

# **Phosphatidylserine as Treatment for PTSD or Other Psychiatric Illness – 2023 Update**

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## **A Rapid Systematic Review**

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## About this report

### Phosphatidylserine as Treatment for PTSD or Other Psychiatric Illness: 2023 Update

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#### About the Evidence-Based Practice Group

The Evidence-Based Practice Group was established to address the many medical and policy issues that WorkSafeBC officers deal with on a regular basis. Members apply established techniques of critical appraisal and evidence-based review of topics solicited from both WorkSafeBC staff and other interested parties such as surgeons, medical specialists, and rehabilitation providers.

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## Objectives

- To determine whether there is any evidence to support the efficacy and/or effectiveness of using phosphatidylserine as a treatment for post-traumatic stress disorder (PTSD) or other psychiatric illnesses.

## Introduction

- In 2017, WorkSafeBC's Evidence-Based Practice Group (EBPG) commissioned a systematic review to investigate the efficacy and/or effectiveness of using phosphatidylserine in treating patients with post-traumatic stress disorder (PTSD) or other psychiatric illnesses<sup>1</sup>.
- The findings concluded that there was no study investigating phosphatidylserine as a treatment for PTSD or other psychiatric illnesses.
- This current update seeks to review the literature from the last update in 2017 in order to determine if phosphatidylserine can be used in the treatment of patients with post-traumatic stress disorder (PTSD) or other psychiatric illnesses.

## Methods

- A systematic literature search was started on October 18, 2023.
- This literature search was conducted on commercial medical literature databases, including, Medline Epub Ahead of Print, Medline In-Process & Other Non-Indexed Citations, Medline Daily Update available through the Ovid platform (1946 to October 10, 2023), CINAHL Complete (Search completed October 18, 2023), EBM Reviews - Cochrane Database of Systematic Reviews 2005 to October 4, 2023, EBM Reviews - ACP Journal Club 1991 to September 2023, EBM Reviews - Database of Abstracts of Reviews of Effects 1st Quarter 2016, EBM Reviews - Cochrane Clinical Answers September 2023, EBM Reviews - Cochrane Central Register of Controlled Trials August 2023, EBM Reviews - Cochrane Methodology Register 3rd Quarter 2012, EBM Reviews - Health Technology Assessment 4th Quarter 2016, and EBM Reviews - NHS Economic Evaluation Database 1st Quarter 2016 (Search completed October 18, 2023), and EMBASE.com (Search completed October 18, 2023).
- The search was done by employing combinations of keywords. Additional keywords (i.e. alternate names for phosphatidylserine, full list of psychiatric disorders) were added to the search strategy compared to the original 2017 systematic review. Full search strategies can be found in Appendix 2. A second search was conducted that looked at phosphatidylserine use in other psychiatric illnesses (Appendix 2, searches 6-10).
- No limitation on date of publication were implemented in any of these searches.
- A manual search was also planned and conducted on the references of the articles that were retrieved in full.

## Results

- Search results:
  - Nineteen published studies were identified through the search - one from MEDLINE, seven from CINAHL, three from PSYCINFO, and eight from EMBASE.
  - After duplicates were removed, 17 published studies were identified - one from MEDLINE, six from CINAHL, three from PSYCINFO, and seven from EMBASE.
  - Upon examination of the titles and abstracts of these published studies, there were no studies thought to be relevant to PTSD; two were excluded due to incorrect population, four due to incorrect interventions, five due to incorrect study design, and six were non-human studies.

