# Evidence Profile – Depression

|  | **Study 1** | **Study 2** |
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| **Authors &** **year** | Van Straten, Hill, Richards & Cuijpers, 2014 | Oosterbaan, Verbraak, Terluin,. Hoogendoorn, Peyrot, Muntingh & van Balkom, 2013 |
| **Design** | Systematic review and meta-analysis (12 RCTs, 2 cluster RCTS) | Cluster RCT |
| **Intervention (I) and Comparison (C)** | (I): Stepped care (SC)(C): Usual care (11 studies) or enhanced usual care (3 studies) | (I): Collaborative stepped care (CSC)(C): Care as usual (CAU) |
| **Focus of intervention** | 8 Treatment studies, 3 Prevention studies | Treatment |
| **Baseline Diagnosis** | The presence or absence of a DSM-IV diagnosis of depressive disorder obtained through interview, or depressive symptoms according to a questionnaire | DSM-IV diagnosis of depressive or anxiety disorder (MINI) |
| **Primary Outcome domain (Measure(s))** | Various, including MINI, SCID, CIDI, CES-D, BDI, PHQ, SCL, K10, CIS-R, GHQ. | - % of patients responding to and remitting after treatment (CGI-I; CGI-S) |
| **Secondary Outcome domain (Measure(s))** | Various | - Anxiety symptoms (HRSA)-Depressive symptoms (CES-D)- Phobic behaviour (FQ)-General symptoms (SCL-90-R)- Quality of life (SF-36). |
| **Setting and characteristics of sample** | Adults in primary care (4 studies), adults with comorbid physical conditions (6 studies), elderly people (5 studies) Countries where studies were conducted:Chile (1 study), India (1 study), Netherlands (6 studies), USA (6 studies) | Adults in primary care in the NetherlandsN=158 |
| **Participants: I** | NA | N = 94Mean age: 37 (12)63% female |
| **Participants: C** | NA | N=64Mean age: 39 (12)61% female |

**Study 1:** Study quality was overall relatively high. A meta-analysis of the 10 studies that were treatment-focused and had post-treatment data found an overall post-intervention effect size of d=0.38 (95% CI 0.18-0.57). Effect sizes at specific time points were d=0.57 (2-4 months; 95% CI 0.21-0.94), d=0.34 (6 months; 95% CI programs 0.20-0.48), d=0.43 (9-12 months; 95% CI 0.20 -0.65) and d=0.26 (18 months; ns). Heterogeneity was high for all effect sizes. SC with interventions arranged by progressive intensity had significantly less effect than SC not arranged as such (d=0.07 vs d=0.41, p <0.01). Location of study, physical health comorbidity and diagnostic status at baseline were not related to effect size. Of the three prevention-focused studies, two found positive effects for SC on 12-month rates of major depressive disorder, while the other found no difference.

**Study 2:** **Description of intervention and comparison:** Step 1: A 3.5-month guided self-help course, with five 45-minute sessions, provided in primary care, with AD medication offered to patients with a moderately severe disorder. Step 2: CBT in combination with AD medication provided by a specialist out-patient mental health service. Within each step, participants were allocated to a depression, anxiety or stress treatment program, depending on their diagnosis. Remission was evaluated after 4 months, using the CGI-S. Participants with scores of at least 3 on the CGI-S (i.e. mild severity or worse) proceeded to the second-step treatment. Patients with stress-related disorders or mild or moderately severe anxiety or depressive disorders started at Step 1. Participants with a severe disorder went directly to Step 2. Participants assigned to CAU could obtain any service normally available in The Netherlands.

**Results**: At 4-month mid-test CSC was superior to CAU: 74.7% v. 50.8% responders (P = 0.003) and 57.8% v. 31.7% (P = 0.002); however, at 8-month post-test and 12-month follow-up no significant differences were found. A similar pattern of response and remission results was found for the specific depression treatment program. Compared with patients in the CAU group, CSC patients had a significantly larger reduction in depressive symptoms (CES-D) after 4 months. However, for the depression treatment programme no significant differences were found between groups at any time point.

