**Supplementary Material**

**Dragioti et al., 2022**

**Impact of Mental Disorders on Clinical Outcomes of Physical Diseases: An Umbrella Review of the Evidence**

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# **eTable 1** Characteristics of systematic reviews with meta-analysis studying the association between neurotic, stress-related and somatoform disorders and outcomes of physical diseases

| Study  (No of associations) | Mental disorder | Disorder definition (standard diagnostic criteria, established diagnostic research criteria, validated assessment instrument with cut-offs) | Physical  disease | Outcome (s)  (Metric) | No of prospective studies (Sample size/ follow-up, range (y) | Mean age of participants (range) | %Male (range) | ROBIS Phase 2 | | | | ROBIS Phase 3 |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Domain 1:  Study eligibility criteria | Domain 2: Identification and selection of studies | Domain 3: Data collection and study appraisal | Domain 4: Synthesis and findings | Risk of bias in the review |
| Neurotic, stress-related and somatoform disorders and cardiovascular diseases | | | | | | | | | | | | |
| Li, 20201  (2) | Anxiety disorder | DSM-IV and validated assessment instruments (HADS-A≥8, GAD-7≥10, HARS ≥18) | Acute coronary syndrome | All-cause mortality; Major cardiac events (RR) | 8 (6,073/  1-10y) | 59-67 | 67-81 | Low risk | High risk | Low risk | Low risk | Low risk |
| Emdin, 20162  (2) | Anxiety disorder | DSM-III-R, DSM-III, DSM-IV, and validated assessment instruments (Zung SAS≥50) | Cardiovascular diseases | Cardiovascular mortality; Major cardiac events (RR) | 6 (156,418/  3-23y) | 41-81 | 0-100 | High risk | Low risk | High risk | Low risk | Low risk |
| Celano, 20153  (2) | Anxiety disorder | DSM-IV and validated assessment instruments (HADS-A≥8, HARS≥18,Zung SAS≥44) | Coronary artery disease | All-cause mortality; Major cardiac events (OR) | 13 (9,644/  11-8y) | 59-67 | 70-82 | Low risk | Low risk | Low risk | High risk | Low risk |
| Roest, 20104  (1) | Anxiety disorder | Validated assessment instruments (HADS-A≥8) | Myocardial infarction | Major cardiac events (OR) | 3 (1,213/  1-5y) | 60-63 | 46-81 | High risk | Low risk | High risk | High risk | Low risk |
| Taggart Wasson, 20185  (1) | Post-traumatic stress disorder | Validated assessment instruments  (IES ≥33) | Myocardial infarction | Medication nonadherence (RR) | 2 (213/  0.3-3y) | 53-61 | 41-58 | Low risk | Low risk | Low risk | Low risk | Low risk |
| Neurotic, stress-related and somatoform disorders and other physical diseases | | | | | | | | | | | | |
| Atlantis, 20136  (1) | Anxiety disorder | Validated assessment instruments (HADS-A≥8) | Chronic obstructive pulmonary disease | All-cause mortality (RR) | 3 (2,099/  1-5y) | 57-69 | 43-69 | High risk | High risk | High risk | High risk | High risk |
| Guo, 20217  (1) | Anxiety disorder | DSM-IV-R and validated assessment instruments (MDS-UPDRS-A≥2) | Parkinson's disease | Cognitive impairment (RR) | 2 (243/  < 5y) | 62-66 | 52-63 | High risk | Low risk | Unclear risk | Low risk | Low risk |
| Li, 20168  (1) | Anxiety disorder | Validated assessment instruments  (HARS≥17) | Neurological diseases with mild cognitive impairment | Alzheimer’s disease progression (RR) | 2 (448/  3-5.5y) | 67-84 | 15-56 | Low risk | High risk | Low risk | Low risk | Low risk |
| Wang, 20209  (2) | Anxiety disorder | Validated assessment instruments (HADS-A≥10) | Breast cancer | All-cause mortality; Cancer recurrence (HR) | 3 (2,874/  8-13y) | 52-60 | 0 | Low risk | Low risk | Low risk | Low risk | Low risk |

DSM— Diagnostic and statistical manual of mental disorders, GAD-7—General anxiety disorder-7, HADS-A—Hospital anxiety and depression scale (anxiety subscale), HARS—Hamilton anxiety rating scale, HR—Hazard ratio, IES— Impact of event scale, MDS-UPDRS-A— Movement disorder society-Unified Parkinson’s disease rating scale (anxiety subscale), OR—Odds ratio, ROBIS— Risk of bias assessment tool for systematic reviews, RR—Risk ratio, Zung SAS— Zung self-rating anxiety scale.

# **eTable 2** Characteristics of systematic reviews with meta-analysis studying the association between mood affective disorders and outcomes of physical diseases