- A second search was conducted that looked at phosphatidylserine use in other psychiatric illnesses (Appendix 2, searches 6-10).
- One hundred-eighty-seven published studies were identified through the search – 75 from MEDLINE, 29 from CINAHL, 32 from PSYCINFO, five from CENTRAL and 47 from EMBASE.
- After duplicates were removed, 159 published studies were identified - 74 from MEDLINE, 27 from CINAHL, 20 from PSYCINFO, and 38 from EMBASE.
- Upon examination of the titles and abstracts of these published studies, there were ten studies thought to be relevant to phosphatidylserine use in other psychiatric illnesses<sup>2-11</sup>; 42 were excluded due to incorrect population, 46 due to incorrect interventions, one due to incorrect outcomes, 19 due to incorrect study design, and 46 were animal/cell culture studies.
- Of the ten studies that were retrieved in full, one was excluded due to incorrect population<sup>8</sup> and five studies were excluded due to incorrect study design<sup>2,3,6,7,11</sup>.
- A hand search of the references from the studies selected for full text screening revealed one additional study<sup>12</sup>.
- Of the three included articles, Brambilla et al., (1995)<sup>4</sup> was the original primary study, with the two other articles providing additional outcomes<sup>5,12</sup>.
- Therefore, three primary studies<sup>4,9,10</sup> comprised of five articles<sup>4,5,9,10,12</sup> are relevant to this systematic review.
- Study Characteristics:
  - A description of study characteristics of included studies is available in Table 1.
- Study Quality:
  - Study quality varied between studies: two had low study quality (Appendix 1, level 3)<sup>4,9</sup>, while one had very low study quality (Appendix 1, level 4)<sup>10</sup>.
  - Study quality was downgraded to very low for the case-controlled studies due to lower levels of evidence, methodological limitations and imprecision.
  - Study quality was lowered for all three studies due to imprecision because of low numbers of participants in the included studies (n < 100).
- Outcomes:
  - One published study, Maggioni et al., (1990), was a small case series of ten depressed elderly women in which oral phosphatidylserine (300 mg/day) was given for 30 days<sup>10</sup>.
  - Treatment with phosphatidylserine significantly decreased Hamilton Rating Scale for Depression (HRSD) score and Nurse's Observation Scale for Inpatient Observation (NOSIE) depression component score compared with pre-treatment (HRSD 7.6±8.1 vs. 24.6±3.6, p≤0.001; NOSIE depression subset 4.9±3.4 vs. 12.4±1.8, p≤0.001).
  - In Brambilla et al., (1995) and associated studies<sup>4,5,12</sup>, 10 elderly women with major depressive disorder (MDD), 10 age- and sex-matched controls, and 10 healthy young women were given treatment with phosphatidylserine (600 mg/day) for 30 days.
  - This case-controlled study showed that treatment with phosphatidylserine significantly, for 30 days, decreased Hamilton Rating Scale for Depression (HRSD) score compared with pre-treatment in the elderly patients with MDD (HRSD 31.3±6.3 vs. 19.6±11.0, p=0.03)<sup>4</sup>.
  - However, beta-endorphin concentration in peripheral blood mononuclear cells, a potential marker for depressive symptomology, did not change after phosphatidylserine therapy vs. pre-treatment, despite significant improvement of the depressive symptomatology<sup>5</sup>.

- Furthermore, interleukin-1 p (IL-1 p), interleukin-6 (IL-6) and tumour necrosis factor-a (TNFa), known markers of major depression, did not change levels in young controls, elderly controls and MDD patients, in spite of significant improvement of the depressive symptomatology<sup>12</sup>.
- In a case-control study, Komori et al., (2015), the study combined supplementation with 100 mg phosphatidylserine, 119 mg docosahexaenoic acid (DHA), and 70 mg eicosapentaenoic acid (EPA) three times a day (300 mg/d) for 12 weeks in 18 elderly patients with major depression<sup>9</sup>.
- Mean 17-item Hamilton depression scale (HAM-D-17) score was significantly improved after 12 weeks in all subjects taking the supplement (HAM-D-17 14.6±5.9 vs. 21.1±3.4, p=0.02). When divided into 8 responders and 10 non-responders, HAM-D-17 score was 8.6±6.3 in responders compared to 18.8±5.1 in non-responders after treatment (P=0.02).

