

# Vitaminer, mineraler og andre kosttilskudd i behandlingen av personer med psykiske lidelser

Notat  
Litteratursøk med sortering  
2009

 kunnskapssenteret

**Bakgrunn:** Nasjonalt kunnskapssenter for helsetjenesten fikk i oppdrag fra HelseDirektoratet å foreta en gjennomgang av internasjonal forskning om effekten av mineraler og vitaminer i behandlingen av mennesker med psykiske lidelser. **Metode:** Vi søkte i databasene OVID MEDLINE, OVID PsycInfo, Cochrane Library. Søket inneholdt termer for psykiske lidelser, vitaminer, mineraler, fiskeolje, diett, terapi og tilskudd. I MEDLINE og EMBASE ble søket avgrenset med søkefilter for systematiske oversikter. Avgrensningen i tid ble satt til fra og med 2004. Det ble også søkt etter retningslinjer. **Resultat:** Vi satt igjen med 29 referanser som vi vurderte som svært sannsynlig relevante treff. Hvis man skal være helt sikker på at de treffer våre inklusjonskriterier må referansematerialet innhentes og leses i fulltekst, men det har vi ikke gjort i dette notatet. Referansematerialet skal nå innhentes og kvalitetssikres og det vil danne grunnlaget for en full kunnskapsoppsummering.

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Nasjonalt kunnskapssenter for helsetjenesten fremskaffer og formidler kunnskap om effekt av metoder, virkemidler og tiltak og om kvalitet innen alle deler av helsetjenesten. Målet er å bidra til gode beslutninger slik at brukerne får best mulig helsetjenester. Senteret er formelt et forvaltningsorgan under Helsedirektoratet, uten myndighetsfunksjoner. Kunnskapssenteret kan ikke instrueres i faglige spørsmål.

Kunnskapssenteret vil takke bibliotekar Hege Sletsjøe i Helsedirektoratet for å ha bidratt med sin ekspertise i dette prosjektet. Kunnskapssenteret tar det fulle ansvaret for synspunktene som er uttrykt i rapporten.

Nasjonalt kunnskapssenter for helsetjenesten  
Oslo, 03.11.2009

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# Oppsummering

Hva er effekten av å bruke kosttilskudd som vitaminer, mineraler og omega-3 i behandlingen av personer med psykiske lidelser?

Nasjonalt kunnskapssenter for helsetjenesten har publisert et notat der grunnlaget er et systematisk og omfattende søk i databasene Cochrane Library, MEDLINE og EMBASE. Søket resulterte totalt i 1831 treff. To personer leste gjennom tittel og sammendrag uavhengig av hverandre. Vi inkluderte 29 referanser i henhold til fastsatte inklusjonskriterier og sorterte disse referansene ut fra to ulike innfallsvinkler, pasientpopulasjon og tiltak. Sammendraget (originale abstract) av hver enkelt oversikt er presentert. Vi har ikke vurdert den metodologiske kvaliteten av oversiktene og minner derfor om at vi har tilgjengelige sjekklister for å vurdere kvaliteten: <http://kunnskapssenteret.no/Verktøy/2031.cms>.

Denne kartleggingen av forskningspublikasjoner viser hva som finnes av oppsummert forskning om en eventuell behandlingseffekt av vitaminer, mineraler, omega 3/6 og andre kosttilskudd for personer med psykiske lidelser.

Oversiktene vi henviser til er ikke nødvendigvis systematiske eller av høy kvalitet. Dette er en svakhet, og det betyr at man bør kritisk vurdere kunnskapen vi henviser til før den eventuelt tas i bruk.

# INNHold

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# Forord

Nasjonalt kunnskapssenter for helsetjenesten fikk i oppdrag fra Helsedirektoratet å foreta en gjennomgang av internasjonal forskning om effekten av mineraler og vitaminer i behandlingen av mennesker med psykiske lidelser. I dette notatet viser vi frem oversiktsartikler som vi har identifisert via et litteratursøk. Vi har ikke vurdert kvaliteten på oversiktene eller forsøkt å sammenstille kunnskapen.

Når forskningsfunn benyttes som beslutningsgrunnlag, bør det tas utgangspunkt i tilgjengelig forskning med best mulig kvalitet. Studiedesign, utførelse og analyser påvirker vår tillit til studienes resultat. I dette arbeidet har vi ikke lest artiklene i fulltekst eller vurdert den metodiske kvaliteten av dem. I vedlegget til Kunnskapssenterets håndbok "Slik oppsummerer vi forskning" finnes det sjekklister som kan brukes til å vurdere kvaliteten av ulike typer studier. Sjekklistene kan være gode hjelpemidler i det videre arbeidet med å ta stilling til forskningens kvalitet, herunder gyldighet og troverdighet. Håndboken med sjekklister er tilgjengelig på nettsiden til Kunnskapssenteret <http://www.kunnskapssenteret.no/Verkt%C3%B8y/2139.cms>.

Dette dokumentet er ment å gi en oversikt over forskningslitteraturen om effekter av kosttilskudd for personer med psykiske lidelser. Vi håper at det vil gjøre det enklere å fatte velinformerte beslutninger i det videre arbeidet med å lage retningslinjer, bestille ny norsk forskning, eller utføre kunnskapsoppsummeringer om effekter av tiltak for å behandle psykiske lidelser.

Gro Jamtvedt  
Avdelingsdirektør

Geir Smedslund  
Seniorforsker og *Fung. forskningsleder*

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# Innledning

Personer som ikke får nok vitaminer og mineraler gjennom sitt vanlige kosthold får gjerne råd om å ta kosttilskudd. Kvinner bør ta folsyre (vitamin B<sub>9</sub>) før, og under, graviditet for å sikre normal utvikling av fosteret og for å selv ikke utvikle mangelsykdom. Det er kjent at vitaminmangel over tid kan føre til en rekke mangelsykdommer, slik som skjorbuk ved vitamin C mangel. Ved store blodtap trenger pasienter jerntilskudd og/eller får beskjed om å spise matprodukter med høyt jerninnhold. Dersom man ikke får nok effekt av å spise riktig mat, tar man gjerne ekstra tilskudd i form av piller eller pulver.

Ved kronisk sykdom får mange i seg for lite vitaminer og/eller mineraler. For å unngå at det utvikles tilleggssykdom, testes pasientene for mangler slik at man eventuelt kan vurdere kostholdstiltak eller kosttilskudd. Personer med psykiske lidelser kan også få i seg for lite vitamin og/eller mineraler. Disse kan få tilbud om å teste for mangler og ut vurderes kostholdsveiledning og ved behov kosttilskudd. Det er derimot usikkert om hvorvidt slike kosttilskudd også kan påvirke personens psykiske lidelse.

Kunnskapssenterets arbeidsform er å først og fremst å lete etter gode og oppdaterte systematiske oversikter som besvarer spørsmål om effekt(er) av tiltak. Årsaksspørsmål om psykiske lidelser eller spørsmål om sammenhenger mellom kosthold og utvikling av psykisk lidelser er utenfor vårt mandat å besvare. I tillegg til å systematisk søke frem kunnskap om effekt av tiltak på denne utvalgte populasjonen og intervensjonen, kan vi kritisk vurdere og re-analysere andres forskningsfunn for slik å si noe om det totale kunnskapsbildet. Hvis vi ikke finner eksisterende systematiske oversikter om dette temaet kan Kunnskapssenteret påta seg å lage en.

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## PROBLEMSTILLING

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Kan kosttilskudd i form av vitaminer og mineraler føre til en bedret psykisk helse hos personer med psykiske lidelser?

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# Metode

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## LITTERATURSØK

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Vi søkte etter systematiske oversikter om effekten av vitaminer, mineraler, og/eller kosttilskudd til personer med psykiske lidelser. Vi søkte i databasene OVID MEDLINE, OVID PsycInfo, Cochrane Library, herunder HTA-rapporter og DARE-rapporter. Søket inneholdt termer for psykiske lidelser, vitaminer, mineraler, fiskeolje, diett, terapi og tilskudd. I MEDLINE og EMBASE ble søket avgrenset med søkefilter for systematiske oversikter. Avgrensningen i tid ble satt til fra og med 2004. Det ble også søkt etter retningslinjer. Detaljert søkestrategi er gjengitt i vedlegget bakerst. I tillegg ble det søkt etter retningslinjer.