| Study  (No of associations) | Mental disorder | Disorder definition (standard diagnostic criteria, established diagnostic research criteria, validated assessment instrument with cut-offs) | Physical  disease | Outcome (s)  (Metric) | No of prospective studies (Sample size/ follow-up, range (y) | Mean age of participants,  range) | %Male (range) | ROBIS Phase 2 | | | | ROBIS Phase 3 |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Domain 1:  Study eligibility criteria | Domain 2: Identification and selection of studies | Domain 3: Data collection and study appraisal | Domain 4: Synthesis and findings | Risk of bias in the review |
| Mood affective disorders and cardiovascular diseases (including stroke) | | | | | | | | | | | | |
| Correll, 201710  (1) | Bipolar disorder | ICD-8,9,10,  RDC | Cardiovascular diseases | Cardiovascular mortality (RR) | 6 (1,309,529/  4-20y) | 37-72 | 42-100 | Low risk | Low risk | Unclear risk | Low risk | Low risk |
| Yuan, 202211  (1) | Bipolar disorder | ICD-9,10 | Stroke | Stroke mortality (HR) | 2 (10,715,313/ 7-20y) | NR | 46-100 | Low risk | Low risk | Unclear risk | Low risk | Low risk |
| Correll, 201710  (1) | Depressive disorders | DSM-IV, ICD-9,10 | Cardiovascular diseases | Cardiovascular mortality (RR) | 5 (650,556/  3-20y) | 44-72 | 34-100 | Low risk | Low risk | Unclear risk | Low risk | Low risk |
| Barth, 200412  (1) | Depressive disorders | Validated assessment instruments  (BDI≥10, HADS-D≥8, Zung SDS≥50) | Coronary artery disease\* | All-cause mortality  (HR) | 6 (7,486/  1-15y) | 53-64 | 31-85 | High risk | Low risk | Unclear risk | High risk | High risk |
| Nicholson, 200613  (1) | DSM-IV, RCD, DIS for DSM-IV, and validated assessment instruments (BDI≥10, CES-D≥16, Zung SDS≥40) | All-cause mortality (RR) | 10 (6,727/ 0.33-15y) | 59-71 | 48-73 | High risk | High risk | High risk | High risk | Unclear risk |
| Wu, 201614  (2) | Depressive disorders | ICD-8, DSM-III, IV and validated assessment instruments (CES-D≥16, HADS-D≥11, MMPI-2 D≥22, Zung SDS≥45) | Coronary artery disease | Cardiovascular mortality; Myocardial infarction (HR) | 12 (161,318/  4.2-24y) | >18-99 | 29-100 | Low risk | Low risk | High risk | Low risk | Low risk |
| Shi, 201715  (2) | Depressive disorders | DIS for DSM-IV and validated assessment instruments (BDI≥10, CES-D≥16, Zung SDS≥50) | Coronary artery disease | Ventricular tachycardia/ fibrillation; Atrial fibrillation recurrence (HR) | 8 (3,805/  < 5y) | 58-64 | 60-82 | Low risk | Low risk | Low risk | Low risk | Low risk |
| Flaherty, 201716 | Depressive disorders | Validated assessment instruments (BDI≥10, CES-D≥16) | Coronary artery bypass graft | All-cause mortality (HR) | 2 (1,126/  >5y) | 62-63 | 67 | High risk | Low risk | Low risk | High risk | High risk |
| Gathright, 201717  (1) | Depressive disorders | Validated assessment instruments (BDI≥10, CES-D≥16, HADS-D≥10, PHQ-9≥10, | Heart failure\* | All-cause mortality (HR) | 9 (3,376/  1-12y) | 57-79 | 40-85 | Low risk | Low risk | Unclear risk | High risk | High risk |
| Sokoreli, 201618  (1) | Validated assessment instruments (BDI≥10, CES-D≥24) | 4 (8,108/  1-3y) | 62-73 | 48-65 | Low risk | Low risk | High risk | High risk | High risk |
| Rutledge, 201619  (1) | Depressive disorders | DIS for DSM-IV and validated assessment instruments (PRIME-MD positive followed by CEG; HADS-D≥8, Zung SDS≥50) | Heart failure | Major cardiac events (RR) | 6 (1,088/  0.5-3y) | 53-66 | 51-72 | Low risk | Low risk | Unclear risk | High risk | High risk |
| Meijer, 201120  (3) | Depressive disorders | CIDI, SCID/DCPR, DIS for DSM-IV, and validated assessment instruments (BDI≥10,  HADS-D≥10, MADRS≥14, Zung SDS ≥40) | Myocardial infarction | All-cause mortality; Cardiovascular mortality; Major cardiac events (OR) | 27 (15,319/  1-5y) | 59-65 | 55-84 | Low risk | Low risk | High risk | High risk | Unclear risk |
| Zhang, 201921  (1) | Depressive disorders | MINI and validated assessment instruments (BDI≥31, HADS-D≥8, Zung SDS≥ 60) | Percutaneous coronary intervention | Major cardiac events (RR) | 7 (3,375/  1-10y) | 57-64 | 63-78 | Low risk | Low risk | High risk | Low risk | Low risk |
| Song, 202022  (1) | Depressive disorders | MINI and validated assessment instruments (HADS-D≥8, CES-D≥16) | Percutaneous coronary intervention | All-cause mortality (RR) | 5 (3,209/  2-10y) | 58-75 | 63-77 | Low risk | High risk | Low risk | Low risk | Low risk |
| Blöchl, 201923  (1) | Depressive disorders | Validated assessment instruments (BDI≥10, HDRS≥7) | Stroke | Poor functional outcome (OR) | 4 (2,663/  0.6-2y) | 61-73 | 44-65 | Low risk | Unclear risk | High risk | Low risk | High risk |
| Bartoli, 201824  (1) | Depressive disorders | ICD-10, CIDI and validated assessment instruments (HDRS≥7, PHQ-9≥10) | Stroke\* | All-cause mortality (RR) | 5 (1,254/  1-10y) | 60-68 | 54-60 | Low risk | Low risk | Low risk | Unclear risk | Low risk |
| Cai, 201925  (1) | ICD-8, DSM-III-R, IV and validated assessment instruments (CES-D≥16, HADS≥11, HDRS≥7) | All-cause mortality (HR) | 8 (79,962/  1-15y) | 39-72 | 42-98 | Low risk | Unclear risk | Low risk | Low risk | Unclear risk |
| Pan, 201126  (1) | Depressive disorders | RCD and validated assessment instruments  (CES-D≥16, Zung SDS≥ 60, HLEQ related to DSM-IV MDD) | Stroke | Stroke mortality (HR) | 4 (35,193/  5-29y) | 46->65 | 43-100 | Low risk | Low risk | Low risk | Low risk | Low risk |
| Wu, 201927  (1) | Depressive disorders | DSM-IV, and validated assessment instruments (BDI≥14, HADS-D≥8, Zung SDS≥50) | Stroke | Stroke recurrence (RR) | 5 (3,547/  1-12y) | 53-82 | 51-66 | Low risk | High risk | Low risk | Low risk | Low risk |
| Mood affective disorders and chronic respiratory diseases | | | | | | | | | | | | |
| Courtwright, 201628  (1) | Depressive disorders | DSM-IV and validated assessment instruments (BDI≥14) | Lung transplant | Posttransplant mortality (HR) | 2 (356/  >5y) | 49-52 | 49 | Low risk | High risk | Low risk | Low risk | Low risk |
| Atlantis, 20136  (1) | Depressive disorders | ICD-10 and validated assessment instruments (BDI≥15, HADS-D≥8, CES-D≥16, Yesavage DI≥11) | Chronic obstructive pulmonary disease | All-cause mortality (RR) | 6 (1,368/  1-7y) | 61-72 | 33-92 | High risk | High risk | High risk | High risk | High risk |
| Mood affective disorders and endocrine system diseases | | | | | | | | | | | | |
| Chow, 202229  (1) | Depressive disorders | ICD-9,10, and validated assessment instruments (HADS-D≥8, PHQ-9≥10) | Diabetes mellitus | Dementia (HR) | 5 (1,945,584/  5-10.6y) | 56-68 | 51-59 | Low risk | Low risk | Low risk | Low risk | Low risk |
| Farooqi, 201930  (3) | Depressive disorders | ICD-9, DSM-III, IV, MINI and validated assessment instruments (PHQ-9≥10) | Diabetes mellitus\* | Coronary artery disease; Stroke; Cardiovascular mortality (HR) | 7 (952,363/  4-20.8y) | 41-65 | 48-67 | High risk | Low risk | Low risk | Low risk | Low risk |
| van Dooren, 201331  (1) | Validated assessment instruments (BDI≥10, CES-D≥16) | Cardiovascular mortality (HR) | 2 (1,045/  6-8y) | 63-65 | 38-70 | Low risk | Low risk | Low risk | High risk | Unclear risk |
| Hofmann, 201332  (2) | Depressive disorders | ICD-9, DSM-IV, CIDI, and validated assessment instruments (BDI≥10, CES-D≥16, HADS-D≥8, PHQ-9≥10, DSQ≥8, GDS≥10) | Diabetes mellitus | All-cause mortality (HR) | 12 (88,648)/  2-10y) | 52-76 | 38-100 | Low risk | Low risk | Low risk | Unclear risk | Low risk |
| Farrokhi, 201433  (1) | Depressive disorders | ICD-9 and validated assessment instruments (BDI≥10, CES-D≥10, PHQ-9≥10) | Kidney failure | All-cause mortality (HR) | 6 (12,600/  1-5y) | >17-60 | 51-57 | Low risk | Low risk | Low risk | Low risk | Low risk |
| Palmer, 201334  (1) | Depressive disorders | SCID, MINI and validated assessment instruments (BDI≥10, PHQ-9≥10, CES-D≥10) | Chronic kidney disease | All-cause mortality (RR) | 13 (17,688/  1-6.5y) | >17-66 | 51-73 | Low risk | Unclear risk | Low risk | Low risk | Unclear risk |
| Mood affective disorders and cancer | | | | | | | | | | | | |
| Satin, 200935  (3) | Depressive disorders | DSM-II, IV, SCID and validated assessment instruments (BDI≥10 HADS-D≥8, CES-D≥16, EDS≥13) | Cancer | All-cause mortality (HR); Cancer progression (RR) | 12 (4,745/  <5 y & ≥5 y) | 35-70 | 0-83 | High risk | Low risk | High risk | High risk | High risk |
| Shi, 201836  (2) | Depressive disorders | DSM-IV and validated assessment instruments (BDI≥10, HADS-D≥8) | Glioma; High-grade brain tumour | All-cause mortality (HR);Glioma mortality(RR) | 5 (1,481/  < 5y) | 45-54 | 34-55 | Low risk | Low risk | High risk | Low risk | Low risk |
| Wang, 20209  (3) | Depressive disorders | ICD-9 and validated assessment instruments (PSSCAN based on DSM-IV-TR≥11 HADS-D≥8, CES-D≥16) | Breast cancer | Breast cancer mortality; All-cause mortality; Cancer recurrence (HR) | 8 (14,316/8-13y) | 52-72 | 0 | Low risk | Low risk | Low risk | Low risk | Low risk |
| Mood affective disorders and other physical diseases | | | | | | | | | | | | |
| Guo, 20217  (1) | Depressive disorders | Validated assessment instruments (HADS-D≥11, MADRS ≥20 and Yesavage DI≥11) | Parkinson's disease | Cognitive impairment (RR) | 2 (547/  < 5y) | 68-69 | 38-63 | High risk | Low risk | Unclear risk | Low risk | Low risk |
| Li, 20168  (1) | Depressive disorders | DSM-IV and validated assessment instruments (GDS≥10, HDRS≥17) | Neurological diseases with mild cognitive impairment | Alzheimer’s disease progression (RR) | 5 (3,629/  3-5.5y) | 67-81 | 36-56 | Low risk | High risk | Low risk | Low risk | Low risk |
| Murao, 201637  (1) | Depressive disorders | MINI and validated assessment instruments  (GDS≥10, CES-D≥16) | Neurological diseases with mild cognitive impairment | Dementia progression (RR) | 3 (7,216/  < 5y) | 65-84 | 15-77 | Low risk | Low risk | Low risk | Low risk | Low risk |
| Ruiz-Grosso, 202038  (2) | Depressive disorders | Validated assessment instruments (CES-D≥16, PHQ-9≥10) | Tuberculosis | Tuberculosis mortality;  Negative outcomes during treatment (OR) | 2 (900/  < 5y) | 26-30 | 53-54 | Low risk | Low risk | Low risk | Low risk | Low risk |
| Schoultz, 202039  (1) | Depressive disorders | Validated assessment instruments  (HADS-D≥10) | Inflammatory bowel disease | Symptom exacerbation (HR) | 2 (480/  1-2y) | 47 | 73 | Low risk | Low risk | Low risk | Low risk | Low risk |
| Scott, 201840  (1) | Depressive disorders | CIDI and validated assessment instruments (BDI≥20) | Human immunodeficiency virus infection | Pain (HR) | 2 (890/  < 5y) | 30-42 | 65-81 | Low risk | Low risk | Low risk | Low risk | Low risk |

BDI— Beck's depression inventory, CES— Center for epidemiologic studies depression scale, CEG — PRIME-MD Clinician evaluation guide, CIDI—composite international diagnostic interview, DIS—Diagnostic interview schedule for DSM-IV, DSM— Diagnostic and statistical manual of mental disorders, DSQ— Depression screening questionnaire, EDS—Edinburgh depression scale, GDS— Geriatric depression scale, HADS-D—Hospital anxiety and depression scale (depression subscale), HDRS— Hamilton depression rating scale, HLEQ—Health and life experiences questionnaire, HR— Hazard ratio, ICD— International classification of diseases, MADRS— Montgomery-Asberg depression rating scale, MINI— Mini international neuropsychiatric interview, MMPI-2 D— Minnesota multiphasic personality inventory-2 (depression subscale), OR—Odds ratio, PHQ-9—Patient health questionnaire-9, PRIME-MD—Primary care evaluation of mental disorders, PSSCAN— Psychological screen for cancer, ROBIS— Risk of bias assessment tool for systematic reviews, RDC—Research diagnostic criteria, RR— Risk ratio, SCID/DCPR— Structured clinical interview for DSM/Diagnostic criteria for psychosomatic research, Yesavage DI- Yesavage depression inventory, Zung SDS— Zung self-rating depression scale. \*Same association but non-overlapping or minimally overlapping primary studies in those systematic reviews with meta-analysis.