## Discussion

- There are no high quality randomized controlled trials, as studies were either case control or case series (Appendix 1, level 3 and 4).
- There is some very low-quality, low-level evidence pointing toward the efficacy of phosphatidylserine for depression.
- Therefore, there is no conclusive evidence for the use of phosphatidylserine therapy in the treatment of PTSD or other psychiatric illnesses, as there are study design and methodological challenges (Table 2).
- In all three studies, phosphatidylserine therapy demonstrated an improvement to depression outcomes compared to pre-treatment levels. However, no between-group comparison was made for depression outcomes for two studies as they were compared to healthy controls<sup>4,9</sup> while one group did not have a comparator group<sup>10</sup>.
- Across all studies, there was no standard protocol for phosphatidylserine therapy as dosage, duration and concomitant therapies were heterogeneous between the three primary studies making it challenging to compare the results.
- Two studies had a total daily dose of 300 mg<sup>9,10</sup> while one study had a daily dose of 600 mg<sup>4</sup>.
- Duration of the studies varied as the duration of one study was 30 days<sup>4</sup>, another study was 45 days<sup>10</sup> and one other study was 12 weeks<sup>9</sup>. Furthermore, two studies had a washout period of 30 days<sup>4,10</sup> while one continued anti-depressant therapy during phosphatidylserine treatment<sup>9</sup>.
- One study had concomitant therapies as a combination pill with other supplements<sup>9</sup> while the other two did not have any concomitant therapies<sup>4,10</sup>.
- While all studies demonstrated some improvement to depression score, all three studies only looked at short term effects (30 days to 12 weeks).
- It also should be noted that performance bias cannot be discounted in the reporting of each of these cases as randomization and blinding of both the patient and assessor was absent for all studies.
- Study quality was lowered for all three studies due to imprecision because of low numbers of participants in the included studies (n < 100).

## Summary

- As reported in the original 2017 systematic review, there was no study investigating the efficacy and/or effectiveness of phosphatidylserine as treatment for PTSD or other psychiatric illnesses. In this update, three additional primary studies were examined. While there was some very low-quality, low-level evidence reporting on the efficacy of

phosphatidylserine for depression, there was still no conclusive evidence that phosphatidylserine improves PTSD nor other psychiatric illnesses, as each study had study design and methodological challenges. Therefore, there are no changes to the conclusions of the 2017 systematic review.

## References

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12. Brambilla F, Maggioni M. Blood levels of cytokines in elderly patients with major depressive disorder. *Acta Psychiatr Scand*. Apr 1998;97(4):309-13. doi:10.1111/j.1600-0447.1998.tb10005.x

## Tables

**Table 1 - Description of studies identified for treatment of depression.**

Primary Study.	N	Primary Population	Experimental Group (n)	Comparison Group(s) (n)	Intervention dosage/frequency	Timepoints	Outcome
Maggioni et al, 1995	10	Patients with dysthymic disorder or MDD	BC-PS (10)	N/A	BC-PS: 300 mg daily for 45 days	Followup: 1 month	HRSD
Brambilla et al, 2005	30	Patients with major depression disorder	BC-PS (10)	Age- and sex-matched control (10), Young healthy volunteers (10)	BC-PS: 600 mg daily (200 mg, 3 times a day) for 1 month	Followup: 1 month	HRSD, NOSIE depression component score
Komori et al, 2015	36	Patients with major depression	Nutrix Kefarin™ plus;) (18)	Age- and sex-matched control (18)	Nutrix Kefarin™ Plus (PS 100 mg, DHA 119 mg, EPA 70 mg, DPA 11 mg, glinolenic acid 50 mg, astaxanthine 2 mg, and Palm Tocotrienol Complex 16 mg) 3 times a day for 12 weeks	Followup: 12 weeks	HAM-D-17

Abbreviations: Bovine cortex phosphatidylserine (BC-PS), Docosahexaenoic acid (DHA), Eicosapentaenoic acid (EPA), Hamilton Rating Scale for Depression (HRSD), Hamilton (HAM-D-17), Major depression disorder (MDD), Nurse's Observation Scale for Inpatient Observation (NOSIE), and phosphatidylserine (PS),



