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Date: August 2013

Bør fastleger tilby pasienter med alvorlig depresjon, tilbakevendende depresjon, kronisk depresjon og dystymi både antidepressiver og psykologisk behandling?

Problem: Alvorlig depresjon, tilbakevendende depresjon, kronisk depresjon og dystymi hos eldre (over 65 år)
Tiltak: Kombinert behandling med både antidepressiver og psykologisk behandling
Sammenlikning: Monoterapi – enten medikamentell behandling eller psykologisk behandling
Setting: Primærhelsetjenesten

Bakgrunn: Depresjon blant eldre er vanlig, og forårsaker redusert livskvalitet. Somatiske sykdommer, redusert funksjon og tapsopplevelser kan øke risiko for depresjon hos eldre. Depresjon hos eldre har oftere et kronisk forløp og depresjon er ledsaget av økt risiko for somatisk sykdom og dødelighet. Depresjon resulterer i høye utgifter til behandling, og virker negativt inn på både personlige, familiære og sosiale forhold. Diagnosen depresjon blir oftere oversett blant eldre pasienter, og eldre pasienter får oftere mangelfull behandling. Det har vært vanskeligere å få gitt adekvate tilbud i spesialisthelsetjenesten til eldre med depresjon som har behov for vurdering og behandling hos psykolog eller psykiater. Studier viser at pasienter med depresjon ikke alltid behandles i tråd med anbefalinger gitt i kunnskapsbaserte kliniske retningslinjer.

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION
PROBLEM	**Is the problem a priority?**	*No* ☐ *Probably No* ☐ *Uncertain* ☐ *Probably Yes* ☐ *Yes* ☒ | *Varies* ☐	.	Alvorlig depresjon innebærer en tung lidelse for den syke og familien, med betydelig funksjonsnedsettelse og risiko for selvmord. Kronisk og tilbakevendende depresjon, og dystymi er også mer belastende enn en enkeltstående episode med mild til moderat depresjon.
	Are a large number of people affected?	*No* ☐ *Probably No* ☒ *Uncertain* ☐ *Probably Yes* ☐ *Yes* ☐ | *Varies* ☐		Depresjon hos eldre er vanligere enn hos yngre. Mange plages med depressive følelser uten å fylle kravene til diagnosen depresjon. Blant dem som lider av depresjon har de fleste mild til moderat depresjon, slik at alvorlig depresjon er relativt sjelden. Alvorlig depresjon er vanligere hos eldre enn hos yngre voksne. Risiko for residiv (tilbakevendende depresjon) og for et kronisk forløp er større hos eldre enn hos yngre voksne.

BENEFITS & HARMS OF THE OPTIONS

CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION
Are the desirable anticipated effects large?	No ☐ Probably No ☒ Uncertain ☐ Probably Yes ☐ Yes ☐ Varies ☐	***Summary of findings:***	Både behandling med antidepressiver og strukturert psykologisk behandling har dokumentert klinisk viktig effekt sammenliknet med placebo eller vanlig behandling for pasienter med avlorlig depresjon. Mange pasienter foretrekker psykologisk behandling framfor medikamentell behandling ved depresjon. En metaanalyse av 67 studier med pasienter med angst og depresjon, herav 40 studier med pasienter med depresjon, viste ingen sikker forskjell i effekt mellom behandling med antidepressiver (AD) og psykoterapi (PT) mht. bedring av symptomer (Cuijpers 2013)[1]. Flere metaanalyser viser tilleggseffekt ved å kombinere AD med PT, sammenliknet med enten AD eller PT alene.
		Antidepressants compared to psychotherapy for elderly with severe depression	
		Bibliography: Depressive symptoms:[1,2]. Hazards/unintended effects: [3]	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects: Risk with Psychotherapy	Anticipated absolute effects: Risk difference with Antidepressants (95% CI)
Depressive symptoms Depression scale	5995 (39 studies[1])	⨁⨁⨁◯ **MODERATE**[2,3] due to inconsistency		The mean change in depressive symptoms in the intervention groups was **0.02 standard deviations higher** (0.1 lower to 0.13 higher)	
All cause mortality (SSRI vs no ADs) Number of events per patient-year - measured with electronic medical record database[4]	241757 (1 study) 1-12 years	⨁⨁◯◯ **LOW**[6]	**HR 1.54** (1.48 to 1.59)[4]	**48 per 1000**[5]	**25 more per 1000** (from 22 more to 27 more)
Falls (SSRIs vs no ADs) Events recorded in electronic medical record, rates per patient-year[4]	204007 (1 study) 1-12 years	⨁⨁◯◯ **LOW**[15]	**HR 1.66** (1.58 to 1.73)	**61 per 1000 patient-years**[16]	**38 more per 1000 patient-years** (from 34 more to 42 more)