# **eTable 3** Characteristics of systematic reviews with meta-analysis studying the association between other mental disorders and outcomes of physical diseases

| Study  (No of associations) | Mental disorder | Disorder definition (standard diagnostic criteria, established diagnostic research criteria, validated assessment instrument with cut-offs) | Physical  disease | Outcome (s)  (Metric) | No of prospective studies (Sample size/follow-up, range(y) | Mean age of participants (range) | %Male (range) | ROBIS Phase 2 | | | | ROBIS Phase 3 |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Domain 1:  Study eligibility criteria | Domain 2: Identification and selection of studies | Domain 3: Data collection and study appraisal | Domain 4: Synthesis and findings | Risk of bias in the review |
| Mental and behavioural disorders due to psychoactive substance use and infectious diseases | | | | | | | | | | | | | |
| Llamosas-Falcón, 202041  (2) | Alcohol use disorder | ICD-9,10 | Hepatitis C virus infection | Decompensated liver cirrhosis; Negative course liver disease  (RR) | 3 (169,506/  1-10y) | 53-61 | 53-10 | Unclear risk | High risk | Unclear risk | Unclear risk | High risk |
| Schizophrenia, schizotypal and delusional disorders and cardiovascular diseases and neoplasms | | | | | | | | | | | | | |
| Correll, 201710  (1) | Schizophrenia | ICD-8,9,10 | Cardiovascular diseases | Cardiovascular mortality (RR) | 7 (821,483/  4-30y) | 39-72 | 42-100 | Low risk | Low risk | Unclear risk | Low risk | Low risk |
| Ni, 201942  (2) | Schizophrenia | ICD-9,10 | Breast cancer; Lung cancer | Breast cancer mortality; Lung cancer mortality (RR) | 2 (3,840/  11-25y) | 39 | 0-64 | Low risk | High risk | Low risk | Low risk | Low risk |
| Zhuo, 201743  (1) | Schizophrenia | ICD-9,10 | Cancer | Cancer mortality(SMR) | 3 (42,102/  11-25y) | 39-72 | 0-100 | High risk | Low risk | High risk | Unclear risk | Unclear risk |
| Organic, including symptomatic, mental disorders and infectious, cardiovascular diseases(including stroke), musculoskeletal system and connective tissue, and neurological disorders | | | | | | | | | | | | | |
| Hariyanto, 202144  (1) | Dementia | ICD-9 | COVID-19\* | All-cause mortality (RR) | 2 (22,796)/  <5y) | 55-71 | 60-92 | Low risk | High risk | Low risk | Low risk | Low risk |
| Liu, 202145  (1) | 2 (551/  <5y) | 70-73 | 52-56 | Low risk | Low risk | Low risk | Low risk | Low risk |
| Ding, 202146  (1) | Dementia | DSM-III, NINDS-AIREN, MINI | Stroke | Delirium (OR) | 7 (1,389/  0.3-10y) | 56-75 | 46-95 | Low risk | High risk | Low risk | Low risk | Low risk |
| Liu, 201847  (2) | Delirium; Dementia | DSM-IV-TR, DSM-IV, MINI, and validated assessment instrument (CAM positive=3) | Hip fracture | All-cause mortality (HR) | 7 (2,874/  <5y) | >65-85 | 18-27 | Low risk | Low risk | Unclear risk | Low risk | Low risk |
| Guo, 20217  (1) | Alzheimer's disease | Validated assessment instruments (DRS-II≤128, MDS-2 ≥1.5) | Parkinson's disease | Cognitive impairment (RR) | 2 (159/  2- 8y) | 63-69 | NR | High risk | Low risk | Unclear risk | Low risk | Low risk |

CAM- Confusion assessment method for delirium (Positive means the presence of acute onset or fluctuating course and inattention, and either disorganized thinking or altered level of consciousness), COVID-19— coronavirus disease 2019, DRS-II—Dementia Rating Scale-II, DSM— Diagnostic and statistical manual of mental disorders, HR— Hazard ratio, ICD— International classification of diseases, MDS-2—Resident Assessment Instrument—Minimum Data Set- 2.0, MINI— Mini international neuropsychiatric interview, NINDS-AIREN-National Institute of Neurological Disorders and the Association Internationale pour la Recherche et l’Enseignement en Neurosciences Criteria, OR—Odds ratio, ROBIS— Risk of a bias assessment tool for systematic reviews, RR— Risk ratio, SMR—standardized mortality ratio. \*Same association but non-overlapping or minimally overlapping primary studies in those systematic reviews with meta-analysis.

# **eTable 4** Level of evidence for the association of neurotic, stress-related and somatoform disorders and secondary outcomes of physical diseases

| Study | Mental disorder | Physical  disease | Outcome | k | Random-effects  measure, ES  (95% CI) | N  cases | p random  effects | I2% | PI (95% CI) | SSE/ESB | LS | eOR | CE | CES |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Neurotic, stress-related and somatoform disorders and cardiovascular diseases | | | | | | | | | | | | | |  |
| Roest, 20104 | Anxiety disorder | Myocardial infarction | Major cardiac events | 3 | OR, 1.71  [1.25, 2.34] | 149 | 7.0e-04 | 0.00 | [0.23,12.86] | No/No | Yes | 1.71 | IV | III |
| Li, 20201 | Anxiety disorder | Acute coronary syndrome | Major cardiac events | 4 | RR, 1.46  [1.19, 1.78] | 484 | 2.4e-04 | 16.34 | [0.79, 2.69] | No/No | No | 1.46 | IV | III |
| Emdin, 20162 | Anxiety disorder | Cardiovascular diseases | Major cardiac events | 3 | RR, 1.64  [0.86, 3.15] | 249 | >0.05 | 67.05 | [0, 2245.45] | No/No | No | 1.64 | NS | NS |
| Celano, 20153 | Anxiety disorder | Coronary artery disease | Major cardiac events | 7 | OR, 1.23  [0.76, 1.99] | 1,067 | >0.05 | 72.52 | [0.25, 6.06] | No/No | No | 1.23 | NS | NS |
| Taggart Wasson,20185 | Post-traumatic stress disorder | Myocardial infarction | Medication nonadherence | 2 | OR, 4.29  [0.99, 18.56] | 76 | >0.05 | 30.16 | NA | NA/NA | No | 4.29 | NS | NS |
| Neurotic, stress-related and somatoform disorders and other physical diseases | | | | | | | | | | | | | |  |
| Guo, 20217 | Anxiety disorder | Parkinson's disease | Cognitive impairment | 2 | RR, 2.59  [1.18, 5.68] | 132 | 1.8e-02 | 0.00 | NA | NA/NA | Yes | 2.59 | IV | IV |
| Wang, 20209 | Anxiety disorder | Breast cancer | Cancer recurrence | 3 | HR, 1.16  [1.01, 1.34] | 1,213 | 3.4e-02 | 0.00 | [1.02, 1.39] | No/No | Yes | 1.16 | IV | IV |
| Li, 20168 | Anxiety disorder | Neurological diseases with mild cognitive impairment | Alzheimer’s disease progression | 2 | RR, 1.06  [0.34, 3.33] | 113 | >0.05 | 91.22 | NA | NA/NA | No | 1.06 | NS | NS |

CE—Class of evidence, CES — Class of evidence after sensitivity analysis (removing the n>1000 cases criterion, C I— Confidence interval, eOR—Equivalent odds ratio, ESB — Excess significance bias, ES — Effect size, HR — Hazard ratio, k—Number of samples for each association, LS — Largest study with significant effect, N cases— Number of cases for each association, NA— Not assessable, NS—Not significant, OR—Odds ratio, RR— Risk ratio, PI— Prediction interval, SSE— Small study effect.

# **eTable 5** Level of evidence for the association between mood affective disorders and secondary outcomes of physical diseases

| Study | Mental disorder | Physical  Disorder | Outcome | k | Random-effects  measure, ES  (95% CI) | N  cases | p random  effects | I2% | PI (95% CI) | | SSE/  ESB | LS | | eOR | | CE | | CES | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Mood affective disorders and cardiovascular diseases (including stroke) | | | | | | | | | | | | | | | | | | | |
| Meijer, 201120 | Depressive disorders | Myocardial infarction | Major cardiac events | 15 | OR, 1.52  [1.36, 1.70] | 1,958 | 3.3e-13 | 24.35 | | [1.15, 1.92] | No/Yes | | Yes | | 1.52 | | II | | II |
| Blöchl, 201923 | Depressive disorders | Stroke | Poor functional outcome | 4 | OR, 2.15  [1.51, 3.07] | 603 | 2.3e-05 | 28.13 | | [0.64, 7.26] | No/Yes | | Yes | | 2.15 | | IV | | III |
| Rutledge, 201619 | Depressive disorders | Heart failure | Major cardiac events | 6 | RR, 2.12  [1.66, 2.72] | 173 | 2.3e-09 | 0.00 | | [1.50, 3.01] | No/Yes | | Yes | | 2.12 | | IV | | II |
| Shi, 201715 | Depressive disorders | Coronary artery disease | Atrial fibrillation recurrence | 2 | HR, 1.85  [1.51, 2.26] | 33 | 1.6e-09 | 0.00 | | NA | NA/NA | | Yes | | 1.85 | | IV | | II |
| Wu, 201927 | Depressive disorders | Stroke | Stroke recurrence | 5 | RR, 1.59  [1.29, 1.95] | 464 | 1.0e-05 | 0.00 | | [1.14, 2.22] | Yes/Yes | | Yes | | 1.59 | | IV | | III |
| Zhang, 201921 | Depressive disorders | Percutaneous coronary intervention | Major cardiac events | 7 | RR, 1.57  [1.27, 1.94] | 714 | 2.8e-05 | 44.15 | | [0.96, 2.58] | No/Yes | | Yes | | 1.57 | | IV | | III |
| Shi, 201715 | Depressive disorders | Coronary artery disease | Ventricular tachycardia/ fibrillation | 6 | HR, 1.49  [1.22, 1.82] | 453 | 7.8e-05 | 24.35 | | [1.13, 1.97] | No/Yes | | Yes | | 1.49 | | IV | | III |
| Wu, 201614 | Depressive disorders | Coronary artery disease | Myocardial infarction | 8 | HR, 1.33  [1.09, 1.63] | 3,781 | 5.3e-03 | 80.91 | | [0.75, 2.37] | Yes/Yes | | Yes | | 1.33 | | IV | | IV |
| Mood affective disorders and endocrine system diseases | | | | | | | | | | | | | | | | | |  | |
| Chow, 202229 | Depressive disorders | Diabetes mellitus | Dementia | 5 | HR, 2.11  [1.77, 2.52] | 95,097 | 8.5e-17 | 84.15 | [1.21, 3.67] | | No/No | Yes | | 2.11 | | II | | II | |
| Farooqi, 201930 | Depressive disorders | Diabetes mellitus | Coronary artery disease | 4 | HR, 1.35  [1.13, 1.6] | 862 | 6.9e-04 | 34.97 | [0.92, 1.96] | | Yes/No | Yes | | 1.35 | | IV | | III | |
| Farooqi, 201930 | Depressive disorders | Diabetes mellitus | Stroke | 2 | HR, 1.96  [0.85, 4.55] | 40,845 | >0.05 | 92.17 | NA | | NA/NA | Yes | | 1.96 | | NS | | NS | |
| Mood affective disorders and cancer | | | | | | | | | | | | | | | | | | | |
| Satin, 200935 | Depressive disorders | Cancer | Cancer progression | 3 | RR, 1.23  [0.85, 1.77] | 538 | >0.05 | 0.00 | [0.11, 13.2] | | No/No | No | | 1.23 | | NS | | NS | |
| Wang, 20209 | Depressive disorders | Breast cancer | Cancer recurrence | 5 | HR, 1.18  [0.96, 1.45] | 1,722 | >0.05 | 42.11 | [0.70, 1.99] | | No/No | Yes | | 1.18 | | NS | | NS | |
| Mood affective disorders and other physical diseases | | | | | | | | | | | | | | | | | | | |
| Ruiz-Grosso, 202038 | Depressive disorders | Tuberculosis | Negative outcomes in treatment | 2 | OR, 4.21  [2.33, 7.58] | 146 | 1.7e-06 | 0.00 | NA | | NA/NA | Yes | | 4.21 | | IV | | III | |
| Scott, 201840 | Depressive disorders | Human immunodeficiency virus infection | Pain | 2 | HR, 2.26  [1.47, 3.46] | 131 | 1.9e-04 | 39.93 | NA | | NA/NA | No | | 2.26 | | IV | | III | |
| Schoultz, 202039 | Depressive disorders | Inflammatory bowel disease | Symptom exacerbation | 2 | HR, 1.05  [1.01, 1.10] | 156 | 2.1e-02 | 0.00 | NA | | NA/NA | No | | 1.05 | | IV | | IV | |
| Murao, 201637 | Depressive disorders | Mild cognitive impairment | Dementia progression | 3 | RR, 1.48  [0.77, 2.84] | 58 | >0.05 | 83.95 | [0, 2925.66] | | No/No | No | | 1.48 | | NS | | NS | |
| Li, 20168 | Depressive disorders | Mild cognitive impairment | Alzheimer’s disease progression | 5 | RR, 1.31  [0.77, 2.22] | 1,121 | >0.05 | 83.74 | [0.20, 8.33] | | No/No | Yes | | 1.31 | | NS | | NS | |
| Guo, 20217 | Depressive disorders | Parkinson's disease | Cognitive impairment | 2 | RR, 0.43  [0.11, 1.65] | 205 | >0.05 | 84.2 | NA | | NA/NA | No | | 0.43 | | NS | | NS | |