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## INKLUSJONSKRITERIER

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Etter en gjennomgang av titler og sammendrag, laget vi en liste over mulig relevante referanser. Listen over ekskluderte referanser er tilgjengelig i arkivet til Kunnskaps-senteret. Fullstendig liste over inkluderte referanser er tilgjengelig i referanselisten, bakerst i rapporten. Komparator, eller type sammenligningstiltak, og situasjonell ramme slik som primærforebygging, spesialisthelsetjenestenivå, institusjon eller lignende var ikke forhåndsdefinert og ble derfor ikke inklusjonskriterier. Kriteriene for å anses som mulig relevant var en eksplisitt bruk (enten i tittel, keyword eller sammendrag) av ord som eksempelvis:

- Systematisk oversikt (eksplisitt søkestrategi, valide kriterier for kvalitetsbedømmelse, og oppsummering av effekter/meta-analyser)

OG

- Vitamin, eller mineral, eller kosttilskudd

OG

- Psykiske lidelser

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## UTVELGELSE OG SORTERING

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Etter at referansene var identifisert som mulig relevante publikasjoner sorterte vi dem i følgende to hovedkategorier:

- 1) Type kosttilskudd, vitaminer eller mineraler og
- 2) Type psykisk lidelse/diagnose



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# Resultat

Bibliotekar Hege Sletsjøe i Helsedirektoratet utførte litteratursøket etter systematiske oversikter den 29. september 2009. Søket ga 612 treff i MEDLINE, 1383 treff i Embase og 28 treff i Cochrane-databasene. Etter duplikatsjekk var det 1813 referanser hvorav 1766 ble ekskludert som åpenbart irrelevant. Vi satt igjen med 29 referanser som vi vurderte som svært sannsynlig relevante treff. Hvis man skal være helt sikker på at de treffer våre inklusjonskriterier må referansematerialet innhentes og leses i fulltekst, men det har vi ikke gjort i dette notatet. I tabellene nedenfor er referanser til mulige oversiktsartikler listet opp. Vi minner om at de kan ha varierende kvalitet og k utdatert. Vi har ikke lest artiklene i fulltekst eller vurdert den metodiske kvaliteten. Ut fra tittel og sammendrag sorterte vi referansene både i forhold til ulike tiltak og pasientpopulasjonene.

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**TABELL 1: REFERANSER SORTERT ETTER TILTAK**

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Tiltak	Antall referanser
<b>Vitaminer, folat/folsyre, inositol, tryptofan (1-4)</b>	4
<b>Mineraler (5)</b>	1
<b>Fiskeoljer, omega 3/6 fettsyrer, (6-21)</b>	16
<b>Uklart hva tiltaket var, eller flere av tiltakene nevnt ovenfor er kombinert (22-29)</b>	8

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**TABELL 2: REFERANSER SORTERT ETTER DIAGNOSE**

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Diagnose	Antall referanser
<b>Angst, depresjon, borderline, stemningslidelser, manisk, affektiv (1-7;9;11;14;18;20-23;25-27)</b>	18
<b>Bipolar, schizofreni (10;12;13;17;19;24)</b>	6
<b>Spiseforstyrrelser</b>	0
<b>Uklart hvilken diagnose det gjaldt, eller kombinasjon av flere av de ovenfor nevnte diagnoser (8;15;16;28;29)</b>	5

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# Diskusjon

Vi søkte ikke etter komplementære eller alternative (CAM) tiltak slik som akupunktur, urter, blomster, krydder eller røtter. Vi søkte heller ikke etter kunnskapsoppsummeringer om populasjoner med atferds-og/eller utviklingsforstyrrelser. Hukommelses- og/eller lærevansker var utenfor vår problemstilling og oversikter om dette ble det ikke søkt etter. Alzheimer og AD/HD var diagnosegrupper som var fremtredende i søkeresultatet. Det finnes en rekke somatiske lidelser tilknyttet vitamin- og/eller mineralmangler, men disse har vi ikke gått inn i her. Personer med psykiske lidelser har også en somatisk helse, og i behandlingen av denne vil det av og til være behov for kostholdstiltak- og veiledning, men vi har bare sett etter kunnskap der kostholdstiltak benyttes for personer med psykiske lidelser i behandlingen av den psykiske diagnosen.

Vi søkte ikke etter enkeltstudier og kan derfor ikke si noe om dette er et forskningsfelt hvor det fremdeles publiseres nye randomiserte kontrollerte studier. Vi søkte ikke eksplisitt etter bivirkninger eller rapporter om uønskede hendelser. Slik kunnskap er selvsagt særlig viktig for pasienter å være klar over når de deltar i beslutninger om å igangsette tiltak. Økonomiske og etiske hensyn er ikke vurdert. Dette bør gjøres hvis man skal lage en fullstendig kunnskapsoppsummering.

Oversiktene vi henviser til er ikke nødvendigvis systematiske eller av høy kvalitet. Dette er en svakhet, og det betyr at man bør kritisk vurdere kunnskapen vi henviser til før den eventuelt tas i bruk.

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# Referanser

1. Frazer CJ, Christensen H, Griffiths KM. Effectiveness of treatments for depression in older people. *Med J Aust* 2005;182(12):627-32.  
Abstract: Objective: To conduct a systematic review of the evidence for the effectiveness of a range of possible-treatments for depression in older people. Data sources: Literature search using the PubMed, PsycInfo and Cochrane Library databases. Data synthesis: Treatments that have been suggested to be effective for depression were grouped under three categories: medical treatments, psychological treatments, and lifestyle changes/alternative treatments. We describe each treatment, review the studies of its effectiveness in people aged [greater-than or equal to] 60 years, and give a rating of the level of evidence. Conclusions: The treatments with the best evidence of effectiveness are antidepressants, electroconvulsive therapy, cognitive behaviour therapy, psychodynamic psychotherapy, reminiscence therapy, problem-solving therapy, bibliotherapy (for mild to moderate depression) and exercise. There is limited evidence to support the effectiveness of transcranial magnetic stimulation, dialectical behaviour therapy, interpersonal therapy, light therapy (for people in nursing homes or hospitals), St John's wort and folate in reducing depressive symptoms
2. Taylor MJ, Wilder H, Bhagwagar Z, Geddes J. Inositol for depressive disorders. *Cochrane Database Syst Rev* 2004;(2):CD004049.  
Abstract: BACKGROUND: There are a number of effective interventions for the treatment of depression. It is possible that the efficacy of these treatments will be improved further by the use of adjunctive therapies such as inositol. OBJECTIVES: 1. To determine the effectiveness of inositol in the treatment of depression. 2. To determine the adverse effects and acceptability of treatment with inositol. SEARCH STRATEGY: The Cochrane Controlled Trials Register (CTTR), The Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Register (CCDANCTR) incorporating results of group searches of EMBASE, MEDLINE, LILACS, CINAHL, PSYINDEX and PsycLIT were searched. Reference lists of relevant papers and major textbooks of affective disorder were checked. Experts in the field and pharmaceutical companies were contacted regarding unpublished material. SELECTION CRITERIA: All randomised controlled trials that compare treatment with inositol, whether as monotherapy or adjunctive therapy, to an alternative treatment, whether another antidepressant medication or placebo, for patients with a diagnosis of depressive disorder (diagnosed according to explicit criteria). DATA COLLECTION AND ANALYSIS: Data were independently extracted from the original reports by two reviewers. Statistical analysis was conducted using Review Manager version 4.2.1. MAIN RESULTS: Four trials were identified, with a total of 141 participants. These were short term trials of double-blind design. The trials did not show clear evi-

dence of a therapeutic benefit, nor any evidence of poor acceptability. REVIEWERS' CONCLUSIONS: It is currently unclear whether or not inositol is of benefit in the treatment of depression. Ongoing studies should reduce this uncertainty. [References: 23]

3. Taylor MJ, Carney SM, Goodwin GM, Geddes JR. Folate for depressive disorders: systematic review and meta-analysis of randomized controlled trials. *J Psychopharmacol* 2004;18(2):251-6.

Abstract: The objective of this review was to determine the effectiveness, adverse effects and acceptability of folate in the treatment of depression. Electronic databases (Cochrane Controlled Trials Register and the Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Register) and reference lists were searched, and authors, experts and pharmaceutical companies contacted to identify randomized controlled trials that compared treatment with folic acid or 5'-methyltetrahydrofolic acid to an alternative treatment, for patients with a diagnosis of depressive disorder. Three randomized trials (247 participants) were included. Two studies assessed the use of folate in addition to other treatment, and found that adding folate reduced Hamilton Depression Rating Scale (HDRS) scores on average by a further 2.65 points [95% confidence interval (CI) 0.38-4.93]. Fewer patients treated with folate experienced a reduction in their HDRS score of less than 50% at 10 weeks (relative risk 0.47, 95% CI 0.24-0.92). The remaining study found no statistically significant difference when folate alone was compared with trazodone. The identified trials did not find evidence of any problems with the acceptability or safety of folate. The limited available evidence suggests folate may have a potential role as a supplement to other treatment for depression. It is currently unclear if this is the case both for people with normal folate levels, and for those with folate deficiency. [References: 28]

4. Williams A-L, Cotter A, Sabina A, Girard C, Goodman J, Katz DL. The role for vitamin B-6 as treatment for depression: A systematic review. *Fam Pract* 2005;22(5):532-7.