CI: Confidence interval; **HR:** Hazard ratio;

[1] Cuijpers included 67 studies on anxiety and mood disorders. We have used the analyses from 39 studies on major depression.
[2] Heterogeneity, I^2 = 46 %.
[3] We did not rate down for indirectness, although studies included all adults, not only elderly with severe depression.
[4] Adjusted for sex, age (five year bands), year, severity of depression, depression before age 65, smoking status, Townsend deprivation score, coronary heart disease, diabetes, hypertension, cancer, dementia, Parkinson's disease, hypothyroidism, obsessive-compulsive disorder, epilepsy/seizures, statins, non-steroidal anti-inflammatory drugs, antipsychotics, lithium, aspirin, antihypertensive drugs, anticonvulsant drugs,

Are the undesirable anticipated effects small?	No ☐ Probably No ☐ Uncertain ☐ Probably Yes ☒ Yes ☐ Varies ☐	
What Is the overall certainty of this evidence?	No included studies ☐ Very low ☐ Low ☐ Moderate ☒ High ☐	

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION

hypnotics/anxiolytics; and stroke/transient ischaemic attack at baseline.
[5] The control rate are patients not currently on ADs
[6] This is a well done large observational study based on a primary care database from 570 general practices in UK. As this is an observational study, it is susceptible to confounding by indication, channelling bias, and residual confounding, so differences in characteristics between patients prescribed different antidepressant drugs that could account for some of the associations between the drugs and the adverse outcomes may remain. We decided not to downgrade further, however.

Antidepressants in combination with psychotherapy compared to antidepressants alone for elderly with severe depression

Bibliography: [4],[5]

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Antidepressants alone	Risk difference with Antidepressants in combination with psychotherapy (95% CI)
Symptom change Scales	11836 (25 [2])	⊕⊕⊕⊖ **MODERATE**[3,4] due to risk of bias		The mean symptom change in the intervention groups (AD+PT) was **0.31 standard deviations higher** (0.2 to 0.43 higher)[1]	
Response rate	1842 (16 [6]) 12 weeks	⊕⊕⊕⊖ **MODERATE**[3,4] due to risk of bias	**OR 1.86** (1.38 to 2.52)	**Moderate**[5]	
				240 per 1000	**130 more per 1000** (from 64 more to 203 more)
Dropout rates all studies	? (16 [6])	⊕⊕⊖⊖ **LOW**[3,7] due to risk of bias, imprecision	**OR 0.86** (0.6 to 1.24)	**Moderate**[1]	
				250 per 1000	**27 fewer per 1000** (from 83 fewer to 42 more)
Dropout rates <12 weeks	? (9)	⊕⊕⊖⊖ **LOW**[3,7] due to risk of bias, imprecision	**OR 1.11** (0.71 to 1.74)	**Moderate**[1]	
				250 per 1000	**20 more per 1000** (from 59 fewer to 117 more)
Dropout	?	⊕⊕⊕⊖	**OR 0.59**	**Moderate**[1]	

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION

rates > 12 weeks	(6 studies[b])	**MODERATE**[3,4] due to risk of bias	(0.39 to 0.88)	**250 per 1000**	**86 fewer per 1000** (from 23 fewer to 135 fewer)