# Evidence Profile – Anxiety

|  | **Study 1** | **Study 2** | **Study 3** | **Study 4** | **Study 5** | **Study 6** | **Study 7** | **Study 8** |
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| **Authors &** **year** | Dozeman, van Marwijk, van Schaik, Smit, Stek, van der Horst, Bohlmeijer & Beekman, 2012 | Kronish, Rieckmann, Burg & Davidson, 2012 | Oosterbaan, Verbraak, Terluin,. Hoogendoorn, Peyrot, Muntingh & van Balkom, 2013 | Seekles, van Straten, Beekman, van Marwijk & Cuijpers, 2011 | Tolin, Diefenbach & Gilliam, 2011 | Primary papervan't Veer-Tazelaar, van Marwijk, van Oppen, van Hout, van der Horst, Cuijpers, Smit & Beekman, 2009Follow-up papervan't Veer-Tazelaar, van Marwijk, van Oppen, van der Horst, Smit, Cuijpers & Beekman, 2011 | Zatzick; Roy-Byrne, Russo, Rivara, Droesch, Wagner, Dunn, Jurkovich, Uehara & Katon, 2004 | Zatzick, Jurkovich, Rivara, Russo, Wagner, Wang, Dunn, Lord, Petrie, O'Connor & Katon, 2013 |
| **Design** | RCT | RCT | Cluster RCT | RCT | RCT | RCT | RCT | RCT |
| **Intervention (I) and Comparison (C)** | (I): Stepped care(C): Usual care | (I): Enhanced depression care (COPES)(C): Care as usual (CAU) | (I): Collaborative stepped care (CSC)(C): Care as usual (CAU) | (I): Stepped care(C): Usual care  | (I): Stepped care exposure and response prevention (ERP)(C): Standard ERP | (I): Preventive stepped care(C): Usual care (UC) | (I): Stepped collaborative care (SCC)(C): Usual care (UC) | (I): Stepped collaborative care (C): Usual care |
| **Focus of intervention** | Prevention | Treatment | Treatment | Treatment | Treatment | Prevention | Treatment | Treatment |
| **Baseline Diagnosis** | A score of at least 8 on the CES-D, but no depressive or anxiety disorder (MINI) | A score from 10-45 on the BDI 1 week and 3 months post hospitalisation for acute coronary syndrome (ACS). | DSM-IV diagnosis of depressive or anxiety disorder (MINI) | DSM-IV diagnosis of major depression, minor depression, dysthymia, panic disorder, social phobia or GAD (CIDI), minor anxiety (score of 12 or more on the HADS) | DSM-IV diagnosis of OCD (ADIS-IV) | A score of at least 16 on the CES-D, but no depressive or anxiety disorder (MINI) | A score of at least 45 on the PCL and/or at 16 on the CES-D in the surgical ward | A score of at least 35 on the PCL in the surgical ward and following discharge. |
| **Primary Outcome domain (Measure(s))** | - Cumulative 12 month incidence of depressive and anxiety disorders (MINI) | - Anxiety (HADS-A) | - % of patients responding to and remitting after treatment (CGI-I; CGI-S) | - Depression symptoms (IDS)- Anxiety symptoms (HADS)- Daily functioning (WSAS) | - OCD symptoms (Y-BOCS) | - Cumulative 12-month incidence of anxiety and depressive disorders (MINI) | - DSM-IV diagnosis of PTSD (PCL) | -PTSD symptoms and diagnosis (CAPS; PCL)-PTSD remission and treatment response (CAPS) |
| **Secondary Outcome domain (Measure(s))** | - Depression symptoms (CES-D)- Anxiety (HADS-A) |  | - Anxiety symptoms (HRSA)- Depressive symptoms (CES-D)- Phobic behaviour (FQ)- General symptoms (SCL-90-R) Quality of life (SF-36) |  |  |  | DSM-IV diagnosis of alcohol abuse or dependence (CIDI) | - Depressive symptoms (PHQ) - Alcohol use (AUDIT-C). |
| **Setting and characteristics of sample** | Elderly people in nursing homes in the NetherlandsTotal sample size: N=185 | US patients with ACSTotal sample size: N=157 | Adults in primary care in the NetherlandsTotal sample size: N=158 | Adults in primary care in the NetherlandsTotal sample size: N=120 | US adults in outpatient mental health careTotal sample size: N=185 | Adults aged over 75 in primary care in the NetherlandsTotal sample size: N=170 | US patients admitted to hospital for surgery after injuryTotal sample size: N=120 | US patients admitted to hospital for surgery after injuryTotal sample size: N=207 |
| **Participants: I** | n= 93Mean age: 85 (7)72% female | n= 80Mean age: 59 (11)54% female | n= 94Mean age: 37 (12)63% female | n= 60Mean age: 51 (10)68% female | n= 19 Mean age: 36 (15)68% female | n= 86Mean age: 82 (4)70% female | n= 59Mean age: 37 (13)32% female | n= 104Mean age: 39 (13)52% female |
| **Participants: C** | N= 92Mean age: 84 (6)73.9% female | n= 77Mean age: 61 (11)53% female | n= 64Mean age: 39 (12)61% female | n= 60Mean age: 49 (12)62% female | n= 15Mean age: 33 (11)47% female | n= 84Mean age: 81 (4)77% female | n= 61Mean age: 44 (16)33% female | n= 103Mean age: 38 (13)44% female |

