/ or *problem solving/ or *social skills).ab,ti.
	4. 1 and 2 and 3

Cochrane library	1. (Depress* or affective)
	2. (onset or first-ever or predictor or prevent* or perspective or risk or vulnerability or longitud* or precipitating or protective or resilience or susceptibility or epidemiology)
	3. (behavioral theory or behavioural theory or behavioral model or behavioural model or behavioral intervention or behavioural intervention or behavioral therapy or behavioural therapy or social learning or self-efficacy or observational learning or self-regulation or conditioning or conditioned or classical condition* or operant condition* or reinforcement or learning theory or behavioral activation or behavioural activation or functional analysis or problem solving or social skills)
	4. 1 and 2 and 3
Embase	1. ('depress*/exp or 'affective'/exp OR depress*:ab,ti)
	2. (onset:ab,ti or first-ever:ab,ti or predictor:ab,ti or prevent*:ab,ti or perspective:ab,ti or risk:ab,ti or vulnerability:ab,ti or 'longitud*':ab,ti or precipitating:ab,ti or protective:ab,ti or resilience:ab,ti or susceptibility:ab,ti or epidemiology:ab,ti)
	3. ('behavior* theory':ab,ti or 'behaviour* theory':ab,ti or 'behavioral model':ab,ti or 'behavioral intervention':ab,ti or 'behaviour* therapy':ab,ti or 'behavioural model':ab,ti or 'behavioural intervention':ab,ti or 'behaviour* therapy':ab,ti or 'social learning':ab,ti or 'self-efficacy':ab,ti or 'observational learning':ab,ti or 'self-regulation':ab,ti or 'conditioning':ab,ti or 'conditioned':ab,ti or 'classical condition*':ab,ti or 'operant condition*':ab,ti or 'reinforcement':ab,ti or 'learning theory':ab,ti or 'behavior* activation':ab,ti or 'behaviour* activation':ab,ti or 'functional analysis':ab,ti or 'problem solving':ab,ti or 'social skills':ab,ti)
	4. 1 and 2 and 3

Search terms Cognitive theories

Database	Search strategy
Pubmed	1. ("depressive disorder"[MeSH Terms] OR "depression"[MeSH Terms] OR depression[Title/Abstract] OR depressive[Title/Abstract] OR depressed [Title/Abstract] OR affective[Title/Abstract])
	2. ("cognitive theory" [Title/Abstract] OR "cognitive model"[Title/Abstract] OR "cognitive therapy"[MeSH Terms] OR "cognitive therapy"[Title/Abstract] OR "cognitive intervention" [Title/Abstract] OR cognitive [Title/Abstract] OR hopelessness[Title/Abstract] OR helplessness[Title/Abstract] OR "dual processing"[Title/Abstract] OR "information processing"[Title/Abstract] OR "information processing bias"[Title/Abstract] OR "cognitive bias"[Title/Abstract] OR "cognitive biased"[Title/Abstract] OR "cognitive biases"[Title/Abstract] OR "scar model"[Title/Abstract] OR "scarring"[Title/Abstract] OR "diathesis-stress"[Title/Abstract] OR "attitude"[MeSH Terms] OR "attitude"[Title/Abstract] OR "attitudes"[Title/Abstract] OR "dysfunctional attitude*"[Title/Abstract] OR "dysfunctional belief"[Title/Abstract] OR "self-control"[Title/Abstract] OR schema[Title/Abstract] OR "automatic negative thought"[Title/Abstract] OR ruminat*[Title/Abstract] OR "repetitive thought"[Title/Abstract] OR "repetitive thinking"[Title/Abstract] OR worry[Title/Abstract] OR persever*[Title/Abstract] OR "intrusive thought"[Title/Abstract] OR "intrusive thinking"[Title/Abstract] OR "negative thought"[Title/Abstract] OR "negative thinking"[Title/Abstract] OR "stress thought"[Title/Abstract] OR "stress thinking"[Title/Abstract] OR "obsessive thought"[Title/Abstract] OR "obsessive thinking"[Title/Abstract] OR "unconscious stress"[Title/Abstract] OR "implicit stress"[Title/Abstract] OR "anticipatory stress"[Title/Abstract] OR "anticipation stress"[Title/Abstract] OR "cognitive intrusion*"[Title/Abstract] OR reflection[Title/Abstract] OR brooding[Title/Abstract] OR "reflect*"[Title/Abstract] OR "self referential thought"[Title/Abstract] OR "counterfactual thinking"[Title/Abstract] OR "mind wandering"[Title/Abstract] OR "post-event processing"[Title/Abstract] OR "habitual negative self-thinking"[Title/Abstract] OR "catastrophizing"[Title/Abstract] OR "automatic thoughts questionnaire"[Title/Abstract] OR "Crandell cognitions inventory"[Title/Abstract] OR "cognitions checklist"[Title/Abstract] OR "cognitive style test"[Title/Abstract] OR "sociotropy-autonomy scale"[Title/Abstract] OR attribution[Title/Abstract] OR schema[Title/Abstract] OR "automatic thoughts"[Title/Abstract] OR "depressive realism"[Title/Abstract] OR "illusion of control"[Title/Abstract] OR "cognitive