**Table 2 - Description of study outcomes for the treatment of depression.**

Primary Study	n	Outcomes
Maggioni et al, 1995	10	<b>Depression score (-):</b> PS significantly decreased HRSD and NOSIE depression subset score compared with pre-treatment (HRSD 7.6±8.1 vs. 24.6±3.6, p≤0.001; NOSIE depression subset 4.9±3.4 vs. 12.4±1.8, p≤0.001). No comparator group.
Brambilla et al, 2005	30	<b>Depression score (-/=):</b> PS significantly decreased HRSD score vs. pre-treatment, in the elderly patients with MDD (HRSD 31.3±6.3 vs. 19.6±11.0, p=0.03). No comparison of depression outcomes was made to age- and sex-matched controls. There were no correlations between β-EP, IL-1p, IL-6, TNFa concentration before or after therapy or between age- and sex-matched controls or young healthy controls.
Komori et al, 2015	36	<b>Depression score (-):</b> HAM-D-17 score was significantly improved after 12 weeks in all subjects taking the supplement (HAM-D-17 14.6±5.9 vs. 21.1±3.4 pre-treatment, p=0.02). When divided into 8 responders and 10 non-responders, HAM-D-17 score was 8.6±6.3 in responders compared to 18.8±5.1 in non-responders after treatment (P=0.02). No between-group comparison of depression outcomes was made to age- and sex-matched controls.

Abbreviations: Beta-Endorphin (β-EP), Bovine cortex phosphatidylserine (BC-PS), Docosahexaenoic acid (DHA), Eicosapentaenoic acid (EPA), Hamilton Rating Scale for Depression (HRSD), Hamilton (HAM-D-17), Interleukin-1 p (IL-1 p), Interleukin-6 (IL-6, Major depression disorder (MDD), Nurse's Observation Scale for Inpatient Observation (NOSIE), phosphatidylserine (PS), ) and tumour necrosis factor-a (TNFa).

## Appendix 1

### WorkSafeBC — Evidence-Based Practice Group levels of evidence (adapted from 1-6)

1	Experimental, randomized controlled trial (RCT), systematic review RCTs with or without meta-analysis.
2	Evidence from controlled trials without randomization (quasi-experimental studies) or systematic reviews of observational studies.
3	Evidence from cohort or case-control analytic studies, preferably from more than 1 centre or research group.
4	Evidence from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments.
5	Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees based on scientific evidence.

## References

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5. (2014). Canadian task force on preventive health care procedure manual. Downloaded from <https://canadiantaskforce.ca/methods/> in May 12, 2022.
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## Appendix 2

### Search 1. Search strategy for MEDLINE (via OVID)

1	exp Stress Disorders, Traumatic/	46168
2	PTSD/	41705
3	((post-traumatic or post traumatic or posttraumatic) and disorder*).tw.	42293
4	PTSD.tw.	32779
5	or/1-4	63803
6	phosphatidylserines/	8496
7	phosphatidylserine.tw.	16792
8	Efalex*.tw.	2
9	PCSO-524*.tw.	15
10	Vayarin*.tw.	0
11	Virtiva*.tw.	1
12	Lyprinol*.tw.	38
13	or/6-12	19141
14	5 and 13	1

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### Search 2. Search strategy for CINAHL (via EBSCO)

1	MH Stress Disorders, Traumatic	27449
2	TI ((stress N2 disorder*)) OR AB ((stress N2 disorder*))	19023
3	TI ((ptsd or posttrauma* or post-trauma* or trauma or traumas)) OR AB ((ptsd or posttrauma* or post-trauma* or trauma or traumas))	120702
4	S1 OR S2 OR S3	128955
5	MA phosphatidylserine	598
6	TI (phosphatidylserine) OR AB (phosphatidylserine)	598
7	TI (Efalex) OR AB (Efalex)	1
8	TI (PCSO-524) OR AB (PCSO-524)	3
9	TI (Vayarin) OR AB (Vayarin)	1
10	TI (Virtiva) OR AB (Virtiva)	0
11	TI (Lyprinol) OR AB (Lyprinol)	8
12	S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11	609
13	S4 AND S12	7