CE—Class of evidence, CES — Class of evidence after sensitivity analysis (removing the n>1000 cases criterion, CI — Confidence interval, eOR—Equivalent odds ratio, ESB — Excess significance bias, ES — Effect size, HR — Hazard ratio, k—Number of samples for each association, LS — Largest study with significant effect, N cases— Number of cases for each association, NA— Not assessable, NS—Not significant, OR—Odds ratio, RR— Risk ratio, PI— Prediction interval, SSE— Small study effect.

# **eTable 6** Level of evidence for the association between mental and behavioural disorders due to psychoactive substance use, schizophrenia, schizotypal and delusional disorders, organic, including symptomatic, mental disorders and secondary outcomes of physical diseases

| Study | Mental disorder | Physical  Disorder | Outcome | k | Random-effects  measure, ES  (95% CI) | N  cases | p random  effects | I2% | PI (95% CI) | SSE/ESB | LS | eOR | CE | CES |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Mental and behavioural disorders due to psychoactive substance use and infectious diseases | | | | | | | | | | | | | |  |
| Llamosas-Falcón, 202041 | Alcohol use disorder | Hepatitis C virus infection | Decompensated liver cirrhosis | 2 | RR, 3.15  [2.87, 3.46] | 6,113 | 7.9e-131 | 0.00 | NA | NA/NA | Yes | 3.15 | II | II |
| Llamosas-Falcón, 202041 | Alcohol use disorder | Hepatitis C virus infection | Negative course liver disease | 3 | RR, 3.83  [1.24, 11.85] | 6,218 | 2.0e-02 | 87.37 | [0.00,3621121.27] | No/Yes | Yes | 3.83 | IV | IV |
| Schizophrenia, schizotypal and delusional disorders and cardiovascular diseases and cancer | | | | | | | | | | | | | |  |
| No secondary outcomes | | | | | | | | | | | | | | |
| Organic, including symptomatic, mental disorders and infectious, cardiovascular diseases, musculoskeletal system and connective tissue, and neurological disorders | | | | | | | | | | | | | | |
| Ding, 202146 | Dementia | Stroke | Delirium | 7 | OR, 5.90  [3.95, 8.83] | 284 | 5.7e-18 | 0.00 | [3.48,10.01] | No/No | Yes | 5.90 | IV | I |
| Guo, 20217 | Alzheimer's disease | Parkinson's disease | Cognitive impairment | 2 | RR, 0.09  [0.00, 6.26] | 22 | >0.05 | 94.36 | NA | NA/NA | No | 0.09 | NS | NS |

CE—Class of evidence, CES — Class of evidence after sensitivity analysis (removing the n>1000 cases criterion, CI — Confidence interval, eOR—Equivalent odds ratio, ESB — Excess significance bias, ES — Effect size, HR — Hazard ratio, k—Number of samples for each association, LS — Largest study with significant effect, N cases— Number of cases for each association, NA— Not assessable, NS—Not significant, OR—Odds ratio, RR— Risk ratio, PI— Prediction interval, SMR—standardized mortality ratio, SSE— Small study effect.

# **eTable 7** Subgroup analyses for associations of mental disorders and outcomes of physical diseases supported by convincing and highly suggestive (I and II) class of evidence