	distortion"[Title/Abstract] OR "judgment of contingency"[Title/Abstract] OR "attentional bias"[Title/Abstract] OR "response styles theory"[Title/Abstract] OR preoccupation[Title/Abstract] OR "self-focus"[Title/Abstract] OR "self-focused attention"[Title/Abstract] OR "emotion regulation" OR "coping strategy"[Title/Abstract] OR "coping style"[Title/Abstract] OR metacognit*[Title/Abstract])
	3. (onset [Title/Abstract] OR first-ever [Title/Abstract] OR predictor [Title/Abstract] OR preventi*[Title/Abstract] OR prospective [Title/Abstract] OR risk [Title/Abstract] OR vulnerability[Title/Abstract] OR longitud*[Title/Abstract] OR precipitating [Title/Abstract] OR protective [Title/Abstract] OR resilience[Title/Abstract] OR susceptibility[Title/Abstract] OR epidemiology[Title/Abstract])
	4. 1 AND 2 AND 3 [Filter: human, English, not review]
PsychInfo	1. (depression/ or depressive/ or depressed/ or affective).ab,ti.
	2. (onset/ or first-ever /or predictor/ or prevention/or preventive/or risk/or vulnerability/or longitud*/or precipitating/or protective/or resilience/or susceptibility/or epidemiology)).ab,ti.
	(*cognitive theory or *cognitive model or cognitive or *cognitive therapy or *cognitive intervention/ or hopelessness or helplessness or *dual processing or *information processing or *cognitive bias or *cognitive biased or *cognitive biases or *scar model or scarring or *diathesis-stress or attitude* or *dysfunctional belief or *dysfunctional attitude or *dysfunctional attitudes or rumination or ruminative or ruminating or *repetitive thought or *repetitive thinking or worry or persev* or *intrusive thought or *intrusive thinking or *negative thought or *negative thinking or *stress thought or *stress thinking or *obsessive thought or *obsessive thinking or *unconscious stress or *implicit stress or *anticipatory stress or *anticipation stress or *cognitive intrusion or reflection or brooding or *reflect or *referential thought or *counterfactual thinking or *mind wandering or *post-event processing or *habitual negative self-thinking or *catastrophizing or *automatic thoughts questionnaire or *Crandell cognitions inventory or *cognitions checklist or *cognitive style test or *sociotropy-autonomy scale or attribution or schema or *automatic thoughts or *depressive realism or *illusion of control or *cognitive distortion or *judgment of contingency or *attentional bias or *response styles theory or preoccupation OR *self-focus OR *self-focused attention OR *emotion regulation OR *coping strategy OR *coping style).ab,ti.
	4. 1 and 2 and 3