### Search 3. Search strategy for CENTRAL (via OVID)

1	exp Stress Disorders, Traumatic/	3911
2	PTSD/	3714
3	((post-traumatic or post traumatic or posttraumatic) and disorder*).tw.	6175
4	PTSD.tw.	5992
5	or/1-4	8468
6	phosphatidylserines/	59
7	phosphatidylserine.tw.	230
8	Efalex*.tw.	4
9	PCSO-524*.tw.	17
10	Vayarin*.tw.	3
11	Virtiva*.tw.	1
12	Lyprinol*.tw.	17
13	or/6-12	272
14	5 and 13	0

### Search 4. Search strategy for EMBASE (via Embase.com)

1	'stress disorders, traumatic'/exp	0
2	'ptsd'/exp	82798
3	('post traumatic':ti,ab OR 'posttraumatic':ti,ab) AND 'disorder':ti,ab	48717
4	ptsd:ti,ab	42521
5	#1 OR #2 OR #3 OR #4	90005
6	'phosphatidylserines'/exp	20095
7	'phosphatidylserine':ti,ab	20227
8	'efalex*':ti,ab	4
9	'pcso-524*':ti,ab	15
10	'vayarin*':ti,ab	3
11	'virtiva*':ti,ab	1
12	'lyprinol*':ti,ab	50
13	#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12	26411
14	#5 AND #13	8

### Search 5. Search strategy for PSYCINFO (via EBSCO)

1	MA Stress Disorders, Traumatic	20798
2	TI ((stress N2 disorder*)) OR AB ((stress N2 disorder*))	46138
3	TI ((ptsd or posttrauma* or post-trauma* or trauma or traumas)) OR AB ((ptsd or posttrauma* or post-trauma* or trauma or traumas))	118200
4	S1 OR S2 OR S3	124397
5	MA phosphatidylserine	93
6	TI (phosphatidylserine) OR AB (phosphatidylserine)	210
7	TI (Efalex) OR AB (Efalex)	0
8	TI (PCSO-524) OR AB (PCSO-524)	3
9	TI (Vayarin) OR AB (Vayarin)	0
10	TI (Virtiva) OR AB (Virtiva)	1
11	TI (Lyprinol) OR AB (Lyprinol)	0
12	S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11	229
13	S4 AND S12	3

### Search 6. Search strategy for MEDLINE (via OVID)

1	eating disorders/ or anorexia nervosa/ or binge-eating disorder/ or bulimia nervosa/ or female athlete triad syndrome/ or pica/ or hyperphagia/ or bulimia/ or self-injurious behavior/ or self mutilation/ or suicide/ or suicidal ideation/ or suicide, attempted/ or mood disorders/ or affective disorders, psychotic/ or bipolar disorder/ or cyclothymic disorder/ or depressive disorder/ or depression, postpartum/ or depressive disorder, major/ or depressive disorder, treatment-resistant/ or dysthymic disorder/ or seasonal affective disorder/ or neurotic disorders/ or depression/ or adjustment disorders/ or antidepressive agents/ or anxiety disorders/ or agoraphobia/ or neurocirculatory asthenia/ or obsessive-compulsive disorder/ or obsessive hoarding/ or panic disorder/ or phobic disorders/ or stress disorders, traumatic/ or combat disorders/ or stress disorders, post-traumatic/ or stress disorders, traumatic, acute/ or anxiety/ or anxiety, castration/ or koro/ or anxiety, separation/ or panic/ or anti-anxiety agents/ or somatoform disorders/ or body dysmorphic disorders/ or conversion disorder/ or hypochondriasis/ or neurasthenia/ or hysteria/ or munchausen syndrome by proxy/ or munchausen syndrome/ or fatigue syndrome, chronic/ or obsessive behavior/ or compulsive behavior/ or behavior, addictive/ or impulse control	984621
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	disorders/ or firesetting behavior/ or gambling/ or trichotillomania/ or stress, psychological/ or burnout, professional/ or sexual dysfunctions, psychological/ or vaginismus/ or Anhedonia/ or Affective Symptoms/ or *Mental Disorders/	
2	(eating disorder* or anorexia nervosa or bulimi* or binge eat* or (self adj (injur* or mutilat*)) or suicide* or parasuicid* or mood disorder* or affective disorder* or bipolar i or bipolar ii or (bipolar and (affective or disorder*)) or mania or manic or cyclothymic* or depression or depressive or dysthymi* or neurotic or neurosis or adjustment disorder* or antidepress* or anxiety disorder* or agoraphobia or obsess* or compulsi* or panic or phobi* or ptsd or posttrauma* or post trauma* or combat or somatoform or somati#ation or medical* unexplained or body dysmorphi* or conversion disorder or hypochondria* or neurastheni* or hysteria or munchausen or chronic fatigue* or gambling or trichotillomania or vaginismus or anhedoni* or affective symptoms or mental disorder* or mental health).ti,kf.	561734
3	or/1-2	1168636
4	phosphatidylserines/	8496
5	phosphatidylserine.tw.	16787
6	Efalex*.tw.	2
7	PCSO-524*.tw.	15
8	Vayarin*.tw.	0
9	Virtiva*.tw.	1
10	Lyprinol*.tw.	38
11	or/4-10	19136
12	3 and 11	172
13	exp animals/ not humans.sh.	5160715
14	12 not 13	113
15	limit 14 to humans	74