Abstract: Background. Major depression is the leading cause of disability worldwide, and among the 10 most frequent indications for using alternative medicine therapies, especially dietary supplements. Objective. To assess the evidence evaluating vitamin B-6 supplementation as treatment for depression. Methods. Medline, Psycinfo, AMED, and Cochrane Controlled Trials Register were searched from database inception through September 2001. All randomized controlled trials, controlled clinical trials, intervention studies, case-control studies, reviews, and case reports examining the evidence behind vitamin B-6 in depression among humans were selected. No limits were placed for demographics or co-morbidities. Only English language papers were abstracted and assessed for trial quality. Two abstractors independently evaluated each study, then reconciled findings. As data were available, between group treatment effect size was noted or, as needed, calculated. When studies reported outcome effects using multiple measures, data were abstracted to permit the greatest possible comparisons among papers. Results. Ten articles met inclusion criteria; three reviews, one case report, five RCTs, and one intervention study. There was no common outcome measure among all studies, eliminating opportunity for direct comparison of effect sizes. As an alternate means of comparison, effects were plotted as they related to the null hypothesis. Conclusion. Viewed as a whole, meaningful treatment effect of vitamin B-6 for depression in general was not apparent. However, examination of papers addressing depression in premenopausal women only, reveals a consistent message about the value of using vitamin B-6 supplementation. Further study of vitamin B-6 as independent and adjuvant therapy for hormone related depression in women is indicated. copyright The Author (2005). Published by Oxford University Press. All rights reserved

5. Parslow R, Morgan AJ, Allen NB, Jorm AF, O'Donnell CP, Purcell R. Effectiveness of complementary and self-help treatments for anxiety in children and adolescents. *Med J Aust* 2008;188(6):355-9.

**Abstract:** **Objective:** To review the evidence for the effectiveness of complementary and self-help treatments for anxiety disorders and situational anxiety in children and adolescents. **Data sources:** Systematic literature search using PubMed, PsycINFO and the Cochrane Library for 111 treatments up to February 2006. **Study selection:** There were 11 treatments for which intervention studies had been undertaken and reported. **Data extraction:** Studies on each treatment were reviewed by one author and checked by a second. A consensus was reached for level of evidence. **Data synthesis:** Relevant evidence was available for bibliotherapy, dance and movement therapy, distraction techniques, humour, massage, melatonin, relaxation training, autogenic training, avoiding marijuana, a mineral-vitamin supplement (EMPower +) and music therapy. Findings from case-control studies, individual cohort studies or low quality randomised controlled trials indicated that several treatments may have potential to reduce anxiety, including bibliotherapy, massage, melatonin, and relaxation training. **Conclusions:** Although some complementary and self-help treatments might be useful for children and adolescents with anxiety, they need to be tested adequately through randomised controlled trials before they could be recommended

6. Abraham PF, Calabrese JR. Evidenced-based pharmacologic treatment of borderline personality disorder: A shift from SSRIs to anticonvulsants and atypical antipsychotics? *J Affect Disord* 2008;111(1):21-30.

**Abstract:** **Objective:** The authors performed a review of double-blind, controlled studies of psychotropic drugs to evaluate the evidence base supporting their use in treatment of borderline personality disorder. **Methods:** English language literature cited in Medline and published between 1970 and 2006 was searched using the following terms: anticonvulsants, antidepressants, antipsychotics, anxiolytics, benzodiazepines, borderline personality disorder, lithium, medication, mood stabilizers, pharmacotherapy, and psychotropics. Only reports of double-blind, randomized, controlled trials were included. **Results:** Twenty eight double-blind, randomized, controlled trials were identified which included anticonvulsants, classical neuroleptics, the benzodiazepine alprazolam, lithium, monoamine oxidase inhibitors, the novel antipsychotic olanzapine, selective serotonin reuptake inhibitors, tricyclic antidepressants, and omega-3 fatty acids. All but three were placebo-controlled. With the exception of alprazolam and tricyclics, the data from these trials revealed evidence of improvements, although often circumscribed and variable. The novel antipsychotic olanzapine appeared to have the most empirical support for having a favorable effect on borderline personality disorder. **Conclusion:** A growing body of data suggests that there are psychotropic agents which appear to be well tolerated, and which to varying degrees may be expected to ameliorate the domains of psychopathology associated with borderline personality disorder. The research literature, on which practice should be optimally based, appears to suggest a need for a shift from antidepressants to anticonvulsants and atypical antipsychotics. copyright 2008 Elsevier B.V. All rights reserved

7. Appleton KM, Hayward RC, Gunnell D, Peters TJ, Rogers PJ, Kessler D, et al. Effects of n-3 long-chain polyunsaturated fatty acids on depressed mood: systematic review of published trials. *Am J Clin Nutr* 2006;84(6):1308-16.

**Abstract:** **BACKGROUND:** Greater dietary intakes of n-3 long-chain polyunsaturated fatty acids (n-3 PUFAs) may be beneficial for depressed mood. **OBJECTIVE:** This study aimed to systematically review all published randomized controlled trials investigating the effects of n-3 PUFAs on depressed mood. **DESIGN:** Eight medical and health databases were searched over all years of records until June 2006 for trials that exposed participants to n-3 PUFAs or fish, measured depressed mood, were conducted on human participants, and included a comparison group. **RESULTS:** Eighteen randomized controlled trials were identified; 12 were included in a meta-analysis. The pooled standardized difference in mean

outcome (fixed-effects model) was 0.13 SDs (95% CI: 0.01, 0.25) in those receiving n-3 PUFAs compared with placebo, with strong evidence of heterogeneity ( $I^2 = 79\%$ ,  $P < 0.001$ ). The presence of funnel plot asymmetry suggested that publication bias was the likely source of heterogeneity. Sensitivity analyses that excluded one large trial increased the effect size estimates but did not reduce heterogeneity. Meta-regression provided some evidence that the effect was stronger in trials involving populations with major depression—the difference in the effect size estimates was 0.73 (95% CI: 0.05, 1.41;  $P = 0.04$ ), but there was still considerable heterogeneity when trials that involved populations with major depression were pooled separately ( $I^2 = 72\%$ ,  $P < 0.001$ ). CONCLUSIONS: Trial evidence that examines the effects of n-3 PUFAs on depressed mood is limited and is difficult to summarize and evaluate because of considerable heterogeneity. The evidence available provides little support for the use of n-3 PUFAs to improve depressed mood. Larger trials with adequate power to detect clinically important benefits are required. [References: 50]

8. Clayton EH, Hanstock TL, Garg ML, Hazell PL. Long chain omega-3 polyunsaturated fatty acids in the treatment of psychiatric illnesses in children and adolescents. *Acta Neuropsychiatrica* 2007;19(2):92-103.

Abstract: Objective: Long chain omega-3 polyunsaturated fatty acids (LCn-3PUFA) are in increasing use in the general population to treat health problems. The objective of the current article is to review the evidence for the rationale and benefit of LCn-3PUFA in the treatment of common psychiatric disorders in children and adolescents. Methods: A search of Psychlit, PubMed and Cochrane Databases was conducted using the terms child, adolescent, bipolar, depression, psychosis, first-episode psychosis, schizophrenia, attention deficit hyperactivity disorder (ADHD), autism, psychiatric, omega-3, n-3, docosahexaenoic acid and eicosapentaenoic acid. Further studies were identified from the bibliographies of published reviews. Results: One small randomized controlled trial with LCn-3PUFA supplementation in depression in children found a small beneficial effect over placebo. Four placebo-controlled trials showed uncertain benefit of LCn-3PUFA for ADHD. Single placebo-controlled trials showed no benefit in autism or bipolar disorder. There is an absence of studies examining benefit for first-episode psychosis or schizophrenia in children and adolescents. Conclusions: While children and adolescents are receiving LCn-3PUFA for a range of psychiatric indications, there is only evidence of likely benefit for unipolar depression. copyright 2007 The Authors

9. Freeman MP. Omega-3 fatty acids and perinatal depression: A review of the literature and recommendations for future research. *Prostaglandins Leukot Essent Fatty Acids* 2006;75(4-5):291-7.

Abstract: Introduction: Perinatal depression refers to major depression in the context of pregnancy and postpartum. In consideration of its prevalence and consequences, the treatment and prevention of perinatal depression should be important public health priorities. Omega-3 fatty acids are attractive for consideration in perinatal women, due to known health benefits for the mother and baby. Anti-depressant medications may pose risks in utero and in breastfeeding. Methods: MEDLINE and manual searches were conducted. Results: Epidemiological and preclinical data support a role of omega-3 fatty acids in perinatal depression. Two studies failed to support a role of omega-3 fatty acids for postpartum depression prophylaxis, although one included a small sample, and the other utilized a low dosage. Two pilot studies suggest good tolerability and potential efficacy in the acute treatment of perinatal depression. Conclusions: Further research studies are warranted to determine the role of omega-3 fatty acids in the treatment of perinatal depression. copyright 2006 Elsevier Ltd. All rights reserved

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rane Database of Systematic Reviews 2006 Issue 3. Chichester (UK): John Wiley & Sons, Ltd; 2006.