<i>Cochrane library</i>	1. (Depress* or affective)
	2. (onset or first-ever or predictor or prevent* or perspective or risk or vulnerability or longitud* or precipitating or protective or resilience or susceptibility or epidemiology)
	3. (cognitive theory or cognitive model or cognitive or cognitive therapy or cognitive intervention or hopelessness or helplessness or dual processing or information processing or cognitive bias or cognitive biased or cognitive biases or scar model or scarring or diathesis-stress or attitude* or dysfunctional belief or dysfunctional attitude or dysfunctional attitudes ruminat* OR 'repetitive thought' OR 'repetitive thinking' OR worry OR persev* OR 'intrusive thought' OR 'intrusive thinking' OR 'negative thought' OR 'negative thinking' OR 'stress thought' OR 'stress thinking' OR 'obsessive thought' OR 'obsessive thinking' OR 'unconscious stress' OR 'implicit stress' OR 'anticipatory stress' OR 'anticipation stress' OR 'cognitive intrusion*' OR reflection OR brooding OR 'reflect*' OR 'self referential thought' OR 'counterfactual thinking' OR 'mind wandering' OR 'post-event processing' OR 'habitual negative self-thinking' OR 'catastrophizing' OR 'automatic thoughts questionnaire' OR 'Crandell cognitions inventory' OR 'cognitions checklist' OR 'cognitive style test' OR 'sociotropy-autonomy scale' OR attribution OR schema OR 'automatic thoughts' OR 'depressive realism' OR 'illusion of control' OR 'cognitive distortion' OR 'judgment of contingency' OR 'attentional bias' OR 'response styles theory' OR preoccupation OR 'self-focus' OR 'self-focused attention' OR 'emotion regulation' OR 'coping strategy' OR 'coping style')
	4. 1 and 2 and 3
<i>Embase</i>	1. ('depress*/exp or 'affective'/exp OR depress*:ab,ti)
	2. (onset:ab,ti or first-ever:ab,ti or predictor:ab,ti or prevent*:ab,ti or perspective:ab,ti or risk:ab,ti or vulnerability:ab,ti or 'longitud*':ab,ti or precipitating:ab,ti or protective:ab,ti or resilience:ab,ti or susceptibility:ab,ti or epidemiology:ab,ti)
	3. ('cognitive theory':ab,ti or 'cognitive model':ab,ti or cognitive:ab,ti or 'cognitive therapy':ab,ti or 'cognitive intervention':ab,ti or hopelessness:ab,ti or helplessness:ab,ti or 'dual processing':ab,ti or 'information process*':ab,ti or 'cognitive bias':ab,ti or 'cognitive bias*':ab,ti or 'scar model':ab,ti or scarring:ab,ti or 'diathesis-stress':ab,ti or attitude*:ab,ti or 'dysfunctional belief':ab,ti or 'dysfunctional attitude*':ab,ti or ruminat*:ab,ti OR 'repetitive thought':ab,ti OR 'repetitive thinking':ab,ti OR worry:ab,ti OR persev*:ab,ti OR 'intrusive thought':ab,ti OR 'intrusive thinking':ab,ti OR 'negative thought':ab,ti OR 'negative thinking':ab,ti OR 'stress thought':ab,ti OR 'stress thinking':ab,ti OR 'obsessive thought':ab,ti OR 'obsessive thinking':ab,ti OR 'unconscious stress':ab,ti OR 'implicit stress':ab,ti OR 'anticipatory stress':ab,ti OR 'anticipation stress':ab,ti OR 'cognitive intrusion*':ab,ti OR reflection:ab,ti OR brooding:ab,ti OR 'reflect*':ab,ti OR 'self referential thought':ab,ti OR 'counterfactual thinking':ab,ti OR 'mind wandering':ab,ti OR 'post-event processing':ab,ti OR 'habitual negative self-thinking':ab,ti OR 'catastrophizing':ab,ti OR 'automatic thoughts questionnaire':ab,ti OR 'Crandell cognitions inventory':ab,ti OR 'cognitions checklist':ab,ti OR 'cognitive style test':ab,ti OR 'sociotropy-autonomy scale':ab,ti OR attribution:ab,ti OR schema:ab,ti OR 'automatic thoughts':ab,ti OR 'depressive realism':ab,ti OR 'illusion of control':ab,ti OR 'cognitive distortion':ab,ti OR 'judgment of contingency':ab,ti OR 'attentional bias':ab,ti OR 'response styles theory':ab,ti OR preoccupation:ab,ti OR 'self-focus':ab,ti OR 'self-focused attention':ab,ti OR 'emotion regulation' OR 'coping strategy':ab,ti OR 'coping style':ab,ti)
	4. 1 and 2 and 3