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## Search 7. Search strategy for CINAHL (via EBSCO)

1	(MH "Mental Health")	58344
2	(MH "Mental Disorders")	67838
3	(MH "Depression+")	137099
4	(MH "Anxiety Disorders")	12368
5	(MH "Stress Disorders, Post-Traumatic") OR (MH "Anxiety Disorders") OR (MH "Obsessive-Compulsive Disorder")	44001
6	(MH "Schizophrenia+")	29873

7	(MH "Psychotic Disorders+")	145361
8	(MH "Eating Disorders+")	21543
9	(MH "Gambling")	3666
10	(MH "Alcohol-Related Disorders") OR (MH "Alcohol-Induced Disorders, Nervous System+") OR (MH "Alcoholism")	23149
11	(MH "Binge Drinking")	2379
12	(MH "Substance Use Disorders+")	187997
13	(MH "Affective Disorders")	8968
14	(MH "Bipolar Disorder")	13546
15	TI ( mental health or mental illness* or mentally ill or mental disorder* or depression or depressive or anxiety or problem drinking or alcoholism or binge drinking or schizophrenia or schizophrenic or psychosis or psychotic or obsessive compulsive or eating disorder* or bulimi* or anorexi* or gambling or post-traumatic stress or PTSD or substance abuse ) OR AB ( mental health or mental illness* or mentally ill or mental disorder* or depression or depressive or anxiety or problem drinking or alc ...	459297
16	TI ( ((drinking or alcohol) N2 (disorder or binge or binges or binging)). ) OR AB ( ((drinking or alcohol) N2 (disorder or binge or binges or binging)). )	14572
17	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16	778444
18	MH phosphatidylserine	0
19	TI (phosphatidylserine) OR AB (phosphatidylserine)	598
20	TI (Efalex) OR AB (Efalex)	1
21	TI (PCSO-524) OR AB (PCSO-524)	3
22	TI (Vayarin) OR AB (Vayarin)	1
23	TI (Virtiva) OR AB (Virtiva)	0
24	TI (Virtiva) OR AB (Virtiva)	0
25	TI (Lyprinol) OR AB (Lyprinol)	8
26	S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25	617
27	S17 AND S26	29