CI: Confidence interval; **OR:** Odds ratio;

[1] No absolute numbers or data on dropout rates given in review. Control group in systematic review of de Maat et al.[6] used here.
[2] Cuijpers et al: Adding psychotherapy to pharmacotherapy in the treatment of depressive disorders in adults: A meta-analysis. Depression and anxiety 2009.[4]
[3] Blinding of patients regarding psychotherapy not possible. Methodological quality of several of the included studies not optimal.
[4] Effect size in favour of combined treatment with psychotherapy and antidepressives compared with AD alone. Studies on adults with depression, not only older adults with severe depression. Subgroup analysis did not find significant differences in effect size based on patient groups, however, except for lower effect sized in patients with dysthymia. Hence we have chosen not rated down for indirectness.
[5] Response rate not stated, 24% in control group in systematic review by Gensichen 2006.[7]
[6] Pampallona Arch Gen Psych 2004.[5]
[7] Wide confidence interval crossing line of no difference.

Antidepressants combined with psychotherapy compared to psychotherapy alone for elderly with severe depression

Bibliography: Cuijpers P et al. 2009 [4]

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Psychotherapy alone	Risk difference with antidepressants combined with psychotherapy (95% CI)
Depressive symptoms Depression scales	?[3] (19 studies)	⊕⊕⊕⊖ **MODERATE**[2] due to risk of bias		The mean change in depressive symptoms in the intervention groups (AD + PT) was **0.35 standard deviations higher** (0.24 to 0.45 higher)	
Recovery rate	?[3] (17 studies)	⊕⊕⊕⊖ **MODERATE**[2] due to risk of	**RR 1.22** (1.14 to 1.29)	**Moderate**[1]	
				344 per 1000	**76 more per 1000** (from 48 more to 100 more)

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION

			bias			
Dropout rate	?[3] (9 studies)	⊕⊕⊕⊖ **MODERATE**[2] due to risk of bias	**RR 0.77** (0.67 to 0.90)	**Moderate**[1] **244 per 1000**	**56 fewer per 1000** (from 24 fewer to 81 fewer)

CI: Confidence interval; **RR:** Risk ratio;

[1] Rates not reported, we have chosen rates in control groups in review of de Maat [6] chosen as illustrative risks for groups receiving psychotherapy only.
[2] Quality if included studies varied.
[3] Number of participants in the studies not stated. Totally 19 studies with 1,838 subjects included in the review (934 in the psychological treatment groups, and 904 in the combined treatment groups).

Antidepressants in combination with psychotherapy compared to antidepressants alone for elderly patients with chronic depression

Bibliography: Spijker J et al. Psychotherapy, antidepressants, and their combination for chronic major depressive disorder: a systematic review. Can J Psychiatry 2013 [8]

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Antidepressants alone	Risk difference with Antidepressants in combination with psychotherapy (95% CI)
Depressive symptoms HRSD	446 (1 study[2]) 12 weeks	⊕⊕⊕⊖ **MODERATE**[3,4] due to indirectness		The mean depressive symptoms in the intervention groups (AD+PT) was **0.59 standard deviations higher** (0 to 0 higher)[1]	
Remission HDRS	446 (1 study[2])	⊕⊕⊕⊖ **MODERATE**[3,5] due to imprecision	**RR 1.66** (1.3 to 2.12)	**291 per 1000**	**192 more per 1000** (from 87 more to 326 more)
Response HDRS	446 (1 study[2]) 12 weeks	⊕⊕⊖⊖ **LOW**[3,5] due to indirectness, imprecision	**RR 1.32** (0.93 to 1.9)	**186 per 1000**	**60 more per 1000** (from 13 fewer to 168 more)

[1] *Confidence interval not stated, but P value for comparison between groups > 0.001*
[2] *Keller et al. A comparison of nefazodone, the cognitive behavioral-analysis system of psychotherapy,*

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION

and their combination for the treatment of chronic depression. N Engl J Med 2000;342:1462-70.
[3] Study from US on adult with chronic major depressive disorder, 681 adults with a chronic nonpsychotic major depressive disorder randomly assigned to 12 weeks of outpatient treatment with nefazodone, the cognitive behavioral-analysis system of psychotherapy (16 to 20sessions), or both. Mean age 43 years.
[4] One study only, but effect size of combination of AD + PT compared with AD only is similar to effect sizes for studies on patients with depression in general. We have chosen not to grade down for imprecision, based on this indirect evidence from other studies.
[5] Wide confidence interval, crossing line of no difference.