Search terms Psychodynamic theories

Database	Search strategy
Pubmed	1. ("depressive disorder"[MeSH Terms] OR "depression"[MeSH Terms] OR depression[Title/Abstract] OR depressive[Title/Abstract] OR depressed [Title/Abstract] OR affective[Title/Abstract])
	2. ("attachment anxiety"[Title/Abstract] OR "secure attachment"[Title/Abstract] OR "insecure attachment"[Title/Abstract] OR "avoidant attachment"[Title/Abstract] OR "withdrawn attachment"[Title/Abstract] OR "attachment style"[Title/Abstract] OR "dismissive attachment"[Title/Abstract] OR "object relations"[Title/Abstract] OR "object relational functioning"[Title/Abstract] OR "self object"[Title/Abstract] OR "loved object"[Title/Abstract] OR "self object representations"[Title/Abstract] OR "depressive position"[Title/Abstract] OR "mirroring"[Title/Abstract] OR "twinship"[Title/Abstract] OR "poignant sadness"[Title/Abstract] OR "remorseful guilt"[Title/Abstract] OR "guilt"[Title/Abstract] OR "shame"[Title/Abstract] OR "compromise formation"[Title/Abstract] OR "narcissistic identification"[Title/Abstract] OR psychodynam*[Title/Abstract] OR psychoanal*[Title/Abstract])
	3. (onset [Title/Abstract] OR first-ever [Title/Abstract] OR predictor [Title/Abstract] OR preventi*[Title/Abstract] OR prospective [Title/Abstract] OR risk [Title/Abstract] OR vulnerability[Title/Abstract] OR longitud*[Title/Abstract] OR precipitating [Title/Abstract] OR protective [Title/Abstract] OR resilience[Title/Abstract] OR susceptibility[Title/Abstract] OR epidemiology[Title/Abstract])
	4. 1 AND 2 AND 3 [Filter: human, English, not review]
PsychInfo	1. (depression/ or depressive/ or depressed/ or affective).ab,ti.
	2. (onset/ or first-ever /or predictor/ or prevention/or preventive/or prospective/or risk/or vulnerability/or longitud*/or precipitating/or protective/or resilience/or susceptibility/or epidemiology)).ab,ti.
	3. (psychoanal*/ or psychodynam*/ or *object relation*/ or *attachment anxiety*/ or *insecure attachment*/ or *enmeshed attachment*/ or *secure attachment*/ or *avoidant attachment*/ or *withdrawn attachment*/ or *dismissive attachment*/ or *self object*/ or twinship/ or mirroring/ or *idealizing transference*/ or *reassurance seeking*/ or *narcissistic identification*).mp.
	4. 1 and 2 and 3
Cochrane library	1. (Depress* or affective)
	2. (onset or first-ever or predictor or preventi* or perspective or risk or vulnerability or longitud* or precipitating or protective or resilience or susceptibility or epidemiology)
	3. (behavioral theory or behavioural theory or behavioral model or behavioural model or behavioral intervention or behavioural intervention or behavioral therapy or behavioural therapy or social learning or self-efficacy or observational learning or self-regulation or conditioning or conditioned or classical condition* or operant condition* or reinforcement or learning theory or behavioral activation or behavioural activation or functional analysis or problem solving or social skills)
	4. 1 and 2 and 3
Embase	1. ('depress*/exp or 'affective'/exp OR depress*:ab,ti)
	2. (onset:ab,ti or first-ever:ab,ti or predictor:ab,ti or preventi*:ab,ti or perspective:ab,ti or risk:ab,ti or vulnerability:ab,ti or 'longitud*':ab,ti or precipitating:ab,ti or protective:ab,ti or resilience:ab,ti or susceptibility:ab,ti or epidemiology:ab,ti)
	3. (object relations or attachment anxiety or insecure attachment or enmeshed attachment or secure attachment or avoidant attachment or withdrawn attachment or dismissive attachment or self object or object relation function or twinship or mirroring or idealizing transference or guilt or shame or reassurance seeking or narcissistic identification or compromise formation or poignant sadness or remorseful guilt or psychodynam* or psychoanal*)
	4. 1 and 2 and 3