### Search 8. Search strategy for CENTRAL (via OVID)

1	eating disorders/ or anorexia nervosa/ or binge-eating disorder/ or bulimia nervosa/ or female athlete triad syndrome/ or pica/ or hyperphagia/ or bulimia/ or self-injurious behavior/ or self mutilation/ or suicide/ or suicidal ideation/ or suicide, attempted/ or mood disorders/ or aDective disorders, psychotic/ or bipolar disorder/ or cyclothymic disorder/ or depressive disorder/ or	79366
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	depression, postpartum/ or depressive disorder, major/ or depressive disorder, treatment-resistant/ or dysthymic disorder/ or seasonal affective disorder/ or neurotic disorders/ or depression/ or adjustment disorders/ or exp antidepressive agents/ or anxiety disorders/ or agoraphobia/ or neurocirculatory asthenia/ or obsessive-compulsive disorder/ or obsessive hoarding/ or panic disorder/ or phobic disorders/ or stress disorders, traumatic/ or combat disorders/ or stress disorders, post-traumatic/ or stress disorders, traumatic, acute/ or anxiety/ or anxiety, castration/ or koro/ or anxiety, separation/ or panic/ or exp anti-anxiety agents/ or somatoform disorders/ or body dysmorphic disorders/ or conversion disorder/ or hypochondriasis/ or neurasthenia/ or hysteria/ or munchausen syndrome by proxy/ or munchausen syndrome/ or fatigue syndrome, chronic/ or obsessive behavior/ or compulsive behavior/ or behavior, addictive/ or impulse control disorders/ or firesetting behavior/ or gambling/ or trichotillomania/ or stress, psychological/ or burnout, professional/ or sexual dysfunctions, psychological/ or vaginismus/ or Anhedonia/ or Affective Symptoms/ or *Mental Disorders/	
2	(eating disorder* or anorexia nervosa or bulimi* or binge eat* or (self adj (injur* or mutilat*)) or suicide* or parasuicid* or mood disorder* or affective disorder* or bipolar i or bipolar ii or (bipolar and (affective or disorder*)) or mania or manic or cyclothymic* or depression or depressive or dysthymi* or neurotic or neurosis or adjustment disorder* or antidepress* or anxiety disorder* or agoraphobia or obsess* or compulsi* or panic or phobi* or ptsd or posttrauma* or post trauma* or combat or somatoform or somati#ation or medical* unexplained or body dysmorphi* or conversion disorder or hypochondria* or neurastheni* or hysteria or munchausen or chronic fatigue* or gambling or trichotillomania or vaginismus or anhedoni* or affective symptoms or mental disorder* or mental health).ti,kf.	66956
3	or/1-2	114903
4	phosphatidylserines/	59
5	phosphatidylserine.tw.	230
6	Efalex*.tw.	4
7	PCSO-524*.tw.	17
8	Vayarin*.tw.	3
9	Virtiva*.tw.	1
10	Lyprinol*.tw.	17
11	or/4-10	272
12	3 and 11	5
13	exp animals/ not humans.sh.	2999



14	12 not 13	5
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### Search 9. Search strategy for EMBASE (via Embase.com)