Antidepressants combined with psychotherapy compared to psychotherapy alone for elderly patients with chronic depression

Bibliography: Spijker et al 2013 [8], Keller et al 2000 [9]

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Psychotherapy alone	Risk difference with Antidepressants combined with psychotherapy (95% CI)
Depressive symptoms HRSD	442 (1 study[2]) 12 weeks	⊕⊕⊖⊖ **LOW**[3] due to risk of bias, indirectness		The mean change in depressive symptoms in the intervention groups (AD+PT) was **0.64 standard deviations higher** (0 to 0 higher)[1]	
Remission HDRS	442 (1 study[2]) 12 weeks	⊕⊕⊕⊖ **MODERATE**[3] due to indirectness	**RR 1.45** (1.15 to 1.82)	**333 per 1000**	**150 more per 1000** (from 50 more to 273 more)
Response HSRD	442 (1 study[2]) 12 weeks	⊕⊕⊕⊖ **MODERATE**[3] due to indirectness	**RR 1.73** (1.16-2.57)	**144 per 1000**	**105 more per 1000** (from 23 more to 225 more)

CI: Confidence interval; **RR:** Risk ratio;

[1] CI not stated, but P value for comparison between groups < 0.001.
[2] Keller et al. A 2000 [9].
[3] One study from US only, mean age 43 years, Study on adult with chronic major depressive disorder, 681 adults with a chronic nonpsychotic major depressive disorder randomly assigned to 2 weeks of outpatient treatment with nefazodone, the cognitive behavioral-analysis system of psychotherapy (16 to 20sessions), or both.

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION

Psychotherapy compared to usual care for elderly patients with dysthymia

Bibliography: Cuijpers P et al. 2010.[10]

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Care as usual or waitlist	Risk difference with Psychotherapy (95% CI)
Depressive symptoms Depression scales	0 (3 studies)	⊕⊕⊕⊖ **MODERATE**[1] due to risk of bias		The mean change in depressive symptoms in the intervention groups was **0.21 standard deviations higher** (0.02 to 0.41 higher)	
Adverse events	0 (0)			No information on potential adverse events with psychotherapy	

CI: Confidence interval; **RR:** Risk ratio;

[1]Quality of studies varied, lack of blinding a problem.

Psychological treatment vs antidepressants for elderly with dysthymia

Bibliography: Cuijpers P et al. 2010. [10]

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Antidepressants	Risk difference with Psychological treatment (95% CI)
Depressive symptoms depression scales	0[3] (3 studies)	⊕⊕⊖⊖ **LOW**[4,5] due to risk of bias, indirectness		The mean change in depressive symptoms in the intervention groups (PT) was **0.47 standard deviations lower** (0.18 to 0.75 lower)[1]	
Dropout rate	0[3] (5 studies)	⊕⊕⊖⊖ **LOW**[4,5] due to risk of bias, indirectness	**RR 0.97** (0.73 to 1.28)	**Moderate**[4]	
				244 per 1000[3]	**7 fewer per 1000** (from 66 fewer to 68 more)

CI: Confidence interval; **RR:** Risk ratio;

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION

[1] Pharmacotherapy more effective in reducing depressive symptoms than psychotherapy for patients with dysthymia.
[2] Rates not reported, we have chosen rates in control groups in review of de Maat [6] as illustrative risks for groups receiving psychotherapy only.
[3] Number of patients not stated.
[4]Quality of trials varied, lack of blinding not possible and a risk of bias.
[5]This analyses included all studies in the review, patients with different types of chronic depression, not only dysthymia, and not only elderly patients.