**Abstract:** **BACKGROUND:** Limited evidence supports a hypothesis suggesting that the symptoms of schizophrenia may be the result of altered neuronal membrane structure and metabolism. The structure and metabolism is dependent on blood plasma levels of certain essential fatty acids and their metabolites. **OBJECTIVES:** To assess the effects of polyunsaturated fatty acids for people with schizophrenia. **SEARCH STRATEGY:** We have updated the initial searches of 1998, 2002 and 2005 with a search of the Cochrane Schizophrenia Group's Register, November 2008, which is based on regular searches of CINAHL, EMBASE, MEDLINE and PsycINFO. Where necessary, we contacted authors and relevant pharmaceutical companies for additional information. **SELECTION CRITERIA:** We included all randomised controlled trials of polyunsaturated fatty acid treatment for schizophrenia. **DATA COLLECTION AND ANALYSIS:** Working independently, we selected studies for quality assessment and extracted relevant data. We analysed on an intention-to-treat basis. Where possible and appropriate we calculated the Relative Risk (RR) and their 95% confidence intervals (CI) and estimated the number needed to treat (NNT). For continuous data we calculated weighted mean differences (WMD) and their 95% confidence intervals. We also inspected the data for heterogeneity. **MAIN RESULTS:** Eight studies are now included in this review. When any dose omega-3 (E-EPA or EPA) is compared with placebo, small short trials suggest that the need for neuroleptics appears to be reduced for people allocated omega-3 supplementation (n=30, 1 RCT, RR 0.73 CI 0.54 to 1.00) and mental state may improve (n=30, 1 RCT, RR not gaining 25% change in PANSS scores 0.54 CI 0.30 to 0.96, NNT 3 CI 2 to 29). There are no differences in the number of people leaving the study early (n=595, 6 RCTs, RR 0.86 CI 0.50 to 1.48). There are few data on the comparison of any dose omega-6 (GLA) with placebo. For movement disorder outcomes, the one small study we found does not show any difference for average short-term endpoint AIMS score (n=16, 1 RCT, WMD 1.30 CI -1.96 to 4.56). When any dose omega-3 (E-EPA or EPA) is compared with any dose omega-3 (DHA) there is no significant difference for mental state outcome of not gaining 25% change in PANSS scores (n=31, 1 RCT, RR 0.66 CI 0.39 to 1.11). When different doses of omega-3 (E-EPA) are compared with placebo there are no differences in measures of global and mental state between the studies. For the outcome of 'experiencing at least one adverse effect' no differences between groups are found for any dose (1 g/day E-EPA vs placebo n=63, 1 RCT, RR 0.97 CI 0.60 to 1.56; 2 g/day E-EPA vs placebo n=63, 1 RCT, RR 0.67 CI 0.37 to 1.20; 4 g/day E-EPA vs placebo n=58, 1 RCT, RR 1.15 CI 0.72 to 1.82). **AUTHORS' CONCLUSIONS:** Three updates of this review have resulted in more included studies and more people randomised but still relatively little useful additional data. The results remain inconclusive. The new trials all compare the omega-3 polyunsaturated fatty acids, in particular eicosapentaenoic acid and its ester, ethyl-eicosapentaenoic acid. The use of omega-3 polyunsaturated fatty acids for schizophrenia still remains experimental and this review highlights the need for large, well designed, conducted and reported studies. **POLYUNSATURATED FATTY ACID SUPPLEMENTATION FOR SCHIZOPHRENIA:** Schizophrenia is a serious, chronic and relapsing mental illness with a worldwide lifetime prevalence of approximately one per cent. Early research suggests dietary supplementation with essential fatty acids (EFAs) may have a positive effect on the symptoms of schizophrenia. We systematically reviewed the effects of EFA supplementation for those suffering from schizophrenia. We included eight studies involving 517 people. Results show one particular type of EFA, ethyl-eicosapentaenoic acid (an omega-3 EFA) may have a positive effect on mental state but, at the moment, results are inconclusive due to the limited number of studies and lack of usable data within these studies

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**Abstract:** Objective: Evidence has indicated an association between depression and low dietary intake of omega-3 polyunsaturated fatty acids (PUFAs). However, clinical trials examining the therapeutic benefit of omega-3 PUFAs in depression showed inconsistent results. The goal of this study is to systematically evaluate the antidepressant efficacy of omega-3 PUFAs by using meta-analytic method. Data Sources: MEDLINE, Embase, and PsycINFO databases were searched from 1966 through August 2006 using the key words (depression OR depressive disorder OR mood disorder) AND (omega-3 OR EPA OR DHA OR polyunsaturated fatty acid OR fish oil). The search was limited to literature in English and clinical trials. Study Selection: Ten double-blind, placebo-controlled studies in patients with mood disorders receiving omega-3 PUFAs with the treatment period lasting 4 weeks or longer were included. Data Extraction: Effect size (ES) of each individual study was derived by computing the standardized mean difference. A random-effects model was used to pool the ESs of all included studies. Data Synthesis: When pooling the results of 10 included studies (N = 329), we found a significant antidepressant effect of omega-3 PUFAs (ES = 0.61, p = .003). Likewise, omega-3 PUFAs significantly improved depression in patients with clearly defined depression (ES = 0.69, p = .002) or with bipolar disorder (ES = 0.69, p = .0009). The dosage of eicosapentaenoic acid (EPA) did not change the antidepressant efficacy significantly. However, significant heterogeneity among these studies and publication bias were noted. Conclusions: Although our meta-analysis showed significant antidepressant efficacy of omega-3 PUFAs, it is still premature to validate this finding due to publication bias and heterogeneity. More large-scale, well-controlled trials are needed to find out the favorable target subjects, therapeutic dose of EPA, and the composition of omega-3 PUFAs in treating depression

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**Abstract:** Several lines of evidence suggest that omega-3 fatty acids may be important in the pathophysiology, treatment or prevention of bipolar disorder (BD). Electronic and manual searches were conducted in order to review the literature relevant to the etiology and treatment of BDs with omega-3 fatty acids. We also present data from a randomized, double-blind, placebo-controlled pilot study conducted at three sites (N=10) comparing an omega-3 fatty acid (docosahexaenoic acid, DHA) versus placebo, added to psychosocial treatment for women with BD who chose to discontinue standard pharmacologic treatment while attempting to conceive. While some epidemiologic and preclinical data support the role of omega-3 fatty acids in BD, clinical trials to date have yielded conflicting results. In our pilot study of 10 Caucasian women taking DHA while attempting to conceive (BP1=9, BP11=1), age 27-42 years, DHA was well tolerated and suggests that a larger study would be feasible. The elucidation of the potential role of omega-3 fatty acids as a treatment for BD requires further study. The current data are not sufficient to support a recommendation of monotherapy treatment as a substitute for standard pharmacologic treatments. However, judicious monotherapy in selected clinical situations, or adjunctive use, may be warranted pending further data from adequately powered controlled clinical trials. Our pilot trial of DHA in women who plan to stop conventional psychotropics in order to conceive suggests that such trials are feasible. copyright 2006 Elsevier Ltd. All rights reserved

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**Abstract:** BACKGROUND: Bipolar disorder is a complex psychiatric disorder and is amongst the top thirty causes of worldwide disability. Mood stabilisers are the primary pharmacological intervention, both in the treatment of acute episodes and in prophylaxis. There is, however, mounting evidence that dietary supplementation with omega-3 fatty acids may be beneficial in psychiatric conditions, particularly those involving disturbances of mood. OBJECTIVES: To review the

efficacy of omega-3 fatty acids as either a monotherapy or an adjunctive treatment for bipolar disorder. **SEARCH STRATEGY:** Electronic searches of the following databases were performed: CCDANCTR-Studies and CCDANCTR-References were searched on 12/2/2008, Supplementary searches were carried out on Biological Abstracts, CINAHL, The Cochrane Library, CCDAN Register, EMBASE, MEDLINE, and PsycINFO. The search strategy also included cited reference searching, personal contact with all authors of studies initially included and contact with the omega-3 producing pharmaceutical companies. **SELECTION CRITERIA:** All relevant randomised controlled trials were included in the review. Studies involving males and females of all ages with a diagnosis of bipolar disorder qualified for inclusion. Studies using any type or dose of omega-3 fatty acid treatment as monotherapy or in addition to standard pharmacotherapy were eligible. The primary outcome was symptom severity; and secondary outcomes were adverse effects, dropout and satisfaction with treatment. **DATA COLLECTION AND ANALYSIS:** Two review authors independently inspected the citations identified from the search. Potentially relevant abstracts were identified and full papers ordered and reassessed for inclusion and methodological quality. All relevant data were extracted. The weighted mean difference (WMD) was used for continuous outcome data, with 95% confidence intervals (CI). **MAIN RESULTS:** Five studies met inclusion criteria for the review, however, methodological quality was highly variable. Only one study, involving 75 participants, provided data for analysis, and showed a benefit of active treatment over control for depression symptom levels (WMD -3.93, 95% CI -7.00 to -0.86) and Clinical Global Impression scores (WMD -0.75, 95% CI -1.33 to -0.17) but not for mania (WMD -2.81, 95% CI -7.68 to 1.90). No serious adverse effects were reported in the five studies. The pattern of dropout was highly variable between studies. **AUTHORS' CONCLUSIONS:** Results from one study showed positive effects of omega-3 as an adjunctive treatment for depressive but not manic symptoms in bipolar disorder. These findings must be regarded with caution owing to the limited data available. There is an acute need for well-designed and executed randomised controlled trials in this field. [References: 69]