**Study 1:** Description of intervention and comparison: Step 1: watchful waiting. Step 2: Activity scheduling. Step 3: life review with GP. Step 4: additional specialist treatment. After one month of watchful waiting, assessments took place in cycles of three months. Failure to improve by at least 5 points on the CES-D determined step-up, while those with a decrease of 0-5 points received further monitoring. Participants who had a CES-D score ≥ 16 after 7 months went to Step 4. Residents in the usual care group had access to any form of health care that was considered appropriate.

Results: The intervention was not effective in reducing the incidence of anxiety disorders relative to the usual care group (IRR = 1.32; 95% CI = 0.48–3.62).

**Study 2:** **Description of intervention and comparison**: Stepped care was embedded within a collaborative care approach, which included participant choice of psychotherapy (PST) and/or pharmacotherapy. Symptoms were reviewed every 8 weeks. Patients who achieved recovery from depression (at least a 50% reduction on PHQ-9 score and fewer than 3 of 9 symptoms) were followed up monthly. Participants who had not responded to treatment at a given time point had a treatment plan developed that could include change and/or augmentation of ADs or a change from ADs to PST or vice versa. Usual care was defined by the patient’s treating physicians, who were informed that their patients were participating in a trial and that they had elevated depressive symptoms or met the criteria for a major depressive episode.

**Results**: At post-treatment, COPES participants showed a significant decrease in HADS-A compared to baseline whereas there was no significant change in usual care patients (effect size of 0.53). Controlling for depression, the effect of enhanced care on anxiety decreased, but remained significant. A subgroup analysis suggested a benefit of enhanced care on anxiety in women but not men.

**Study 3:** **Description of intervention and comparison:** Step 1: A 3.5-month guided self-help course, with five 45-minute sessions, provided in primary care, with AD medication offered to patients with a moderately severe disorder. Step 2: CBT in combination with AD medication provided by a specialist out-patient mental health service. Within each step, participants were allocated to a depression, anxiety or stress treatment program, depending on their diagnosis. Remission was evaluated after 4 months, using the CGI-S. Participants with scores of at least 3 on the CGI-S (i.e. mild severity or worse) proceeded to the second-step treatment. Patients with stress-related disorders or mild or moderately severe anxiety or depressive disorders started at Step 1. Participants with a severe disorder went directly to Step 2. Participants assigned to CAU could obtain any service normally available in The Netherlands.