Combined therapy (antidepressants and psychotherapy) compared to antidepressants alone for elderly with dysthymia

Bibliography: Cuijpers P et al. 2010.[10]

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Antidepressants alone	Risk difference with combined therapy (ADs and PT) (95% CI)
Depressive symptoms depression scales	?[2] (4 studies)	⊕⊕⊕⊖ **VERY LOW**[3,4,5] due to risk of bias, inconsistency, imprecision		The mean change in depressive symptoms in the intervention groups was **0.04 standard deviations lower** (0.24 lower to 0.17 higher)	
Dropout rate	?[2] (7 studies)	⊕⊕⊖⊖ **LOW**[3,6] due to risk of bias, imprecision	**RR 0.82** (0.62 to 1.08)	**Moderate**[1]	
				244 per 1000[2]	**44 fewer per 1000** (from 93 fewer to 20 more)

CI: Confidence interval; **RR:** Risk ratio;

[1] Rates not reported, we have chosen rates in control groups in review of de Maat[6] chosen as illustrative risks for groups receiving psychotherapy only.
[2] Number of participants not stated.
[3] The quality of studies varied.
[4]This is a subgroup analysis in a series of 9 studies on chronic major depression (2 studies), double depression (2 studies), dysthymia (4 studies) and mixed population (1 study). Overall combined treatment seemed to be more effective than AD alone (SMD = 0.23, 95% CI +0.01-0.47), but not in the 4 studies on dysthymia.
[5]Wide confidence interval crossing line of no difference, few events.

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION

[6]This analyses included all studies in the review, patients with different types of chronic depression, not only dysthymia, and not only elderly patients, but we decided not to rate down.

Psychotherapy in combination with antidepressants compared to psychotherapy alone for elderly with dysthymia

Bibliography: Cuijpers P et al. 2010.[10]

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Psychotherapy alone	Risk difference with Psychotherapy in combination with antidepressants (95% CI)
Depressive symptoms Depression scales	0 (4 studies)	⨁⨁⨀⨀ **LOW**[3,4] due to risk of bias, imprecision		The mean change in depressive symptoms in the intervention groups was **0.45 standard deviations higher** (0.20 to 0.70 higher)	
Dropout rate	0 (3 studies)	⨁⨁⨁⨀ **VERY LOW**[3,5,6] due to risk of bias, inconsistency, imprecision	**RR 1.10** (0.79 to 1.52)	**Moderate**[1]	
				244 per 1000[2]	**24 more per 1000** (from 51 fewer to 127 more)

CI: Confidence interval; **RR:** Risk ratio;

[1] Rates not reported, we have chosen rates in control groups in review of de Maat [6] chosen as illustrative risks for groups receiving psychotherapy only.
[2] Number of patients not stated.
[3] Quality of studies varied.
[4] Four studies with different patient groups included in the analyses, not only elderly patients, and not only patients with dysthymia, also patients with other form of chronic depression. Too few data to do subgroup based on diagnosis.
[5] Studies on patients with all types of chronic depression included, not only dysthymia, and not only elderly patients. We decided not to rate down for this, however.
[6] Wide confidence interval, crossing line of no difference, few observations.

GRADE DECIDE

Problem: Moderate and severe depression in adults ***Option:*** Collaborative care to augment primary care ***Comparison:*** Usual care ***Setting:*** Primary care

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION
VALUES	**Are the desirable effects large relative to undesirable effects?**	*No* ☐ *Probably No* ☐ *Uncertain* ☐ *Probably Yes* ☐ *Yes* ☒ | ***Varies*** ☐		

GRADE DECIDE **Problem:** Moderate and severe depression in adults **Option:** Collaborative care to augment primary care **Comparison:** Usual care **Setting:** Primary care