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**Abstract:** Objectives: To consider the possible rationale and utility of omega-3 fatty acids as a treatment for depression in the perinatal period. Method: A review of published and unpublished research was undertaken, using electronic databases, conferences proceedings and expert informants. Results: Relevant bodies of evidence include an epidemiological link between low fish intake and depression. Laboratory studies show correlations between low omega-3 fatty acid levels and depression, as well as reduced levels of omega-3 in non-depressed women during the perinatal period. Treatment studies using omega-3 in patients with mood disorders further support an omega-3 contribution, as do neuroscientific theories. Research into omega-3 and infant development also highlights potential effects of depletion in the perinatal period and supports infant safety and benefits of supplementation. Conclusions: There is a relative lack of knowledge about the safety of standard antidepressants in the perinatal period. There is a clear need for more research into alternative treatments, such as omega-3 fatty acids, in the management of depression in the perinatal period
  
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**Abstract:** Background. A growing number of observational and epidemiological studies have suggested that mental illness, in particular mood disorders, is associated with reduced dietary intake and/or cellular abundance of omega-3 polyunsaturated fatty acids (PUFA). This has prompted researchers to test the efficacy of omega-3 PUFA in a range of different psychiatric disorders. We have critically reviewed the double blind placebo controlled clinical trials published prior to April 2007 to determine whether omega-3 PUFA are likely to be efficacious in these

disorders. Results. Most trials involved a small number of participants but were largely well designed. Omega-3 PUFA were well tolerated by both children and adults with mild gastrointestinal effects being the only consistently reported adverse event. For schizophrenia and borderline personality disorder we found little evidence of a robust clinically relevant effect. In the case of attention deficit hyperactivity disorder and related disorders, most trials showed at most small benefits over placebo. A limited meta-analysis of these trials suggested that benefits of omega-3 PUFA supplementation may be greater in a classroom setting than at home. Some evidence indicates that omega-3 PUFA may reduce symptoms of anxiety although the data is preliminary and inconclusive. The most convincing evidence for beneficial effects of omega-3 PUFA is to be found in mood disorders. A meta-analysis of trials involving patients with major depressive disorder and bipolar disorder provided evidence that omega-3 PUFA supplementation reduces symptoms of depression. Furthermore, meta-regression analysis suggests that supplementation with eicosapentaenoic acid may be more beneficial in mood disorders than with docosahexaenoic acid, although several confounding factors prevented a definitive conclusion being made regarding which species of omega-3 PUFA is most beneficial. The mechanisms underlying the apparent efficacy of omega-3 PUFA in mood disorders compared to schizophrenia are discussed as is a rationale for the possibly greater efficacy of EPA compared to DHA Conclusion. While it is not currently possible to recommend omega-3 PUFA as either a mono- or adjunctive-therapy in any mental illness, the available evidence is strong enough to justify continued study, especially with regard to attentional, anxiety and mood disorders. copyright 2007 Ross et al; licensee BioMed Central Ltd

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17. Sempels C, Sienaert P. The role of omega-3 fatty acids in the treatment of bipolar disorders: The current situation. *Tijdschr Psychiatr* 2007;49(9):639-47.  
 Abstract: BACKGROUND: There is great interest in the use of omega-3 fatty acids in the treatment of various psychiatric disorders. Epidemiological investigations show that a high consumption of omega-3 fatty acids is in inverse proportion to the prevalence of affective disorders. AIM: To provide an overview of current research reports on the use of omega-3 fatty acids and bipolar disorders. METHOD: Medline was searched with the following MeSH terms: 'mood disorders', 'affective disorders', 'bipolar disorders', 'fish oil', 'unsaturated dietary fats', 'omega-3 fatty acids', 'eicosapentaenoic acid', 'docosahexaenoic acid' and 'alpha-linolenic acid'. RESULTS: To date, articles have been published about four randomized controlled trials and one open-label study. Omega-3 fatty acids, when added to an existing psychopharmacological maintenance treatment for bipolar disorder, can have a slight beneficial effect on depressive symptoms. There is no clear evidence that this combination has a beneficial effect on manic symptoms. CONCLUSION: Current data on the efficacy of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) in the treatment of bipolar disorder are insufficient for us to draw definite conclusions that can guide clinical practice. Further investigations are required into the effects of omega-3 fatty acids on the various phases of bipolar disorder
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 Abstract: Several lines of evidence indicate an association between omega-3 polyunsaturated fatty acids (PUFAs) and depression. The purpose of this review was to evaluate the evidence to date within the context of the study design and methodology used. In case-control and cohort studies, concentrations of omega-3 PUFAs were lower in participants with unipolar and postpartum depression. Fish are the major dietary source of omega-3 PUFAs, and infrequent fish consumption is associated with depression in epidemiological studies. While these

findings do not appear to be the result of confounding, in some studies failure to detect confounding may be due to a lack of power or incomplete control. In four of seven double-blind randomized controlled trials, depression was significantly improved upon treatment with at least 1 g/day of eicosapentaenoic acid, an omega-3 PUFA. While clinical significance was demonstrated, preservation of blinding may be a limitation in this area of research. It remains unclear whether omega-3 supplementation is effective independently of antidepressant treatment, for depressed patients in general or only those with abnormally low concentrations of these PUFAs. The relationship between omega-3 PUFAs and depression is biologically plausible and is consistent across study designs, study groups, and diverse populations, which increases the likelihood of a causal relationship. copyright 2005 Elsevier Inc. All rights reserved

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20. Van Strater ACP, Bouvy PF. Omega-3 fatty acids in the treatment of affective disorders: An overview of the literature. *Tijdschr Psychiatr* 2007;49(2):85-94.  
Abstract: BACKGROUND: More and more interest is being shown in fish oil because it contains omega-3 fatty acids which may have beneficial effects in a wide range of somatic and psychiatric disorders. AIM: To search the literature for evidence of the effectiveness of omega-3 fatty acids in affective disorders. METHOD: We studied the literature with the help of Pubmed (1966-March 2006) using the keywords 'depression', 'affective disorder', 'bipolar disorder', 'seasonal affective disorder', 'postpartum depression', 'puerperal depression', 'fatty acids', 'eicosapentaenoic acid', 'arachidonic acid', 'docosahexaenoic acid' and 'fish oil'. We obtained additional information from the bibliographic references attached to the articles concerned. RESULTS: Epidemiological studies and studies on fatty acid concentrations suggest a link between omega-3 fatty acids and affective disorders, although some of the results are contradictory. Some clinical investigations found that treatment with omega-3 fatty acids did have a positive effect, but the number of test subjects was very limited and some investigations even produced negative results. CONCLUSION: There is insufficient clinical evidence to prove conclusively that treatment with omega-3 fatty acids has a beneficial effect on affective disorders
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Abstract: Background: Complementary and alternative medicine (CAM) therapies are used more than conventional therapies by people with self-defined anxiety and depression. Preliminary evidence supports a hypothesis that low plasma concentration of essential fatty acids is associated with depression. Reported here is the result of a systematic review examining the therapeutic efficacy of essential fatty acids for depression. Methods: Data sources included Medline, Psychinfo, AMED (Allied and Complementary Medicine), and Cochrane Controlled Trials Register databases searched from inception through September 2001. English language randomized controlled trials, controlled clinical trials, intervention studies, case control studies, reviews, and case reports of humans were selected, without limits for demographics or co-morbidities. Two abstractors independently evaluated each study, then reconciled findings. When possible, between group treatment effect size was noted or calculated. Results: Six articles met inclusion criteria: one RCT, two reviews, and three case control trials. A common outcome measure among the case control trials allowed for direct comparison of effect sizes. Conclusions: The evidence implies promise of a treatment effect of omega-3 fatty acids for depression in adults; although a statement of definitive clinical efficacy is premature. Further study of essential fatty acids as independent and adjuvant therapy for adult depression is indicated, including more sophisticated investigation of dose-response in particular populations. copyright 2006 Elsevier B.V. All rights reserved