| Subgroup | k | Random-effects  measure, ES  (95% CI) | N cases | p random  effects | I2% | PI (95% CI) | SSE/ESB | LS | eOR | CE/  CES |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Mood affective disorders and cardiovascular diseases (including stroke)** | | | | | | | | | | |
| **Depressive disorders / Heart failure/ All-cause mortality**18 | | | | | | | | | | |
| *a) Diagnostic method* |  |  |  |  |  |  |  |  |  |  |
| Standard diagnostic criteria |  | No data available or only one study | | | | | | | | |
| Research criteria |  | No data available or only one study | | | | | | | | |
| Validated assessment instruments with cut-offs that map onto discrete categories | 3 | HR, 1.43 [1.22, 1.67] | 896 | 1.2e-05 | 0.00 | [0.51, 4.00] | No/No | Yes | 1.43 | I/IV |
| *b) Timing of mental diagnosis* |  |  |  |  |  |  |  |  |  |  |
| Diagnosis of mental disorder before the diagnosis of physical disease |  | No data available or only one study | | | | | | | | |
| Diagnosis of mental disorder after the diagnosis of physical disease | 3 | HR, 1.43 [1.22, 1.67] | 896 | 1.2e-05 | 0.00 | [0.51, 4.00] | No/No | Yes | 1.43 | I/IV |
| *c) Follow-up duration* |  |  |  |  |  |  |  |  |  |  |
| >5 years |  | No data available or only one study | | | | | | | | |
| ≤5 years | 4 | HR, 1.44 [1.26, 1.65] | 1,377 | 1.4e-07 | 0.00 | [1.07, 1.94] | No/No | Yes | 1.44 | I/I |
| *d) Type of estimates* |  |  |  |  |  |  |  |  |  |  |
| Adjusted estimates | 4 | HR, 1.44 [1.26, 1.65] | 1,377 | 1.4e-07 | 0.00 | [1.07, 1.94] | No/No | Yes | 1.44 | I/I |
| Unadjusted estimates |  | No data available or only one study | | | | | | | | |
| *e) Age of participants* |  |  |  |  |  |  |  |  |  |  |
| <50 years old |  | No data available or only one study | | | | | | | | |
| ≥50 years old | 4 | HR, 1.44 [1.26, 1.65] | 1,377 | 1.4e-07 | 0.00 | [1.07, 1.94] | No/No | Yes | 1.44 | I/I |
| *f) Exposure to psychiatric medications* |  |  |  |  |  |  |  |  |  |  |
| Yes | 2 | HR, 1.43 [1.19, 1.71] | 794 | 1.1e-04 | 0.00 | NA | NA/NA | Yes | 1.43 | I/IV |
| No |  | No data available or only one study | | | | | | | | |
| *g) Sex* |  |  |  |  |  |  |  |  |  |  |
| Majority of male | 3 | HR, 1.43 [1.22, 1.67] | 896 | 1.2e-05 | 0.00 | [0.51, 4.00] | No/No | Yes | 1.43 | I/IV |
| Majority of female |  | No data available or only one study | | | | | | | | |
| **Depressive disorders /Myocardial infraction/Major cardiac events**20 | | | | | | | | | | |
| *a) Diagnostic method* |  |  |  |  |  |  |  |  |  |  |
| Standard diagnostic criteria |  | No data available or only one study | | | | | | | | |
| Research criteria | 4 | OR, 1.69 [0.38, 7.44] | 142 | >0.05 | 69.66 | [0.00, 980.31] | No/No | No | 1.69 | II/NS |
| Validated assessment instruments with cut-offs that map onto discrete categories | 11 | OR, 1.51 [1.35, 1.7] | 1,816 | 3.0e-12 | 0.00 | [1.32, 1.73] | No/Yes | Yes | 1.51 | II/II |
| *b) Timing of mental diagnosis* |  |  |  |  |  |  |  |  |  |  |
| Diagnosis of mental disorder before the diagnosis of physical disease |  | No data available or only one study | | | | | | | | |
| Diagnosis of mental disorder after the diagnosis of physical disease | 15 | OR, 1.52 [1.36, 1.7] | 1,958 | 3.3e-13 | 24.35 | [1.34, 1.72] | No/Yes | Yes | 1.52 | II/II |
| *c) Follow-up duration* |  |  |  |  |  |  |  |  |  |  |
| >5 years |  | No data available or only one study | | | | | | | | |
| ≤5 years | 15 | OR, 1.52 [1.36, 1.7] | 1,958 | 3.3e-13 | 24.35 | [1.34, 1.72] | No/Yes | Yes | 1.52 | II/II |
| *d) Type of estimates* |  |  |  |  |  |  |  |  |  |  |
| Adjusted estimates |  | No data available or only one study | | | | | | | | |
| Unadjusted estimates | 15 | OR, 1.52 [1.36, 1.7] | 1,958 | 3.3e-13 | 24.35 | [1.34, 1.72] | No/Yes | Yes | 1.52 | II/II |
| *e) Age of participants* |  |  |  |  |  |  |  |  |  |  |
| <50 years old |  | No data available or only one study | | | | | | | | |
| ≥50 years old | 13 | OR, 1.53 [1.33, 1.76] | 1,337 | 1.8e-09 | 29.6 | [1.31, 1.8] | No/No | Yes | 1.53 | II/I |
| *f) Exposure to psychiatric medications* |  |  |  |  |  |  |  |  |  |  |
| Yes |  | No data available or only one study | | | | | | | | |
| No |  | No data available or only one study | | | | | | | | |
| *g) Sex* |  |  |  |  |  |  |  |  |  |  |
| Majority of male | 13 | OR, 1.53 [1.33, 1.76] | 1,337 | 1.8e-09 | 29.6 | [1.31, 1.8] | No/No | Yes | 1.53 | II/I |
| Majority of female |  | No data available or only one study | | | | | | | | |
| **Mood affective disorders and endocrine system diseases** | | | | | | | | | | |
| **Depressive disorders/ Kidney failure/All-cause mortality**33 | | | | | | | | | | |
| *a) Diagnostic method* |  |  |  |  |  |  |  |  |  |  |
| Standard diagnostic criteria |  | No data available or only one study | | | | | | | | |
| Research criteria |  | No data available or only one study | | | | | | | | |
| Validated assessment instruments with cut-offs that map onto discrete categories | 5 | HR, 1.41 [1.30, 1.53] | 221 | 1.4e-16 | 29.65 | [1.24, 1.62] | No/Yes | Yes | 1.41 | II/IV |
| *b) Timing of mental diagnosis* |  |  |  |  |  |  |  |  |  |  |
| Diagnosis of mental disorder before the diagnosis of physical disease | 2 | HR, 1.41 [1.31, 1.52] | 1,613 | 1.8e-18 | 0.00 | NA | NA/NA | Yes | 1.41 | II/II |
| Diagnosis of mental disorder after the diagnosis of physical disease | 4 | HR, 1.71 [1.16, 2.5] | 221 | 6.4e-03 | 46.86 | [0.42, 7.00] | Yes/Yes | Yes | 1.71 | II/IV |
| *c) Follow-up duration* |  |  |  |  |  |  |  |  |  |  |
| >5 years | 2 | HR, 1.92 [1.2, 3.06] | 83 | 6.3e-03 | 0.00 | NA | NA/NA | Yes | 1.92 | II/IV |
| ≤5 years | 4 | HR, 1.40 [1.30, 1.50] | 1,751 | 1.9e-21 | 16.31 | [1.20, 1.62] | No/Yes | Yes | 1.40 | II/IV |
| *d) Type of estimates* |  |  |  |  |  |  |  |  |  |  |
| Adjusted estimates | 6 | HR, 1.41 [1.31, 1.51] | 1,834 | 1.0e-22 | 12.85 | [1.28, 1.55] | Yes/Yes | Yes | 1.41 | II/II |
| Unadjusted estimates | No data available or only one study | | | | | | | | | |
| *e) Age of participants* |  |  |  |  |  |  |  |  |  |  |
| <50 years old |  | No data available or only one study | | | | | | | | |
| ≥50 years old | 3 | HR, 1.91 [1.03, 3.55] | 165 | 4.1e-02 | 61.19 | [0, 1623.27] | Yes/Yes | Yes | 1.91 | II/IV |
| *f) Exposure to psychiatric medications* |  |  |  |  |  |  |  |  |  |  |
| Yes |  | No data available or only one study | | | | | | | | |
| No |  | No data available or only one study | | | | | | | | |
| *g) Sex* |  |  |  |  |  |  |  |  |  |  |
| Majority of male | 3 | HR, 1.92 [1.08, 3.42] | 1,664 | 2.7e-02 | 56.91 | [0.00, 959.04] | No/Yes | Yes | 1.92 | II/IV |
| Majority of female |  | No data available or only one study | | | | | | | | |
| **Depressive disorders/Diabetes mellitus/All-cause mortality32** | | | | | | | | | | |
| *a) Diagnostic method* |  |  |  |  |  |  |  |  |  |  |
| Standard diagnostic criteria | 6 | HR, 1.54 [1.09, 2.18] | 3,725 | 1.4e-02 | 85.18 | [0.48, 4.99] | No/Yes | No | 1.54 | II/IV |
| Research criteria |  | No data available or only one study | | | | | | | | |
| Validated assessment instruments with cut-offs that map onto discrete categories | 6 | HR, 2.57 [1.82, 3.64] | 1,872 | 9.9e-08 | 88.08 | [0.81, 8.19] | No/No | Yes | 2.57 | II/II |
| *b) Timing of mental diagnosis* |  |  |  |  |  |  |  |  |  |  |
| Diagnosis of mental disorder before the diagnosis of physical disease |  | No data available or only one study | | | | | | | | |
| Diagnosis of mental disorder after the diagnosis of physical disease | 2 | HR, 2.57 [0.73, 9.03] | 783 | >0.05 | 96.65 | NA | NA/NA | Yes | 2.57 | II/NS |
| *c) Follow-up duration* |  |  |  |  |  |  |  |  |  |  |
| >5 years | 5 | HR, 2.81 [1.82, 4.34] | 1,828 | 3.2e-06 | 92.39 | [0.53, 14.85] | No/No | Yes | 2.81 | II/III |
| ≤5 years | 2 | HR, 2.79 [1.71, 4.54] | 280 | 3.8e-05 | 0.00 | NA | NA/NA | Yes | 2.79 | II/IV |
| *d) Type of estimates* |  |  |  |  |  |  |  |  |  |  |
| Adjusted estimates | 7 | HR, 2.84 [2.00, 4.03] | 2,108 | 4.7e-09 | 88.81 | [0.88, 9.15] | No/No | Yes | 2.84 | II/II |
| Unadjusted estimates |  | No data available or only one study | | | | | | | | |
| *e) Age of participants* |  |  |  |  |  |  |  |  |  |  |
| <50 years old |  | No data available or only one study | | | | | | | | |
| ≥50 years old | 4 | HR, 2.91 [2.27, 3.73] | 1,312 | 2.7e-17 | 64.63 | [1.07, 7.96] | No/No | Yes | 2.91 | II/II |
| *f) Exposure to psychiatric medications* |  |  |  |  |  |  |  |  |  |  |
| Yes |  | No data available or only one study | | | | | | | | |
| No |  | No data available or only one study | | | | | | | | |
| *g) Sex* |  |  |  |  |  |  |  |  |  |  |
| Majority of male | 4 | HR, 2.46 [1.46, 4.13] | 1,305 | 7.0e-04 | 89.37 | [0.24, 25.3] | No/Yes | Yes | 2.46 | I/III |