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION
RESOURCE USE	**Are the resources required small?**	No ☐ / Probably No ☐ / Uncertain ☒ / Probably Yes ☐ / Yes ☐ / **Varies** ☐		Kostnadene for pasienten og familien antas å være relativt små. Utgifter til medikamenter er i dag relativt små, mens utgifter til strukturert psykologisk behandling er større. Hovedutfordringen kan være at det er mangel på denne type tilbud, og at eldre med alvorlig depresjon har vanskeligere for å få tilbudet enn yngre med depresjon.
RESOURCE USE	**Is the incremental cost small relative to the net benefits?**	No ☐ / Probably No ☐ / Uncertain ☐ / Probably Yes ☒ / Yes ☐ / **Varies** ☐	Flere kosteffektivitetsanalyser har konkludert med at kombinasjonsbehandling er effektivt ved alvorlig depresjon. Kostnadene for hver pasient som ble vellykket behandlet ble i en engelsk studie beregnet til £ 4056 (95 % CI 1400 -18 300 £); kostnaden per vunnet kvalitetsjusterte leveår var £ 5777 (95 % CI 1900-33 800 £) for alvorlig depresjon (1). Kombinasjonsbehandling ble også vurdert å være kostnadseffektiv i en japansk undersøkelse (2). I disse analysene er også samfunnsmessige tap pga. redusert produktivitet ved sykefravær tatt med i beregningen, slik at kostnadseffektiviteten vil være noe mindre blant eldre som ikke lenger er i arbeid. Fortsatt antar vi imidlertid at kombinasjonsbehandlingen er kostnadseffektiv ved alvorlig depresjon.	
EQUITY	**What would be the impact on health inequities?**	Increased ☐ / Probably increased ☐ / Uncertain ☒ / Probably reduced ☐ / Reduced ☐ / **Varies** ☐	Vi har ingen dokumentasjon om mulige effecter på ulikheter.	
ACCEPTABILITY	**Is the option acceptable to key stakeholders?**	No ☐ / Probably No ☐ / Uncertain ☐ / Probably Yes ☒ / Yes ☐ / **Varies** ☐	Vi har lite solid dokumentasjon om hvilken behandling eldre med depresjon foretrekker. Erfaringsmessig er både medikamentell og psykologisk behandling akseptabelt for pasienter og familie.	
FEASIBILITY	**Is the option feasible to implement?**	No ☐ / Probably No ☐ / Uncertain ☐ / Probably Yes ☒ / Yes ☐ / **Varies** ☐		Det er mangel på tilbud om strukturert psykologisk behandling. Det bør være mulig både å øke kompetansen blant fastleger, samt å sikre at eldre med alvorlig depresjon kan få tilbud om psykologisk behandling i spesialisthelsetjenesten om nødvendig.

Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings ☐	Undesirable consequences *probably outweigh* desirable consequences in most settings ☐	The balance between desirable and undesirable consequences *is closely balanced or uncertain* ☐	Desirable consequences *probably outweigh* undesirable consequences in most settings ☒	Desirable consequences *clearly outweigh* undesirable consequences in most settings ☐
Type of recommendation	**We recommend against the option** ☐		**We suggest considering the option** ☐ Only in the context of rigorous research ☐ Only with targeted monitoring and evaluation ☐ Only in specific contexts		**We recommend the option** ☒
Recommendation (text)	**Vi anbefaler:** **Behandling av pasienter med alvorlig depresjon, tilbakevendende depresjon, kronisk depresjon og dystymi** **Fastleger bør tilby pasienter med alvorlig depresjon, tilbakevendende depresjon, kronisk depresjon og dystymi både antidepressiver og psykoterapi/strukturert psykologisk behandling.** **Dersom fastlegen ikke selv har kompetanse til å gi psykoterapi, bør fastlegen henvise pasienten til helsepersonell som har slik kompetanse. Kognitiv terapi, kognitiv atferdsterapi og interpersonlig terapi har best dokumentasjon**.				
Justification	Det er dokumentasjon av moderat til høy kvalitet på at kombinasjonsbehandling med antidepressiver og psykoterapi er mer effektivt enn en av behandlingene alene for å redusere depresjonssymptomer og øke andelen som blir bra av sin depresjon. Det er mulig at frafall reduseres ved lang tids oppfølging. Kombinasjonsbehandlingen er kostnadseffektiv ved alvorlig depresjon, kanskje også ved moderat depresjon.				
Implementation considerations	Utfordringen er å sikre tilgang til strukturert psykologisk behandling til alle eldre med alvorlig depresjon, samt pasienter med kronisk depresjon, tilbakevendende depresjon og dystymi. Opplæring av fastleger i enkle prinsipper for kognitiv atferdsterapi eller interpersonlig terapi er viktig. Samtidig er det viktig at disse pasientene sikres tilbud i spesialisthelsetjenesten (DPS og alderspsykiatri eller hos privatpraktiserende psykologer og psykiatere) ved henvisning.				
Monitoring and evaluation	Monitorering og evaluering vil bli gjort i TICD prosjektet.				
Research priorities	Det er behov for mer forskning om effektene av kombinasjonsbehandling versus monoterapi spesielt ved dystymi. Det er også behov for mer informasjon om kostnadseffektivitet av de ulike behandlingsmulighetene.				