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**Abstract:** Introduction: Perinatal Major Depressive Disorder (MDD) is common and poses particular treatment dilemmas. Complementary and Alternative Medicine (CAM) treatments are widely used, accessible, and understudied for well-defined psychiatric indications. Women are more likely than men to both suffer from MDD and use CAM. Methods: A PubMed/Medline search was conducted to assess the evidence base for commonly utilized CAM treatments, MDD, and perinatal depression. Results: Among CAM treatments, omega-3 fatty acids have received the most specific study in terms of epidemiological, preclinical, and clinical research for perinatal depression. Three randomized placebo-controlled trials have been conducted in which investigators assessed omega-3 fatty acids vs. placebo for perinatal depression, with conflicting results. CAM interventions that can be easily added to a treatment plan with little risk and general health benefits for most women include omega-3 fatty acids, exercise, and folate, although data are insufficient at this time to recommend any of these as monotherapy for perinatal depression. S-adenosyl-methionine (SAME) and bright light therapy may be reasonable to consider based on the evidence in MDD. St. John's Wort requires further study with regard to safety in pregnancy, and drug interactions can be a potential problem. Discussion: Further study is required to elucidate the role of CAM treatments for perinatal depression, and the clinical context of perinatal depression requires safe, effective, and accessible treatment options. copyright 2008 Elsevier B.V. All rights reserved

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**Abstract:** This review evaluates the research published between 1966 and 2004 on several integrative treatments for depression, including omega-3 fatty acids, *Hypericum perforatum* (St. John's Wort), S-adenosyl-methionine, folate, 5-Hydroxytryptophan, acupuncture, exercise, and light therapy, with a particular emphasis on issues pertinent to women. Data from double-blind, placebo-controlled trials support each of these as treatment interventions for depression. We discuss both the strength of the evidence for each treatment and methodological issues related to interpretation of efficacy. Available data pertaining to considerations in women, including use during pregnancy and breastfeeding and interactions with hormonal therapies are discussed. The reviewed treatments deserve further research. Their appropriate place in the armamentarium of depression treatments for women must be defined. An evidence-based integrative medicine approach brings together treatment options with proven efficacy and the public's desire for complementary and alternative medicine treatments. [References: 127]

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**Abstract:** Objective: Depressive symptoms of bipolar disorder have more negative impact on a patient's life than manic symptoms. This review focused on the emerging efficacy data for treatments in bipolar depression. Methods: English-language literature cited in Medline was searched with terms bipolar depression, clinical trial, and trial. Randomized, placebo-controlled trials of newer studies with older agents and all studies with newer or novel agents were prioritized. Open-label studies of novel agents presented at major scientific meetings were also included. Results: Olanzapine, olanzapine-fluoxetine combination (OFC), and quetiapine were superior to placebo in the acute treatment of bipolar depression. Lamotrigine only significantly reduced core symptoms of depression compared with placebo. Pramipexole, a dopamine D2/D3 receptor agonist and omega-3 fatty acids, a polyunsaturated fatty acid, augmentation to mood stabilizer (MS) had superiority to placebo in reducing depressive symptoms. Topiramate augmentation of an MS was equally as effective as Bupropion-SR. Patients treated with an MS responded well to the addition of agomelatine, a mela-

tonin receptor agonist with 5-HT<sub>2C</sub> antagonist properties. However, inositol and repetitive transcranial magnetic stimulation did not separate from placebo. Lamotrigine and olanzapine, and to a lesser extent, divalproex, are superior to placebo in preventing depressive relapses. All agents were relatively well tolerated. Conclusions: Olanzapine, OFC, and quetiapine are effective in the acute treatment of bipolar depression. Compared with lithium and divalproex, lamotrigine is more effective in preventing bipolar depression. Larger controlled studies of the other agents in the acute and maintenance treatment of bipolar depression are warranted. copyright Blackwell Munksgaard, 2005

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Abstract: Background: There is increasing speculation that diet has an important impact on mental health and that the outcomes of certain mental health disorders, including depression may be influenced by nutritional factors. Although considerable research has focused on understanding the biochemistry and assessing the efficacy of pharmaceutical interventions for depression, it is only recently that research attention has focused on the impact of diet. Emerging evidence suggests that certain nutrients may be important in the pathogenesis and treatment of depression. Aims: This review seeks to establish the current evidence base supporting nutritional interventions in unipolar depression. Methods: Literature searches identified articles relating to nutritional supplementation in unipolar depression. These were subdivided into categories. All randomized controlled trials were graded using SIGN 50 criteria, with an overall grading recommendation assigned to the evidence for each nutrient. Results: Ten randomized controlled trials were graded, comprising two tryptophan studies, four omega 3 studies and one zinc study. All categories except the single zinc trial achieved a combined B grading level. Conclusion: At present the evidence base is extremely weak but hints at a potential benefit of adjunctive nutritional supplementation in the treatment of depression and highlights the urgent need for more research in this area. Declaration of interest: This review was carried out independently, with no financial support obtained from any party. The authors declare no interests. copyright Shadowfax Publishing and Informa Healthcare USA, Inc

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Abstract: Objective: To review the evidence for the effectiveness of complementary and self-help treatments for depression in children and adolescents. Data sources: Systematic literature search using PubMed, PsycINFO and the Cochrane Library for 131 treatments up to February 2006. Study selection: There were 13 treatments that had been evaluated in intervention studies. Data extraction: Studies on each treatment were reviewed by one author and checked by a second. A consensus was reached for level of evidence. Data synthesis: Relevant evidence was available for glutamine, S-adenosylmethionine, St John's wort, vitamin C, omega-3 fatty acids, light therapy, massage, art therapy, bibliotherapy, distraction techniques, exercise, relaxation therapy and sleep deprivation. However, the evidence was limited and generally of poor quality. The only treatment with reasonable supporting evidence was light therapy for winter depression. Conclusions: Given that antidepressant medication is not recommended as a first line treatment for children and adolescents with mild to moderate depression, and that the effects of psychological treatments are modest, there is a pressing need to extend the range of treatments available for this age group

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**Abstract:** Background: Research suggests that depressive disorders exist on a continuum, with subthreshold symptoms causing considerable population burden and increasing individual risk of developing major depressive disorder. An alternative strategy to professional treatment of subthreshold depression is population promotion of effective self-help interventions that can be easily applied by an individual without professional guidance. The evidence for self-help interventions for depressive symptoms is reviewed in the present work, with the aim of identifying promising interventions that could inform future health promotion campaigns or stimulate further research. Methods: A literature search for randomised controlled trials investigating self-help interventions for depressive disorders or depressive symptoms was performed using PubMed, PsycINFO and the Cochrane Database of Systematic Reviews. Reference lists and citations of included studies were also checked. Studies were grouped into those involving participants with depressive disorders or a high level of depressive symptoms, or non-clinically depressed participants not selected for depression. A number of exclusion criteria were applied, including trials with small sample sizes and where the intervention was adjunctive to antidepressants or psychotherapy. Results: The majority of interventions searched had no relevant evidence to review. Of the 38 interventions reviewed, the ones with the best evidence of efficacy in depressive disorders were S-adenosylmethionine, St John's wort, bibliotherapy, computerised interventions, distraction, relaxation training, exercise, pleasant activities, sleep deprivation, and light therapy. A number of other interventions showed promise but had received less research attention. Research in non-clinical samples indicated immediate beneficial effects on depressed mood for distraction, exercise, humour, music, negative air ionisation, and singing; while potential for helpful longer-term effects was found for autogenic training, light therapy, omega 3 fatty acids, pets, and prayer. Many of the trials were poor quality and may not generalise to self-help without professional guidance. Conclusion: A number of self-help interventions have promising evidence for reducing subthreshold depressive symptoms. Other forms of evidence such as expert consensus may be more appropriate for interventions that are not feasible to evaluate in randomised controlled trials. There needs to be evaluation of whether promotion to the public of effective self-help strategies for subthreshold depressive symptoms could delay or prevent onset of depressive illness, reduce functional impairment, and prevent progression to other undesirable outcomes such as harmful use of substances. copyright 2008 Morgan and Jorm; licensee BioMed Central Ltd

28. Ramakrishnan U, Imhoff-Kunsch B, Digirolamo AM. Role of docosahexaenoic acid in maternal and child mental health. *Am J Clin Nutr* 2009;89(3):958S-62S.