Search terms Personality-based theories

Database	Search strategy
Pubmed	1. ("depressive disorder"[MeSH Terms] OR "depression"[MeSH Terms] OR depression[Title/Abstract] OR depressive[Title/Abstract] OR depressed [Title/Abstract] OR affective[Title/Abstract])
	2. (personality[Title/Abstract] OR Eysenck[Title/Abstract] OR Neuroticism[Title/Abstract] OR Psychoticism[Title/Abstract] OR BAS[Title/Abstract] OR FFFS[Title/Abstract] OR BIS[Title/Abstract] OR Big Five[Title/Abstract] OR volatility[Title/Abstract] OR Agreeableness[Title/Abstract] OR "Openness to experience"[Title/Abstract] OR Conscientiousness[Title/Abstract] OR Cloninger[Title/Abstract] OR "Novelty seeking"[Title/Abstract] OR "Harm avoidance"[Title/Abstract] OR Persistence[Title/Abstract] OR "Reward dependence"[Title/Abstract] OR "Self-directedness"[Title/Abstract] OR "Watson & Tellegen"[Title/Abstract] OR Constraint[Title/Abstract])
	3. (onset [Title/Abstract] OR first-ever [Title/Abstract] OR predictor [Title/Abstract] OR preventi* [Title/Abstract] OR prospective [Title/Abstract] OR risk [Title/Abstract] OR vulnerability[Title/Abstract] OR longitud* [Title/Abstract] OR precipitating [Title/Abstract] OR protective [Title/Abstract] OR resilience[Title/Abstract] OR susceptibility[Title/Abstract] OR epidemiology[Title/Abstract])
	4. 1 AND 2 AND 3 [Filter: human, English, not review]
PsychInfo	1. (depression/ or depressive/ or depressed/ or affective).ab,ti.
	2. (onset/ or first-ever /or predictor/ or prevention/or preventive/or prospective/or risk/or vulnerability/or longitud*/or precipitating/or protective/or resilience/or susceptibility/or epidemiology)).ab,ti.
	3. (personality or Eysenck or Neuroticism or Psychoticism or BAS or FFFS or BIS or *Big Five or volatility or Agreeableness or *Openness to experience or Conscientiousness or Cloninger or *Novelty seeking or *Harm avoidance or *Reward dependence or *Self-directedness or *Watson & Tellegen).ab,ti.
	4. 1 and 2 and 3
Cochrane library	1. (Depress* or affective)
	2. (onset or first-ever or predictor or preventi* or perspective or risk or vulnerability or longitud* or precipitating or protective or resilience or susceptibility or epidemiology)
	3. (personality or Eysenck or Neuroticism or Psychoticism or BAS or FFFS or BIS or "Big Five" or volatility or Agreeableness or "Openness to experience" or Conscientiousness or Cloninger or "Novelty seeking" or "Harm avoidance" or "Reward dependence" or "Self-directedness" or "Watson & Tellegen")
	4. 1 and 2 and 3
Embase	1. ('depress*/exp or 'affective'/exp OR depress*:ab,ti)
	2. (onset:ab,ti or first-ever:ab,ti or predictor:ab,ti or preventi*:ab,ti or perspective:ab,ti or risk:ab,ti or vulnerability:ab,ti or 'longitud*':ab,ti or precipitating:ab,ti or protective:ab,ti or resilience:ab,ti or susceptibility:ab,ti or epidemiology:ab,ti)
	3. (personality:ab,ti OR eyenck:ab,ti OR neuroticism:ab,ti OR psychoticism:ab,ti OR bas:ab,ti OR fffs:ab,ti OR bis:ab,ti OR 'big five':ab,ti OR volatility:ab,ti OR agreeableness:ab,ti OR 'openness to experience':ab,ti OR conscientiousness:ab,ti OR cloninger:ab,ti OR 'novelty seeking':ab,ti OR 'harm avoidance':ab,ti OR 'reward dependence':ab,ti OR 'self-directedness':ab,ti OR 'watson & tellegen':ab,ti)
	4. 1 and 2 and 3