| Majority of female | 3 | HR, 3.49 [2.51, 4.86] | 803 | 1.4e-13 | 57.37 | [0.1, 124.03] | No/No | Yes | 3.49 | I/IV |
| **Depressive disorders/Diabetes mellitus /Dementia**29 | | | | | | | | | | |
| *a) Diagnostic method* |  |  |  |  |  |  |  |  |  |  |
| Standard diagnostic criteria | 3 | HR, 1.99 [1.62, 2.45] | 94,793 | 3.8e-11 | 90.16 | [0.19, 21.4] | No/No | Yes | 1.99 | II/II |
| Research criteria |  | No data available or only one study | | | | | | | | |
| Validated assessment instruments with cut-offs that map onto discrete categories | 2 | HR, 2.63 [1.90, 3.64] | 304 | 6.0e-09 | 0.00 | NA | NA/NA | Yes | 2.63 | II/IV |
| *b) Timing of mental diagnosis* |  |  |  |  |  |  |  |  |  |  |
| Diagnosis of mental disorder before the diagnosis of physical disease | 3 | HR, 1.99 [1.62, 2.45] | 94,793 | 3.8e-11 | 90.16 | [0.19, 21.4] | No/No | Yes | 1.99 | II/II |
| Diagnosis of mental disorder after the diagnosis of physical disease | 2 | HR, 2.63 [1.90, 3.64] | 304 | 6.0e-09 | 0.00 | NA | NA/NA | Yes | 2.63 | II/IV |
| *c) Follow-up duration* |  |  |  |  |  |  |  |  |  |  |
| >5 years | 5 | HR, 2.11 [1.77, 2.52] | 95,097 | 8.5e-17 | 84.15 | [1.21, 3.67] | No/No | Yes | 2.11 | II/II |
| ≤5 years |  | No data available or only one study | | | | | | | | |
| *d) Type of estimates* |  |  |  |  |  |  |  |  |  |  |
| Adjusted estimates | 5 | HR, 2.11 [1.77, 2.52] | 95,097 | 8.5e-17 | 84.15 | [1.21, 3.67] | No/No | Yes | 2.11 | II/II |
| Unadjusted estimates |  | No data available or only one study | | | | | | | | |
| *e) Age of participants* |  |  |  |  |  |  |  |  |  |  |
| <50 years old |  | No data available or only one study | | | | | | | | |
| ≥50 years old | 5 | HR, 2.11 [1.77, 2.52] | 95,097 | 8.5e-17 | 84.15 | [1.21, 3.67] | No/No | Yes | 2.11 | II/II |
| *f) Exposure to psychiatric medications* |  |  |  |  |  |  |  |  |  |  |
| Yes |  | No data available or only one study | | | | | | | | |
| No |  | No data available or only one study | | | | | | | | |
| *g) Sex* |  |  |  |  |  |  |  |  |  |  |
| Majority of male | 5 | HR, 2.11 [1.77, 2.52] | 95,097 | 8.5e-17 | 84.15 | [1.21, 3.67] | No/No | Yes | 2.11 | II/II |
| Majority of female |  | No data available or only one study | | | | | | | | |
| **Mental and behavioural disorders due to psychoactive substance use and infectious diseases** | | | | | | | | | | |
| **Alcohol use disorder/ Hepatitis C virus infection/ Decompensated liver cirrhosis**41 | | | | | | | | | | |
| *a) Diagnostic method* |  |  |  |  |  |  |  |  |  |  |
| Standard diagnostic criteria | 2 | OR, 3.15 [2.87, 3.46] | 6,113 | 7.9e-131 | 0.00 | NA | NA/NA | Yes | 3.15 | II/II |
| Research criteria |  | No data available or only one study | | | | | | | | |
| Validated assessment instruments with cut-offs that map onto discrete categories |  | No data available or only one study | | | | | | | | |
| *b) Timing of mental diagnosis* |  |  |  |  |  |  |  |  |  |  |
| Diagnosis of mental disorder before the diagnosis of physical disease |  | No data available or only one study | | | | | | | | |
| Diagnosis of mental disorder after the diagnosis of physical disease | 2 | OR, 3.15 [2.87, 3.46] | 6,113 | 7.9e-131 | 0.00 | NA | NA/NA | Yes | 3.15 | II/II |
| *c) Follow-up duration* |  |  |  |  |  |  |  |  |  |  |
| >5 years |  | No data available or only one study | | | | | | | | |
| ≤5 years |  | No data available or only one study | | | | | | | | |
| *d) Type of estimates* |  |  |  |  |  |  |  |  |  |  |
| Adjusted estimates | 2 | OR, 3.15 [2.87, 3.46] | 6,113 | 7.9e-131 | 0.00 | NA | NA/NA | Yes | 3.15 | II/II |
| Unadjusted estimates |  | No data available or only one study | | | | | | | | |
| *e) Age of participants* |  |  |  |  |  |  |  |  |  |  |
| <50 years old |  | No data available or only one study | | | | | | | | |
| ≥50 years old |  | No data available or only one study | | | | | | | | |
| *f) Exposure to psychiatric medications* |  |  |  |  |  |  |  |  |  |  |
| Yes |  | No data available or only one study | | | | | | | | |
| No |  | No data available or only one study | | | | | | | | |
| *g) Sex* |  |  |  |  |  |  |  |  |  |  |
| Majority of male |  | No data available or only one study | | | | | | | | |
| Majority of female |  | No data available or only one study | | | | | | | | |
| **Schizophrenia, schizotypal and delusional disorders and cardiovascular diseases and cancer** | | | | | | | | | | |
| **Schizophrenia/ Cardiovascular diseases/ Cardiovascular mortality**10 | | | | | | | | | | |
| *a) Diagnostic method* |  |  |  |  |  |  |  |  |  |  |
| Standard diagnostic criteria | 6 | RR, 1.54 [1.35, 1.76] | 8,356 | 1.1e-10 | 39.62 | [1.15, 2.07] | No/No | No | 1.54 | I/I |
| Research criteria |  | No data available or only one study | | | | | | | | |
| Validated assessment instruments with cut-offs that map onto discrete categories |  | No data available or only one study | | | | | | | | |
| *b) Timing of mental diagnosis* |  |  |  |  |  |  |  |  |  |  |
| Diagnosis of mental disorder before the diagnosis of physical disease | 7 | RR, 1.54 [1.36, 1.75] | 9,097 | 2.2e-11 | 27.82 | [1.19, 2.00] | No/No | No | 1.54 | I/I |
| Diagnosis of mental disorder after the diagnosis of physical disease |  | No data available or only one study | | | | | | | | |
| *c) Follow-up duration* |  |  |  |  |  |  |  |  |  |  |
| >5 years | 3 | RR, 1.91 [1.22, 2.98] | 7,338 | 4.4e-03 | 55.45 | [0.02, 210.9] | No/No | Yes | 1.91 | I/IV |
| ≤5 years | 4 | RR, 1.46 [1.29, 1.66] | 1,759 | 1.3e-09 | 0.00 | [1.05, 2.04] | No/No | No | 1.46 | I/I |
| *d) Type of estimates* |  |  |  |  |  |  |  |  |  |  |
| Adjusted estimates | 5 | RR, 1.78 [1.22, 2.61] | 2,299 | 2.8e-03 | 49.05 | [0.59, 5.40] | No/No | No | 1.78 | I/IV |
| Unadjusted estimates |  | No data available or only one study | | | | | | | | |
| *e) Age of participants* |  |  |  |  |  |  |  |  |  |  |
| <50 years old | 2 | RR, 1.56 [1.32, 1.84] | 646 | 1.5e-07 | 0.00 | NA | NA/NA | Yes | 1.56 | I/IV |
| ≥50 years old | 3 | RR, 1.43 [1.27, 1.61] | 7,391 | 5.0e-09 | 0.00 | [0.66, 3.11] | No/No | No | 1.43 | I/III |
| *f) Exposure to psychiatric medications* |  |  |  |  |  |  |  |  |  |  |
| Yes | 4 | RR, 1.92 [1.31, 2.81] | 1,039 | 8.8e-04 | 41.35 | [0.47, 7.75] | No/No | No | 1.92 | I/III |
| No |  | No data available or only one study | | | | | | | | |
| *g) Sex* |  |  |  |  |  |  |  |  |  |  |
| Majority of male | 4 | RR, 1.53 [1.34, 1.74] | 8,156 | 2.2e-10 | 60.39 | [0.98, 2.38] | No/No | Yes | 1.53 | I/I |
| Majority of female | 2 | RR, 1.89 [0.97, 3.70] | 200 | >0.05 | 0.00 | NA | NA/NA | No | 1.89 | I/NS |
| **Schizophrenia/Cancer/Cancer mortality**43 | | | | | | | | | | |
| *a) Diagnostic method* |  |  |  |  |  |  |  |  |  |  |
| Standard diagnostic criteria | 3 | SMR, 1.74 [1.41, 2.15] | 6,145 | 2.9e-07 | 66.53 | [0.17, 17.56] | No/No | Yes | 1.74 | II/II |
| Research criteria |  | No data available or only one study | | | | | | | | |
| Validated assessment instruments with cut-offs that map onto discrete categories |  | No data available or only one study | | | | | | | | |
| *b) Timing of mental diagnosis* |  |  |  |  |  |  |  |  |  |  |
| Diagnosis of mental disorder before the diagnosis of physical disease | 3 | SMR, 1.74 [1.41, 2.15] | 6,145 | 2.9e-07 | 66.53 | [0.17, 17.56] | No/No | Yes | 1.74 | II/II |
| Diagnosis of mental disorder after the diagnosis of physical disease |  | No data available or only one study | | | | | | | | |
| *c) Follow-up duration* |  |  |  |  |  |  |  |  |  |  |
| >5 years | 3 | SMR, 1.74 [1.41, 2.15] | 6,145 | 2.9e-07 | 66.53 | [0.17, 17.56] | No/No | Yes | 1.74 | II/II |
| ≤5 years |  | No data available or only one study | | | | | | | | |
| *d) Type of estimates* |  |  |  |  |  |  |  |  |  |  |
| Adjusted estimates |  | No data available or only one study | | | | | | | | |
| Unadjusted estimates |  | No data available or only one study | | | | | | | | |
| *e) Age of participants* |  |  |  |  |  |  |  |  |  |  |
| <50 years old |  | No data available or only one study | | | | | | | | |
| ≥50 years old |  | No data available or only one study | | | | | | | | |
| *f) Exposure to psychiatric medications* |  |  |  |  |  |  |  |  |  |  |
| Yes | 2 | SMR, 1.52 [1.25, 1.85] | 108 | 3.5e-05 | 0.00 | NA | NA/NA | Yes | 1.52 | II/IV |
| No |  | No data available or only one study | | | | | | | | |
| *g) Sex* |  |  |  |  |  |  |  |  |  |  |
| Majority of male | 3 | SMR, 1.80 [1.47, 2.22] | 6141 | 2.8e-08 | 60.13 | [0.19, 16.78] | No/No | Yes | 1.80 | II/II |
| Majority of female |  | No data available or only one study | | | | | | | | |