**Abstract:** Mental health problems in women and children represent a significant public health problem worldwide, especially in developing countries. The role of nutrition as a cost-effective approach in the prevention and management of these conditions has received recent attention, particularly nutrients such as iron, zinc, and n-3 (omega-3) fatty acids, which play a role in brain structure and function. The objective of this article was to review current evidence on the relation between n-3 fatty acids, especially docosahexaenoic acid (DHA), and maternal and child mental health disorders. Human studies published in English were identified from Medline databases (1966 to June 2008) by using key search terms and review articles. A summary of the role of DHA in the human brain is followed by a review of human studies, both observational and intervention trials, that examine the relation between n-3 fatty acids such as DHA and depression and child mental health disorders. Observational studies support a direct association between poor n-3 fatty acid status and increased risk of maternal depression and childhood behavioral disorders such as attention-deficit hyperactivity disorder (ADHD). However, evidence from intervention trials is weak. Most of the studies reviewed had small sample sizes and were conducted in clinically diagnosed samples, with no placebo-controlled groups. Little is known about the benefits of DHA in the prevention of maternal depression and ADHD. Large, well-designed,

community-based prevention trials are needed. copyright 2009 American Society for Nutrition

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**Abstract:** **BACKGROUND:** The use of complementary medicines in those with mental health problems is well documented. However, their effectiveness is often not established and they may be less harmless than commonly assumed. **AIMS:** To review the complementary medicines routinely encountered in psychiatric practice, their effectiveness, potential adverse effects and interactions. **METHOD:** Electronic and manual literature search on the effectiveness and safety of psychotropic complementary medicines. **RESULTS:** Potentially useful substances include ginkgo and hydergine as cognitive enhancers, passion flower and valerian as sedatives, St John's wort and s-adenosylmethionine as antidepressants, and selenium and folate to complement antidepressants. The evidence is less conclusive for the use of omega-3 fatty acids as augmentation treatment in schizophrenia, melatonin for tardive dyskinesia and 18-methoxycoronaridine, an ibogaine derivative, for the treatment of cocaine and heroin addiction. **CONCLUSIONS:** Systematic clinical trials are needed to test promising substances. Meanwhile, those wishing to take psychotropic complementary medicines require appropriate advice. [References: 156]



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# Vedlegg

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## SØKESTRATEGI

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### Cochrane

**Søk:** Hege Sletsjøe

**Database:** Cochrane Library, issue 3, 2009

**Dato:** 29.09.2009

**Antall treff:** Cochrane reviews (12), Other reviews – DARE (13), HTA (3)

- #1 [MeSH descriptor \*\*Mental Disorders\*\* explode all trees](#)  
[\(\(mental or behavior or adjustment or anxiety or cognitive or dissociative or eating or factitious or mood or neurotic or personality or somatoform or substance related or amnes\\* or delerium or impulse control\) NEAR/1 \(disorder\\* or disease\\*\)\):ti,ab](#)
- #2 [\(demntia\\* or schizophren\\*\):ti,ab](#)
- #3 [\(#1 OR #2 OR #3\)](#)
- #4 [MeSH descriptor \*\*Fish Oils\*\* explode all trees](#)
- #5 [MeSH descriptor \*\*Plant Oils\*\* explode all trees](#)
- #6 [MeSH descriptor \*\*Dietary Fats, Unsaturated\*\* explode all trees](#)
- #7 [MeSH descriptor \*\*Dietary Fats, Unsaturated\*\* explode all trees](#)
- #8 [MeSH descriptor \*\*Fatty Acids, Omega-3\*\* explode all trees](#)
- #9 [MeSH descriptor \*\*Fatty Acids, this term only\*\*](#)
- #10 [MeSH descriptor \*\*Fatty Acids, Unsaturated\*\* explode all trees](#)
- #11 [MeSH descriptor \*\*Fatty Acids, Unsaturated\*\* explode all trees](#)
- #12 [MeSH descriptor \*\*Nutrition Therapy\*\* explode all trees](#)
- #13 [MeSH descriptor \*\*Diet Therapy\*\* explode all trees](#)
- #14 [MeSH descriptor \*\*Vitamins\*\* explode all trees](#)
- #15 [MeSH descriptor \*\*Minerals\*\* explode all trees](#)
- #16

- #17 [\(supplement\\* or therapy\\*\):ti,ab](#)
- #18 [\(\( #15 OR #16 \) AND #17\)](#)
- #19 [\(\(fish or flax or linseed or plant\) NEAR/1 oil\):ti,ab](#)
- #20 [\(\(fatty NEAR/1 acid\\*\) or \(n-3 or n-6 or omega-3 or omega-6\)\):ti,ab](#)
- #21 [\(\(vitamin\\* or diet\\* or mineral\\*\) NEAR/1 \(supplement\\* or therapy\)\):ti,ab](#)
- #22 [\(#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #19 OR #20 OR #21\)](#)
- #23 [\(#4 AND #22\)](#)

## Medline

**Søk:** Hege Sletsjøe

**Database:** Ovid MEDLINE(R) <1950 to September Week 3 2009>

**Dato:** 29.09.2009

**Antall treff:** 612

**Kommentar:** Brukt SR-filteret som ligger i Ovid Medline (Clinical queries – Reviews (optimized))

- 1 exp Mental Disorders/ (753949)
- 2 ((mental or behavior or adjustment or anxiety or cognitive or dissociative or eating or factitious or mood or neurotic or personality or somatoform or substance related or amnes\* or delerium or impulse control) adj1 (disorder\* or disease\*)).tw. (45840)
- 3 (dementi\* or schizophren\*).tw. (112263)
- 4 or/1-3 (775013)
- 5 exp fish oils/ or exp plant oils/ (29835)
- 6 exp dietary fats, unsaturated/ or fatty acids, omega-3/ (17712)
- 7 fatty acids/ or exp fatty acids, unsaturated/ (214723)
- 8 exp Nutrition Therapy/ (66360)
- 9 exp Diet Therapy/ (33611)
- 10 exp Vitamins/ (221577)
- 11 exp Minerals/ (84977)
- 12 (supplement\* or therapy\*).tw. (1034899)
- 13 therapy.fs. (1161222)
- 14 or/10-11 (300795)
- 15 or/12-13 (1964049)
- 16 15 and 14 (46762)

17 ((fish or flax or linseed or plant) adj1 oil).tw.  
(5321)  
18 (fatty adj1 acid\* adj1 (n-3 or n-6)).tw. (3388)  
19 ((vitamin\* or diet\* or mineral\*) adj1 (supplement\* or  
therapy)).tw. (20099)  
20 (omega-3 or omega-6).tw. (4972)  
21 6 or 11 or 7 or 17 or 20 or 18 or 10 or 19 or 5  
(535450)  
22 21 and 15 (78376)  
23 8 or 22 or 9 (141251)  
24 23 and 4 (5085)  
25 limit 24 to (yr="2004 -Current" and "reviews (opti-  
mized)") (421)  
26 6 or 7 or 9 or 17 or 20 or 8 or 18 or 16 or 19 or 5  
(350868)  
27 4 and 26 (7232)  
28 limit 27 to (yr="2004 -Current" and "reviews (opti-  
mized)") (612)  
29 from 28 keep 1-612 (612)

## Embase

**Søk:** Hege Sletsjøe

**Database:** EMBASE <1980 to 2009 Week 39>

**Dato:** 29.09.2009

**Antall treff:** 1383

**Kommentar:** Brukt SR-filteret som ligger i Ovid Medline (reviews (2 or more terms min difference)). På grunn av stor treffmengde har jeg kombinert linje 7-14 med (supplement\* or therapy\*).tw. og (dt or dm).fs. – den siste søker på drug therapy og disease management som floating subheading.

1 exp mental disease/ (739183)  
2 ((mental or behavior or adjustment or anxiety or cognitive or dissociative or eating or factitious or mood or neurotic or personality or somatoform or substance related or amnes\* or delerium or impulse control) adj1 (disorder\* or disease\*)).tw. (43738)  
3 (dementi\* or schizophren\*).tw. (98116)  
4 or/1-3 (748365)  
5 exp diet supplementation/ or exp vitamin supplementation/ (41227)

```
6      ((vitamin* or diet* or mineral*) adj1 (supplement* or
therapy)).tw. (15116)
7      exp vegetable oil/ (24773)
8      exp fish oil/ (6937)
9      fatty acid/ or essential fatty acid/ (36660)
10     exp omega 3 fatty acid/ (8391)
11     exp mineral/ (7844)
12     ((fish or flax or linseed or plant) adj1 oil).tw.
(4970)
13     (fatty adj1 acid* adj1 (n-3 or n-6)).tw. (3096)
14     (omega-3 or omega-6).tw. (3969)
15     (supplement* or therapy*).tw. (862572)
16     (dt or dm).fs. (1647823)
17     16 or 15 (2101345)
18     or/7-14 (78098)
19     18 and 17 (19434)
20     6 or 19 or 5 (62287)
21     4 and 20 (5009)
22     limit 21 to ("reviews (2 or more terms min difference)"
and yr="2004 -Current") (1383)
23     from 22 keep 1 (1)
```

# Søk etter retningslinjer

Oppdrag: Retningslinjer om mineraler og vitaminer i behandlingen av mennesker med psykiske lidelser