**Results**: At 4-month mid-test CSC was superior to CAU: 74.7% v. 50.8% responders (P = 0.003) and 57.8% v. 31.7% (P = 0.002); however, at 8-month post-test and 12-month follow-up no significant differences were found. A similar pattern of response and remission results was found for the specific anxiety treatment program. Compared with those in the CAU group, CSC participants had a significantly larger reduction in anxiety symptoms (HRSA, FQ) after 4 months. In the anxiety treatment programme scores on the HRSA were also significantly more reduced at 4 months for CSC compared with CAU.

**Study 4:** Description of intervention and comparison: Step 1: watchful waiting. Step 2: guided self-help. Step 3: problem-solving therapy. Step 4: pharmacotherapy and/or referral for specialized mental health care. Scores of at least 14 on the IDS, at least 8 on the HADS and at least 6 on the WSAS CES-D determined step-up. Usual care participants were advised to see their GP to discuss treatment options.

Results: Symptoms of anxiety decreased significantly over 24 weeks for both groups; however, there was no significant difference in symptom reduction between the two groups.

**Study 5:** **Description of intervention and comparison**: Step 1: bibliotherapy plus counselling. The therapist answered questions regarding ERP, and provided suggestions for implementing ERP; however, no ERP was performed or modelled within these sessions. Step 2: Standard ERP, including modelling within sessions. Participants assigned to the standard ERP condition received ERP as per Step 2. Failure to improve by at least 5 points on the Y-BOCS determined step-up.

**Results:** No significant differences in response rates were found between the two samples at posttreatment (50% stepped care versus 42% standard ERP, p=.66).

**Study 6:** **Description of intervention and comparison**: Step 1: watchful waiting. Step 2: CBT-based bibliotherapy. Step 3: brief CBT-based problem solving therapy. Step 4:referral to primary care. A score of at least 16 on CES-D, administered every three months, determined step-up. Participants assigned to UC had unrestricted access to usual care for their depression or anxiety concerns.

**Results**: The 12 month rate of depressive and anxiety disorders was significantly lower in the intervention group than in the UC group (12 % v.24%; relative risk, 0.49; 95% CI 0.24 to 0.98). The rate of anxiety disorders in the intervention group after 12 months was not significantly different from that of depressive disorders. These results were maintained at 24-month follow-up.

**Study 7:** **Description of intervention and comparison**: Stepped care was embedded within a collaborative care approach. For the first 6 months after injury, all SCC participants received case management. All participants with positive alcohol toxicology test results on admission, or who demonstrated post-injury alcohol abuse received motivational interviewing (MI). Three months after the injury, each SCC participant was administered the SCID PTSD module, and participants with PTSD were given their preference of CBT, pharmacotherapy, or combined treatment. During the PTSD intervention, the TSS performed brief assessments of adherence to medication and symptom relapse, outside scheduled sessions. From 6 to 12 months after the injury, participants had their symptoms periodically reassessed and participants who remained symptomatic with PTSD and/or alcohol abuse received ongoing support and MI and PTSD treatments. All participants, including those in the UC condition, received a list of community referrals.

**Results**: The SCC group demonstrated no difference (−0.07%; 95% CI, −4.2% to 4.3%) in the adjusted rates of change in PTSD from baseline to 12 months, whereas the UC group had a 6% increase (95% CI, 3.1%-9.3%). The intervention effect on PTSD commenced at 3 months, with between-group differences reaching trend level at 6 months, and significance at 12 months.

**Study 8: Description of intervention and comparison**: As for Zatzick et al (2004). Behavioural activation was also part of case management. UC participants underwent PTSD screening, and baseline and follow-up interviews

**Results:** Regression analyses demonstrated significant CAPS (p < 0.01), and PCL-C (p < 0.001) group by time interaction effects in favour of SCC over the course of the year. The intervention also achieved a significant impact on PTSD treatment response (OR = 1.93, 95% CI = 1.0 -3.7). PTSD remission criteria also demonstrated significant reductions over the course of the year (p < 0.01). No significant treatment effects were observed for PTSD diagnostic criteria over the course of the year (OR = 1.4, 95% CI = 0.8, 2.5).