Search terms Diathesis-stress theories

Database	Search strategy
Pubmed	1. ("depressive disorder"[MeSH Terms] OR "depression"[MeSH Terms] OR depression[Title/Abstract] OR depressive[Title/Abstract] OR depressed [Title/Abstract] OR affective[Title/Abstract])
	2. ("predisposition nature" [Title/Abstract] OR "predisposition nurture" [Title/Abstract] OR "diathesis stress"[Title/Abstract] OR "diathesis-stress"[Title/Abstract] OR "diathesis stressor"[Title/Abstract] OR diathesis[Title/Abstract] OR diatheses [Title/Abstract] OR interaction [Title/Abstract] OR "nurture nature" [Title/Abstract] OR "nature/nurture model"[Title/Abstract] OR "social support" [Title/Abstract] OR coping [Title/Abstract] OR OR vulnerab* [Title/Abstract])
	3. ("stress/stressor" [Title/Abstract] "stress/trauma" [Title/Abstract] OR "stress/vulnerability" [Title/Abstract] OR "stress/vulnerability stress" [Title/Abstract] OR "stress/death" [Title/Abstract] OR "stress/stressful" [Title/Abstract] OR "stress/stressors" [Title/Abstract] OR "stress/adversity" [Title/Abstract] OR "stress/affect" [Title/Abstract] OR "stress/anxiety/depression" [Title/Abstract] OR "adverse event*" [Title/Abstract] OR trauma[Title/Abstract] OR "life event*" [Title/Abstract] OR "traumatic" [Title/Abstract] OR "bereavement" [Title/Abstract] OR "grief" [Title/Abstract] OR "humiliation" [Title/Abstract] OR "social rejection" [Title/Abstract] or maltreatment [Title/Abstract] OR "childhood trauma" [Title/Abstract] OR "early trauma" [Title/Abstract])
	4. (onset [Title/Abstract] OR first-ever [Title/Abstract] OR predictor [Title/Abstract] OR preventi* [Title/Abstract] OR prospective [Title/Abstract] OR risk [Title/Abstract] OR vulnerability[Title/Abstract] OR longitudi*[Title/Abstract] OR precipitating [Title/Abstract] OR protective [Title/Abstract] OR resilience[Title/Abstract] OR susceptibility[Title/Abstract] OR epidemiology[Title/Abstract])
	5. 1 AND 2 AND 3 AND 4 [Filter: human, English, not review]
PsychInfo	1. (depression/ or depressive/ or depressed/ or affective).ab,ti.
	2. (onset/ or first-ever /or predictor/ or prevention/or preventive/or prospective/or risk/or vulnerability/or longitudi*/or precipitating/or protective/or resilience/or susceptibility/or epidemiology)).ab,ti.
	3. (*predisposition or diathesis or diatheses or interaction or * nature nurture or *social support or coping or vulnerability or vulnerable or vulnerabilities).ab,ti
	4. (Stress or *adverse event or trauma or *life event or traumatic or bereavement or grief or humiliation or *social rejection or maltreatment or *childhood trauma or *early trauma).ab,ti
	5. 1 and 2 and 3 and 4

<i>Cochrane library</i>	1. (Depress* or affective)
	2. (onset or first-ever or predictor or prevent* or perspective or risk or vulnerability or longitud* or precipitating or protective or resilience or susceptibility or epidemiology)
	3. (predisposition OR “nature*nurture*” OR “diathesis stress” OR diathesis-stress OR “diathesis stressor” OR diathesis OR diatheses OR “social support” OR coping or vulnerability or vulnerable or vulnerabilities)
	4. (stress OR “adverse event*” OR trauma or maltreatment” OR “childhood trauma” OR “early trauma” OR “life event*” OR “life-event*” or traumatic or bereavement or grief or humiliation or “social rejection”)
	5. 1 and 2 and 3 and 4
<i>Embase</i>	1. (‘depress*’/exp or ‘affective’/exp OR depress*:ab,ti)
	2. (onset:ab,ti or first-ever:ab,ti or predictor:ab,ti or prevent*:ab,ti or perspective:ab,ti or risk:ab,ti or vulnerability:ab,ti or ‘longitud*’:ab,ti or precipitating:ab,ti or protective:ab,ti or resilience:ab,ti or susceptibility:ab,ti or epidemiology:ab,ti)
	3. (predisposition:ab,ti OR “nature-nurture”:ab,ti OR “diathesis stress”:ab,ti OR diathesis-stress:ab,ti OR “diathesis stressor”:ab,ti OR diathesis:ab,ti OR diatheses:ab,ti OR “social support”:ab,ti or coping:ab,ti or vulnerability:ab,ti or vulnerable:ab,ti or vulnerabilities:ab,ti)
	4. (stress:ab,ti OR “adverse event”:ab,ti or “adverse events”:ab,ti OR trauma:ab,ti or “life event”:ab,ti or traumatic:ab,ti or bereavement:ab,ti or grief:ab,ti or humiliation:ab,ti OR “life events”:ab,ti or “social rejection”:ab,ti or maltreatment:ab,ti)
	5. 1 and 2 and 3 and 4