Søk: Astrid Nøstberg

Dato: 28.-29. september 2009

<b>Søk: (mental disorder* OR mental illness*) AND (vitamin* OR mineral* OR nutrition* OR micronutrient* OR nutritional support* OR dietary supplement* OR acid*)</b>		
<b>Database</b>	<b>Antall treff</b>	<b>Kommentar / Trefflister</b>
TRIP+ <a href="http://www.tripdatabase.com/">http://www.tripdatabase.com/</a>	0	("mental disorder*" or "mental illness*") and (vitamin* or mineral* or acid* or nutrition* or supplement* or micronutrient* or "nutritional support*" or "dietary supplement*")
G-I-N <a href="http://www.g-in.net/">http://www.g-in.net/</a>	0	(mental disorder* or mental illness*) and (vitamin* or mineral* or nutrition* or micronutrient* or nutritional support* or dietary supplement* or acid*)
NLH National Library of Guidelines <a href="http://www.library.nhs.uk/guidelinesFinder/">http://www.library.nhs.uk/guidelinesFinder/</a>	2	Treffliste: <a href="http://www.library.nhs.uk/guidelinesFinder/SearchResults.aspx?searchText=%28mental%20disorder%20or%20mental%20illness%29%20and%20%28vitamin%20or%20mineral%20or%20nutrition%20or%20micronutrient%20or%20nutritional%20support%20or%20dietary%20supplement%20or%20acid%29">http://www.library.nhs.uk/guidelinesFinder/SearchResults.aspx?searchText=%28mental%20disorder%20or%20mental%20illness%29%20and%20%28vitamin%20or%20mineral%20or%20nutrition%20or%20micronutrient%20or%20nutritional%20support%20or%20dietary%20supplement%20or%20acid%29</a>  Se også treffliste nedenfor  Man må registrere seg for å lese fulltekst, men det er gratis.
CMA INFO-BASE <a href="http://mdm.ca/cpgsnew/cpgs/i">http://mdm.ca/cpgsnew/cpgs/i</a>	0	

<a href="#">ndex.asp</a>		
<b>Søk: ( psykisk? lidelse? )</b>		
<b>Database</b>	<b>Antall treff</b>	<b>Kommentar / Trefflister</b>
Sundhedsstyrelsen <a href="http://www.sst.dk/">http://www.sst.dk/</a>	2	Treffliste nedenfor
<b>Søk:</b> <b>psykisk* lidelse* eller mental* lidelse* og vitamin* eller mineral* eller kosttilskudd eller ernæring eller syre* eller kosthold og retningslinje* eller veiled*</b>		
<b>Database</b>	<b>Antall treff</b>	<b>Kommentar / Trefflister</b>
BIBSYS ASK <a href="http://ask.bibsys.no/ask/action/resources">http://ask.bibsys.no/ask/action/resources</a>	0	
<b>Manuell leting på siden (kilder uten søkemotor, eller lite innhold)</b>		
<b>Database</b>	<b>Antall treff</b>	<b>Kommentar / Trefflister</b>
Socialstyrelsen <a href="http://www.socialstyrelsen.se">http://www.socialstyrelsen.se</a>	2	Treffliste nedenfor
National Guideline Clearinghouse <a href="http://www.guideline.gov/">http://www.guideline.gov/</a>	24	Lett gjennom hierarkiet  Treffliste: <a href="http://www.guideline.gov/browse/browsemode.aspx?node=16873&amp;type=1">http://www.guideline.gov/browse/browsemode.aspx?node=16873&amp;type=1</a>
SIGN <a href="http://www.sign.ac.uk/">http://www.sign.ac.uk/</a>	8	Retningslinjer under fagområdet Mental health: <a href="http://www.sign.ac.uk/guidelines/published/index.html#Mental">http://www.sign.ac.uk/guidelines/published/index.html#Mental</a>
NHS evidence: <a href="http://www.evidence.nhs.uk/default.aspx">http://www.evidence.nhs.uk/default.aspx</a>	94	<a %22+or+%22mental+illness"%22)+and+(vitamin*+or+mineral*+or+micronutrient*+or+%22nutritional+support"%22+or+%22dietary+supplement"%22+or+acid*)&amp;m='itn.Guidelines&amp;ps=50&amp;pa=1&amp;s=Relevance&amp;exp=""' href="http://www.evidence.nhs.uk/Search.aspx?t=(%22mental+disorder">http://www.evidence.nhs.uk/Search.aspx?t=(%22mental+disorder"%22+or+%22mental+illness"%22)+AND+(vitamin*+or+mineral*+or+micronutrient*+or+%22nutritional+support"%22+or+%22dietary+supplement"%22+or+acid*)&amp;m=itn.Guidelines&amp;ps=50&amp;pa=1&amp;s=Relevance&amp;exp=</a> (For at lenka skal fungere, må du kopiere og lime den inn i URLen)
New Zealand Guidelines Group <a href="http://www.nzg.org.nz">http://www.nzg.org.nz</a>	18	<a href="http://www.nzg.org.nz/index.cfm?fuseaction=fuseaction_10&amp;fusesubaction=docs&amp;documentID=22#Mental%20Health">http://www.nzg.org.nz/index.cfm?fuseaction=fuseaction_10&amp;fusesubaction=docs&amp;documentID=22#Mental%20Health</a>

<a href="http://gacguidelines.ca/">g.org.nz/</a>		(Lenka virker ikke som den skal, men gå til "Mental Health" under Category links)
GAC (Guideline Advisory Committee) <a href="http://gacguidelines.ca/">http://gacguidelines.ca/</a>	15	Treffliste nedenfor
CTFPHC (Canadian Task Force on Preventive Health Care) <a href="http://www.ctfpchc.org/">http://www.ctfpchc.org/</a>	0 aktuelle	Lette gjennom kategoriene, men fant ingen ting som var aktuelt. Ikke mulig å lenke direkte til oversikten over retningslinjene

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## TREFFLISTE FRA NATIONAL LIBRARY OF GUIDELINES:

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### Guidelines for the nutritional management of anorexia nervosa

- **Publisher:** [Royal College of Psychiatrists](#)
- **Publication Type:** Care Guideline
- **Publication Date:** 01 Jul 2005

- [View detail](#)
- [Link to full text here, Portable Document File / PDF](#)

### Routine postnatal care of women and their babies

- **Publisher:** [NICE](#)
- **Publication Type:** Care Guideline
- **Publication Date:** 26 Jul 2006

- [View detail](#)
- [Link to full text here, Portable Document File / PDF](#)

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## TREFFLISTE FRA SUNDHEDSSTYRELSEN:

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#	<u>Titel</u>	<u>Udg.år</u>	<u>Kategori</u>
1	<a href="#">Fremme af mental sundhed : -baggrund, begreber og determinanter</a>	2008	Udredning
2	<a href="#">Vejledning om medikamentel behandling af børn og unge med psykiske lidelser</a>	2008	Vejledning A. Lov-baseret

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## TREFFLISTE FRA SOCIALSTYRELSEN:

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### Riktlinjer som är under produktion:

Nationella riktlinjer för psykosociala insatser för personer med schizofreni

<http://www.socialstyrelsen.se/riktlinjer/nationellariktlinjer/schizofreni>

### Preliminära riktlinjer:

Nationella riktlinjer för depressionssjukdom och ångestsyndrom

<http://www.socialstyrelsen.se/riktlinjer/nationellariktlinjer/depressionochangest>

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## TREFFLISTE FRA GAC (GUIDELINE ADVISORY COMMITTEE):

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### Anxiety

[Anxiety](#)

September 2007

September  
2010



### Bipolar Disorder

[Bipolar Disorder](#)

May 2007

September 2008

### Dementia

[Managing Dementing Disorders: Behavioural Disturbances](#)

June  
2002

June  
2006



[Managing Dementing Disorders: Caregiving](#)

June  
2002

June  
2006



[Managing Dementing Disorders: Depression](#)

June  
2002

June  
2006



[Managing Dementing Disorders: Diagnosis and Assessment](#)

June  
2002

June  
2006



[Managing Dementing Disorders: Ethical Issues](#)

June  
2002

June  
2006



[Managing Dementing Disorders: Pharmacologic Therapy](#)

June  
2002

June  
2006



[Managing Dementing Disorders: Prevention](#)

June  
2002

June  
2006



[Managing Dementing Disorders: Referral](#)

June  
2002

June  
2006



[Managing Dementing Disorders: Screening and Case Finding](#)

June  
2002

June  
2006





**Depression, Adults**

<a href="#">Screening for Depression</a>	June 2007	October 2009	
<a href="#">Management of Moderate to Severe Depression</a>	June 2007	October 2009	
<a href="#">Management of Mild Depression</a>	June 2007	October 2009	

**Psychotherapy**

<a href="#">Psychological Therapy and Counseling</a>	June 2002	June 2007	
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