1	'mental health'/exp	243362
2	'mood disorders'/exp	700881
3	'mental disorder*':ti	13407
4	'mental illness':ti,ab	47438
5	((serious* OR sever*) NEXT/2 mental* NEXT/2 (ill* OR disorder*)):ti,ab	18299
6	'schizophrenia'/exp	220914
7	schizophreni*:ab,ti	194662
8	'bipolar disorder'/exp	90997
9	((bipolar OR 'bi polar') NEXT/3 (disorder* OR depress* OR ill*)):ti,ab	64109
10	'psychotic disorders'/exp	354143
11	psychotic*:ti,ab OR psychosis:ti,ab OR psychoses:ti,ab	119389
12	schizoaffective:ti,ab OR 'schizo affective':ti,ab	10129
13	hypomania*:ti,ab OR mania*:ti,ab OR manic:ti,ab	30434
14	'anxiety':ti,ab	374516
15	'depressive disorder'/exp	651917
16	'depression'/exp OR 'chronic depression'/exp OR 'dysthymia'/exp OR 'adjustment disorder'/exp OR 'affective psychosis'/exp	655401
17	'depress*':ab,ti OR 'melancholia*':ab,ti OR 'adjustment disorder*':ab,ti OR 'disorder*, adjustment':ab,ti OR 'reactive disorder*':ab,ti OR 'disorder*, reactive*':ab,ti OR 'transient situational disturbance*':ab,ti OR 'affective disorder*, psychotic':ab,ti OR 'psychoses, affective':ab,ti OR 'affective psychoses':ab,ti OR 'psychotic affective disorder*':ab,ti OR 'disorder*, psychotic affective':ab,ti OR 'psychotic mood disorder*':ab,ti OR 'mood disorder*, psychotic':ab,ti OR 'dysthymic disorder':ab,ti OR 'adjustment reaction':ab,ti OR 'transient situational disorder':ab,ti OR 'patient health questionnaire-9':ab,ti OR 'hamd':ab,ti OR 'bdi':ab,ti OR 'sds':ab,ti OR 'dsi':ab,ti OR 'madr':ab,ti OR 'phq-9':ab,ti OR 'hds':ab,ti	882115
18	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17	1747411
19	'phosphatidylserine'/exp	20103
20	'phosphatidylserine':ti,ab	20235
21	'efalex*':ti,ab	4
22	'pcso-524*':ti,ab	15

23	'vayarin*':ti,ab	3
24	'virtiva*':ti,ab	1
25	'lyprinol*':ti,ab	50
26	#19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25	26420
27	'drug therapy'/exp	3560327
28	'treatment response'/exp	344266
29	'treatment outcome'/exp	2333232
30	'drug efficacy'/exp	1033650
31	'outcome assessment'/exp	897000
32	#27 OR #28 OR #29 OR #30 OR #31	5968244
33	#18 AND #26 AND #32	52
34	[animals]/lim NOT [humans]/lim	6405800
35	#33 NOT #34	47

### Search 10. Search strategy for PSYCINFO (via EBSCO)

1	(MA "Mental Health")	41899
2	(MA "Mental Disorders")	81288
3	(MA "Depression")	58329
4	(MA "Anxiety Disorders")	20487
5	(MA "Stress Disorders, Post-Traumatic") OR (MA "Anxiety Disorders") OR (MA "Obsessive-Compulsive Disorder")	47446
6	(MA "Schizophrenia")	58776
7	(MA "Psychotic Disorders")	23842
8	(MA "Eating Disorders")	7832
9	(MA "Gambling")	3918
10	(MA "Alcohol-Related Disorders") OR (MA "Alcohol-Induced Disorders, Nervous System") OR (MA "Alcoholism")	30692
11	(MA "Binge Drinking")	1098
12	(MA "Substance Use Disorders")	168135
13	(MA "Affective Disorders")	1343
14	(MA "Bipolar Disorder")	24120
15	TI ( mental health or mental illness* or mentally ill or mental disorder* or depression or depressive or anxiety or problem drinking or alcoholism or binge drinking or schizophrenia or schizophrenic or psychosis or psychotic or obsessive compulsive or eating disorder* or bulimi* or anorexi* or gambling or post-traumatic stress or PTSD or substance abuse ) OR AB ( mental health or mental illness* or mentally ill or mental disorder* or depression or depressive or anxiety or problem drinking or alc ...	949883

16	TI ( ((drinking or alcohol) N2 (disorder or binge or binges or binging)). ) OR AB ( ((drinking or alcohol) N2 (disorder or binge or binges or binging)). )	20593
17	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16	1025457
18	MA phosphatidylserine	93
19	TI (phosphatidylserine) OR AB (phosphatidylserine)	210
20	TI (Efalex) OR AB (Efalex)	0
21	TI (PCSO-524) OR AB (PCSO-524)	3
22	TI (Vayarin) OR AB (Vayarin)	0
23	TI (Virtiva) OR AB (Virtiva)	1
24	TI (Virtiva) OR AB (Virtiva)	0
25	TI (Lyprinol) OR AB (Lyprinol)	0
26	S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25	245
27	S17 AND S26	32