CE—Class of evidence, CES — Class of evidence after subgroup analysis, CI — Confidence interval, eOR—Equivalent odds ratio, ESB — Excess significance bias, ES — Effect size, HR — Hazard ratio, k—Number of samples for each association, LS — Largest study with significant effect, N cases— Number of cases for each association, NA— Not assessable, NS—Not significant, OR—Odds ratio, RR— Risk ratio, PI— Prediction interval, SMR—standardized mortality ratio, SSE— Small study effect.

# **eMethods 1.** Search strategy

*PubMed:* (Somatic disease OR Cardiovascular Diseases OR coronary disease OR Coronary Heart Disease OR Heart Failure OR Myocardial Failure OR myocardial infarction OR Rheumatic Heart Disease OR stroke OR CAD OR abnormal heart rhythms OR arrhythmia OR sudden cardiac death OR cerebrovascular disease OR cerebrovascular diseases OR cerebro vascular disease OR cerebro vascular diseases OR cerebral vascular disease OR cerebral vascular diseases OR hypertension OR hypertensive OR myocarditis OR angina OR transient ischemic attack OR transient ischemic attacks OR transient ischaemic attack OR peripheral artery disease OR peripheral artery diseases OR hypertrophic cardiomyopathy OR chronic respiratory diseases OR pulmonary hypertension OR pneumonia OR asthma OR asthmatic OR chronic obstructive pulmonary disease OR chronic obstructive pulmonary diseases OR COPD OR obstructive sleep apnea syndrome OR neurocognitive disorder OR neurocognitive disorders OR Lewy Bodies OR Huntington Neurodegenerative Diseases OR multiple sclerosis OR Alzheimer Disease OR autoimmune encephalopathy OR paraneoplastic encephalitis OR peripheral neuropathy OR dementia OR Parkinson disease OR Amyotrophic Lateral Sclerosis OR ALS OR epilepsy OR epileptic OR seizure OR seizures OR Obesity OR obese OR overweight OR over weight OR dyslipidemia OR Cushing OR hidradenitis suppurativa OR metabolic syndrome OR chronic renal failure OR myeloproliferative disorder OR myeloproliferative disorders OR diabetes mellitus OR diabetes OR diabetic OR thyroid disorder OR thyroid disorders OR sarcoidosis OR liver disease OR liver diseases OR functional gastrointestinal disorder OR functional gastrointestinal disorders OR ulcerative colitis OR Crohn disease OR gastroesophageal reflux disease OR gastroesophageal reflux diseases OR GERD OR chronic pancreatitis OR chronic kidney disease OR kidney disease OR kidney diseases OR acute kidney injury OR acute kidney injuries OR dialysis OR benign prostatic hyperplasia OR kidney stone OR kidney stones OR Neoplasm OR Neoplasms OR cancer OR cancers OR tumor OR tumors OR liver disease cirrhosis OR Irritable bowel syndrome OR vitiligo OR acne OR melanoma OR systemic lupus OR atopic eczema OR celiac disease OR ankylosing spondylitis OR Bechterew OR psoriasis OR rheumatoid arthritis OR RA OR inflammatory bowel disease OR Graves disease OR osteoporosis OR fracture OR fractures OR lymphoma OR anemia OR anemias OR anaemia OR anaemias OR ΗΙV/AIDS OR infectious OR infection OR virus infection OR musculoskeletal disorders OR low back pain OR fibromyalgia OR osteoarthritis OR arthritis OR chronic pain) AND ("Mental Disorders"[Mesh] OR mental disorder OR mental disorders OR psychiatric disorder OR psychiatric disorders OR psychopathological disorder OR psychopathological disorders OR psychopathological condition OR psychopathological conditions OR ADHD OR attention-deficit hyperactivity disorder OR attention deficit OR hyperkinetic disorder OR hyperkinetic syndrome OR Autism OR autistic OR Asperger OR neurodevelopmental disorder OR neurodevelopmental disorders OR Intellectual Disability OR Intellectual Disabilities OR mental retardation OR learning disability OR Schizophrenia OR schizophrenic OR psychotic disorder OR psychotic disorders OR psychosis OR Schizotypal OR Delusional Disorder OR Brief Psychotic Disorder OR Schizophreniform Disorder OR Schizoaffective disorder OR Bipolar disorder OR bipolar disorders OR Depression OR depressive OR mood OR Anxiety OR anxious OR panic disorder OR agoraphobia OR Obsessive-compulsive disorder OR Obsessive compulsive disorder OR OCD OR PTSD OR Trauma-related disorder OR Trauma-related disorders OR Stress-related disorder OR Stress-related disorders OR Substance-related disorder OR Substance-related disorders OR addictive disorder OR addiction disorders OR drug abuse OR eating disorder OR eating disorders OR anorexia OR bulimia OR binge-eating OR binge eating OR sleep disorder OR sleep disorders OR sleep disturbance OR sleep disturbances OR insomnia OR Body Dysmorphic Disorder OR Trichotillomania OR Hair-Pulling Disorder OR Excoriation Disorder OR Skin-Picking Disorder OR dissociative disorder OR dissociative disorders Dissociative Identity Disorder OR Restless Legs Syndrome OR Gender Dysphoria OR Personality disorder OR Personality disorders OR Antisocial Personality Disorder OR Paranoid Personality Disorder OR Schizoid Personality Disorder OR Schizotypal Personality Disorder OR Borderline Personality Disorder OR Histrionic Personality Disorder OR Narcissistic Personality Disorder OR Avoidant Personality Disorder OR Dependent Personality Disorder OR Obsessive-Compulsive Personality Disorder) AND ("Mortality"[Mesh] OR "mortality\*" [tiab] OR "mortality rate\*"[tiab] OR "death"[MeSH Terms] OR "death\*" [tiab] OR "death rate\*"[tiab] OR "crude death rate\*"[tiab] OR "age-specific death rate\*" [tiab] OR "survival"[MeSH Terms] OR "survival\*" [tiab] OR "prognosis"[MeSH Terms] OR "prognosis\*"[tiab] OR disability [tiab] OR disease-specific symptom severity [tiab] OR "disability-adjusted life years") AND ("Systematic Review"[Publication Type:NoExp] OR "Systematic Reviews as Topic"[mesh:noexp] OR "meta-analysis as topic"[MESH:NOEXP] OR "Meta-Analysis"[Publication Type:NoExp] OR "meta analyses"[ot] OR "meta analyses"[Title/Abstract] OR "meta analysis"[Title/Abstract] OR "meta analysis"[Title/Abstract] OR "meta analytic"[ot] OR "meta analytic"[Title/Abstract] OR "meta analytical"[ot] OR "meta analytical"[Title/Abstract] OR "meta analytics"[Title/Abstract] OR "meta analyze"[ot] OR "meta analyze"[Title/Abstract] OR ("meta"[ot] AND "analyzed"[ot]) OR "meta analyzed"[Title/Abstract] OR "meta regression"[Title/Abstract] OR "metaanalyses"[ot] OR "metaanalyses"[Title/Abstract] OR "metaanalysis"[ot] OR "metaanalysis"[Title/Abstract] OR "metaanalytic"[Title/Abstract] OR "metaanalyze"[Title/Abstract] OR "metaanalyzed"[Title/Abstract])

*EMBASE*: #1 somatic AND ('disease'/exp OR disease) OR 'cardiovascular disease' OR 'coronary artery disease' OR 'ischemic heart disease' OR 'heart failure' OR 'heart infarction' OR 'rheumatic heart disease' OR 'cerebrovascular accident' OR 'heart arrhythmia' OR 'sudden cardiac death' OR 'cerebrovascular disease' OR 'hypertension' OR 'myocarditis' OR 'angina pectoris' OR 'transient ischemic attack' OR 'peripheral occlusive artery disease' OR 'hypertrophic cardiomyopathy' OR 'chronic respiratory tract disease' OR 'pulmonary hypertension' OR 'pneumonia' OR 'asthma' OR 'chronic obstructive lung disease' OR 'sleep disordered breathing' OR 'disorders of higher cerebral function' OR 'lewy body' OR 'parkinson disease' OR 'huntington chorea' OR 'multiple sclerosis' OR 'alzheimer disease' OR 'autoimmune encephalitis' OR 'paraneoplastic encephalitis' OR 'peripheral neuropathy' OR 'dementia' OR 'amyotrophic lateral sclerosis' OR 'epilepsy' OR 'seizure' OR 'obesity' OR 'dyslipidemia' OR 'cushing syndrome' OR 'suppurative hidradenitis' OR 'metabolic disorder' OR 'chronic kidney failure' OR 'myeloproliferative disorder' OR 'diabetes mellitus' OR 'non insulin dependent diabetes mellitus' OR 'insulin dependent diabetes mellitus' OR 'thyroid disease' OR 'sarcoidosis' OR 'liver disease' OR 'digestive system function disorder' OR 'ulcerative colitis' OR 'crohn disease' OR 'pancreas disease' OR 'dialysis' OR 'prostate hypertrophy' OR 'nephrolithiasis' OR 'neoplasm' OR 'malignant neoplasm' OR 'liver cirrhosis' OR 'irritable colon' OR 'vitiligo' OR 'acne' OR 'melanoma' OR 'systemic lupus erythematosus' OR 'atopic dermatitis' OR 'celiac disease' OR 'ankylosing spondylitis' OR 'inflammatory bowel disease' OR 'graves disease' OR 'osteoporosis' OR 'fracture' OR 'lymphoma' OR 'anemia' OR 'human immunodeficiency virus' OR 'infection' OR 'virus infection' OR 'musculoskeletal disorders' OR 'chronic pain' OR 'low back pain' OR 'fibromyalgia' OR 'osteoarthritis' OR 'arthritis'

#2 'mental disease' OR 'attention deficit hyperactivity disorder' OR 'hyperkinetic disorder' OR 'autism' OR 'asperger syndrome' OR 'schizophrenia' OR 'psychosis' OR 'bipolar disorder' OR 'depression' OR 'dysthymia' OR 'mood disorder' OR 'anxiety disorder' OR 'anxiety' OR 'obsessive compulsive disorder' OR 'posttraumatic stress disorder' OR 'stress related disorder' OR 'drug dependence' OR 'addiction' OR 'eating disorder' OR 'anorexia' OR 'bulimia' OR 'binge eating disorder' OR 'sleep disorder' OR 'insomnia' OR 'personality disorder' OR 'borderline state' OR 'body dysmorphic disorder' OR 'antisocial personality disorder' OR 'paranoid personality disorder' OR 'schizoidism' OR 'histrionic personality disorder' OR 'narcissism' OR 'avoidant personality disorder' OR 'compulsive personality disorder'

#3 'mortality ' OR 'mortality rate' OR 'mortality risk' OR 'survival' ' OR 'incidence' OR 'survival rate' OR 'death' OR 'prognosis' OR 'function' OR 'disability' OR 'symptom severity' OR 'quality of life' OR 'disability-adjusted life year'

#4 'systematic review' OR 'systematic review (topic)' OR 'meta analysis' OR 'meta analysis (topic)'

#1 AND #2 AND #3 AND #4 AND ([systematic review]/lim OR [meta analysis]/lim)

*APA PsycInfo:* ( somatic disease or cardiovascular diseases or coronary disease or coronary heart disease or heart failure or myocardial failure or myocardial infarction or rheumatic heart disease or stroke or cad or abnormal heart rhythms or arrhythmia or sudden cardiac death or cerebrovascular disease or cerebrovascular diseases or cerebro vascular disease or cerebro vascular diseases or cerebral vascular disease or cerebral vascular diseases or hypertension or hypertensive or myocarditis or angina or transient ischemic attack or transient ischemic attacks or transient ischaemic attack or peripheral artery disease or peripheral artery diseases or hypertrophic cardiomyopathy or chronic respiratory diseases or pulmonary hypertension or pneumonia or asthma or asthmatic or chronic obstructive pulmonary disease or chronic obstructive pulmonary diseases or copd or obstructive sleep apnea syndrome or neurocognitive disorder or neurocognitive disorders or lewy bodies or huntington neurodegenerative diseases or multiple sclerosis or alzheimer disease or autoimmune encephalopathy or paraneoplastic encephalitis or peripheral neuropathy or dementia or parkinson disease or amyotrophic lateral sclerosis or als or epilepsy or epileptic or seizure or seizures or obesity or obese or overweight or over weight or dyslipidemia or cushing or hidradenitis suppurativa or metabolic syndrome or chronic renal failure or myeloproliferative disorder or myeloproliferative disorders or diabetes mellitus or diabetes or diabetic or thyroid disorder or thyroid disorders or sarcoidosis or liver disease or liver diseases or functional gastrointestinal disorder or functional gastrointestinal disorders or ulcerative colitis or crohn disease or gastroesophageal reflux disease or gastroesophageal reflux diseases or gerd or chronic pancreatitis or chronic kidney disease or kidney disease or kidney diseases or acute kidney injury or acute kidney injuries or dialysis or benign prostatic hyperplasia or kidney stone or kidney stones or neoplasm or neoplasms or cancer or cancers or tumor or tumors or liver disease cirrhosis or irritable bowel syndrome or vitiligo or acne or melanoma or systemic lupus or atopic eczema or celiac disease or ankylosing spondylitis or bechterew or psoriasis or rheumatoid arthritis or ra or inflammatory bowel disease or graves disease or osteoporosis or fracture or fractures or lymphoma or anemia or anemias or anaemia or anaemias or ηιv/aids or infectious or infection or virus infection or musculoskeletal disorders or low back pain or fibromyalgia or osteoarthritis or arthritis or chronic pain ) AND ( mental health or mental illness or mental disorder or psychiatric illness ) AND ( survival or mortality or cancer or rejection or infection or hospitalization for health or treatment outcome ) AND ( meta-analysis or systematic review )

Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects

*JBI database of systematic reviews and implementation reports:* (Somatic disease OR Cardiovascular Diseases OR coronary disease OR Coronary Heart Disease OR Heart Failure OR Myocardial Failure OR myocardial infarction OR Rheumatic Heart Disease OR stroke OR CAD OR abnormal heart rhythms OR arrhythmia OR sudden cardiac death OR cerebrovascular disease OR cerebrovascular diseases OR cerebro vascular disease OR cerebro vascular diseases OR cerebral vascular disease OR cerebral vascular diseases OR hypertension OR hypertensive OR myocarditis OR angina OR transient ischemic attack OR transient ischemic attacks OR transient ischaemic attack OR peripheral artery disease OR peripheral artery diseases OR hypertrophic cardiomyopathy OR chronic respiratory diseases OR pulmonary hypertension OR pneumonia OR asthma OR asthmatic OR chronic obstructive pulmonary disease OR chronic obstructive pulmonary diseases OR COPD OR obstructive sleep apnea syndrome OR neurocognitive disorder OR neurocognitive disorders OR Lewy Bodies OR Huntington Neurodegenerative Diseases OR multiple sclerosis OR Alzheimer Disease OR autoimmune encephalopathy OR paraneoplastic encephalitis OR peripheral neuropathy OR dementia OR Parkinson disease OR Amyotrophic Lateral Sclerosis OR ALS OR epilepsy OR epileptic OR seizure OR seizures OR Obesity OR obese OR overweight OR over weight OR dyslipidemia OR Cushing OR hidradenitis suppurativa OR metabolic syndrome OR chronic renal failure OR myeloproliferative disorder OR myeloproliferative disorders OR diabetes mellitus OR diabetes OR diabetic OR thyroid disorder OR thyroid disorders OR sarcoidosis OR liver disease OR liver diseases OR functional gastrointestinal disorder OR functional gastrointestinal disorders OR ulcerative colitis OR Crohn disease OR gastroesophageal reflux disease OR gastroesophageal reflux diseases OR GERD OR chronic pancreatitis OR chronic kidney disease OR kidney disease OR kidney diseases OR acute kidney injury OR acute kidney injuries OR dialysis OR benign prostatic hyperplasia OR kidney stone OR kidney stones OR Neoplasm OR Neoplasms OR cancer OR cancers OR tumor OR tumors OR liver disease cirrhosis OR Irritable bowel syndrome OR vitiligo OR acne OR melanoma OR systemic lupus OR atopic eczema OR celiac disease OR ankylosing spondylitis OR Bechterew OR psoriasis OR rheumatoid arthritis OR RA OR inflammatory bowel disease OR Graves disease OR osteoporosis OR fracture OR fractures OR lymphoma OR anemia OR anemias OR anaemia OR anaemias OR ΗΙV/AIDS OR infectious OR infection OR virus infection OR musculoskeletal disorders OR low back pain OR fibromyalgia OR osteoarthritis OR arthritis OR chronic pain) AND (mental disorder OR mental disorders OR psychiatric disorder OR psychiatric disorders OR psychopathological disorder OR psychopathological disorders OR psychopathological condition OR psychopathological conditions OR ADHD OR attention-deficit hyperactivity disorder OR attention deficit OR hyperkinetic disorder OR hyperkinetic syndrome OR Autism OR autistic OR Asperger OR neurodevelopmental disorder OR neurodevelopmental disorders OR Intellectual Disability OR Intellectual Disabilities OR mental retardation OR learning disability OR Schizophrenia OR schizophrenic OR psychotic disorder OR psychotic disorders OR psychosis OR Schizotypal OR Delusional Disorder OR Brief Psychotic Disorder OR Schizophreniform Disorder OR Schizoaffective disorder OR Bipolar disorder OR bipolar disorders OR Depression OR depressive OR mood OR Anxiety OR anxious OR panic disorder OR agoraphobia OR Obsessive-compulsive disorder OR Obsessive compulsive disorder OR OCD OR PTSD OR Trauma-related disorder OR Trauma-related disorders OR Stress-related disorder OR Stress-related disorders OR Substance-related disorder OR Substance-related disorders OR addictive disorder OR addiction disorders OR drug abuse OR eating disorder OR eating disorders OR anorexia OR bulimia OR binge-eating OR binge eating OR sleep disorder OR sleep disorders OR sleep disturbance OR sleep disturbances OR insomnia OR Body Dysmorphic Disorder OR Trichotillomania OR Hair-Pulling Disorder OR Excoriation Disorder OR Skin-Picking Disorder OR dissociative disorder OR dissociative disorders Dissociative Identity Disorder OR Restless Legs Syndrome OR Gender Dysphoria OR Personality disorder OR Personality disorders OR Antisocial Personality Disorder OR Paranoid Personality Disorder OR Schizoid Personality Disorder OR Schizotypal Personality Disorder OR Borderline Personality Disorder OR Histrionic Personality Disorder OR Narcissistic Personality Disorder OR Avoidant Personality Disorder OR Dependent Personality Disorder OR Obsessive-Compulsive Personality Disorder) AND ( mortality OR survival OR death\* OR prognosis OR function OR disability OR disease-specific symptom severity, OR quality of life OR HRQOL OR disability-adjusted life years)

# **eResults 1.** ROBIS assessments for Phase 2 across the four domains and for Phase 3

In phase 2 and in Domain 1: Study eligibility criteria, 35 (74.5%) of the systematic reviews with meta-analysis were evaluated as low risk, 11 (23.4%) as high risk, and one (2.1%) as unclear risk of bias. In Domain 2: Identification and selection of studies, 34 (72.3%) were evaluated as low risk, 10 (21.3%) as high risk, and three (6.4%) as unclear risk of bias. In Domain 3: Data collection and study appraisal, 26 (55.3%) were evaluated as low risk, 13 (27.6%) as high risk of bias, and eight (17.1%) as unclear risk. In Domain 4: Synthesis and findings, 31 (66%) were evaluated as low risk, 12 (25.5%) as high risk, and four (8.5%) as unclear risk of bias. In Phase 3, 32 (68.1%) systematic reviews with meta-analysis were evaluated as low risk, nine (19.1%) were evaluated as high risk, and six (12.8%) were evaluated as low unclear risk of bias.

# **eResults 2.** Findings from other subgroup analyses

When restricting the analyses to studies formulating a diagnosis of mental disorder before the diagnosis of physical disease (NB: the clinical outcomes always followed the diagnosis of psychiatric disorders), the level of evidence of class I and II associations remained unchanged. When restricting the analyses to studies formulating a diagnosis of mental disorder after the diagnosis of physical disease, the class I and II associations between depression and all-cause mortality in patients with heart failure, kidney failure, and diabetes mellitus, as well as between depression and dementia in patients with diabetes mellitus were downgraded to weak evidence (class IV, number of primary studies, k, ranging from 2 to 4) or to non-significant level (NS, k=2 studies).

When restricting the analyses to follow-up duration >5 years, the class I association between schizophrenia and cardiovascular mortality in cardiovascular diseases and the class II associations between depression and all-cause mortality in kidney failure and diabetes mellitus were downgraded to suggestive or weak evidence (class III and IV, k ranging from 2 to 5). When restricting the analyses to follow-up duration ≤5 years, only the class II association between depression and all-cause mortality in diabetes mellitus was downgraded to weak (class IV, k=2 studies) evidence. There was no change in the level of evidence for the remaining associations.

When restricting the analyses to adjusted estimates, only the class I association between schizophrenia and cardiovascular mortality in cardiovascular diseases was downgraded to weak (class IV, k=5) evidence. There was no change in the level of evidence for the remaining associations, as most of the included associations were preferably adjusted. When restricting to unadjusted estimates, there was no change in the level of evidence.

When restricting the analyses to age of participants <50 years old, the class I association between schizophrenia and cardiovascular mortality in cardiovascular diseases was downgraded to weak (class IV, k=2) evidence. When restricting the analyses to an age of participants ≥ 50 years old, the class I association between schizophrenia and cardiovascular mortality in cardiovascular diseases and the class II association between depression and all-cause mortality in kidney failure were downgraded to suggestive (class III) or weak evidence (class IV, k=3 studies per association)

When restricting the analyses to studies including in their samples a majority of males, the class I association between schizophrenia and cardiovascular mortality in cardiovascular diseases and between depression and all-cause mortality in heart failure were downgraded to highly suggestive (class II) or weak (class IV) evidence (k ranging from 3 to 4). The class II associations between depression and all-cause mortality in kidney failure and diabetes mellitus were downgraded to suggestive or weak evidence (class III and IV, k ranging from 3 to 4). When restricting the analyses to studies including in their samples a majority of females, the class II association between depression and all-cause mortality in diabetes mellitus was downgraded to weak evidence (class IV, k=3 studies).

However, it is important to note that all these subgroup analyses were conducted in a very small number of primary studies and are therefore highly underpowered.

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