Appendix B: PRISMA Checklist

Section/topic	#	PRISMA Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2,3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4, 5, 6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7,8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7, Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8,9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8,9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	9
Section/topic	#	PRISMA Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	10
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	10

RESULTS				
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.		Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.		Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).		11, Table1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.		Figure 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.		11,12
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).		11,12
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).		NA
DISCUSSION				
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).		13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).		14
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.		15
FUNDING				
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.		Author disclosure

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed10000

Appendix C: Articles included in the systematic review (reference with asterisk were included in the meta-analysis)

- *Alloy, L. B., Abramson, L. Y., Whitehouse, W. G., Hogan, M. E., Panzarella, C., & Rose, D. T. (2006). Prospective incidence of first onsets and recurrences of depression in individuals at high and low cognitive risk for depression. *Journal of Abnormal Psychology*, 115(1), 145–156. <https://doi.org/10.1037/0021-843X.115.1.145>
- Bijl, R. V., Graaf, R. de, Ravelli, A., Smit, F., & Vollebergh, W. A. (2002). Gender and age-specific first incidence of DSM-III-R psychiatric disorders in the general population. Results from the Netherlands mental health survey and incidence study (NEMESIS). *Social Psychiatry and Psychiatric Epidemiology*, 37(8), 372–379. <https://doi.org/10.1007/s00127-002-0566-3>
- Carter, J. S., & Garber, J. (2011). Predictors of the first onset of a major depressive episode and changes in depressive symptoms across adolescence: Stress and negative cognitions. *Journal of Abnormal Psychology*, 120(4), 779–796. <https://doi.org/10.1037/a0025441>
- Coventry, W. L., Medland, S. E., Wray, N. R., Thorsteinsson, E. B., Heath, A. C., & Byrne, B. (2009). Phenotypic and discordant-monozygotic analyses of stress and perceived social support as antecedents to or sequelae of risk for depression. *Twin Research and Human Genetics*, 12(5), 469–488. <https://doi.org/10.1375/twin.12.5.469>
- *Eldesouky, L., Thompson, R. J., Oltmanns, T. F., & English, T. (2018). Affective instability predicts the course of depression in late middle-age and older adulthood. *Journal of Affective Disorders*, 239, 72–78. <https://doi.org/10.1016/j.jad.2018.06.038>

- *Fanous, A. H., Neale, M. C., Aggen, S. H., & Kendler, K. S. (2007). A longitudinal study of personality and major depression in a population-based sample of male twins. *Psychological Medicine*, 37(8), 1163–1172. <https://doi.org/10.1017/S0033291707000244>
- *Giollabhui, N. M., Hamilton, J. L., Nielsen, J., Connolly, S. L., Stange, J. P., Varga, S., ... Alloy, L. B. (2018). Negative cognitive style interacts with negative life events to predict first onset of a major depressive episode in adolescence via hopelessness. *Journal of Abnormal Psychology*, 127(1), 1–11. <https://doi.org/10.1037/abn0000301>
- *Goldstein, B. L., Kotov, R., Perlman, G., Watson, D., & Klein, D. N. (2018). Trait and facet-level predictors of first-onset depressive and anxiety disorders in a community sample of adolescent girls. *Psychological Medicine*, 48(8), 1282–1290. <https://doi.org/10.1017/S0033291717002719>
- Goodyer, I. M., Herbert, J., Tamplin, A., & Altham, P. M. (2000). First-episode major depression in adolescents: Affective, cognitive and endocrine characteristics of risk status and predictors of onset. *British Journal of Psychiatry*, 176(FEB.), 142–149. <https://doi.org/10.1192/bjp.176.2.142>
- Kendler, K. S., Gatz, M., Gardner, C. O., & Pedersen, N. L. (2006). Personality and major depression: A Swedish longitudinal, population-based twin study. *Archives of General Psychiatry*, 63(10), 1113–1120. <https://doi.org/10.1001/archpsyc.63.10.1113>
- Kendler, K. S., Neale, M. C., Kessler, R. C., Heath, A. C., & Eaves, L. J. (1993). A Longitudinal Twin Study of 1-Year Prevalence of Major Depression in Women. *Archives of General Psychiatry*, 50(11), 843–852. <https://doi.org/10.1001/archpsyc.1993.01820230009001>

*Kessler, R. C., Gruber, M., Hettema, J. M., Hwang, I., Sampson, N., & Yonkers, K. A. (2008).

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