Skal antidepressiver vs psykoterapi brukes ved alvorlig depresjon hos eldre, skal kombinasjon av antidepressiver og psykoterapier brukes vs antidepressiver alene, skal kombinasjon av antidepressiver og psykoterapi brukes vs psykoterapi alene

Author(s): Flottorp, Aakhus
Date: 2013-08-25
Question: Should antidepressants vs psychotherapy be used for depression in the elderly?
Settings:
Bibliography: Cuijpers et al. The efficacy of psychotherapy and pharmacotherapy in treating depressive and anxiety disorders: a meta-analysis of direct comparisons. World Psychiatry 2013. Pinquart et al.Treatments for later-life depressive conditions: a meta-analytic comparison of pharmacotherapy and psychotherapy. Am J Psychiatry 2006.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antidepressants	Psychotherapy	Relative (95% CI)	Absolute		
Depressive symptoms (measured with: Depression scale; Better indicated by lower values)												
67	randomised trials	no serious risk of bias	serious[1]	no serious indirectness[2]	no serious imprecision	none	3142[3]	2853[4]	-	SMD 0.02 higher (0.1 lower to 0.13 higher)	⊕⊕⊕O MODERATE	CRITICAL

[1] Both clinical and statistical heterogeneity: studies on depression and anxiety in all adults, not only elderly. 40 studies on depression, 27 on anxiety.
[2] The 67 studies were on both depression and anxiety, and not only with elderly, But subgroup analysis of 39 studies on MDD showed similar results as all studies.
[3] pharmacotherapy
[4] psychotherapy

Author(s): Flottorp, Aakhus
Date: 2013-08-25
Question: Should antidepressants in combination with psychotherapy vs antidepressants alone be used for elderly patients with depression?
Settings:
Bibliography: Cuijpers et al. Adding psychotherapy to pharmacotherapy in the treatment of depressive disorders in adults: a meta-analysis. J Clin Psychiatry 2009. Pampallona et al. Combined pharmacotherapy and psychological treatment for depression: a systematic review. Arch Gen Psychiatry 2004.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antidepressants in combination with psychotherapy	Antidepressants alone	Relative (95% CI)	Absolute		
Symptom change (measured with: Depression scales; Better indicated by higher values)												
25[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness[3]	no serious imprecision	none	10818	1018	-	SMD 0.31 higher (0.2 to 0.43 higher)	⊕⊕⊕O MODERATE	CRITICAL

Dropout rate												
19[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	0%	OR 0.65 (0.5 to 0.83)	-[4]	⊕⊕⊕O MODERATE	IMPORTANT
Response rate (follow-up median 12 weeks)												
16[5]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/932 (0%)	24%[6]	OR 1.86 (1.38 to 2.52)	130 more per 1000 (from 64 more to 203 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Dropout rates all studies (follow-up median 12 weeks)												
16[5]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[7]	none	-	25%[8]	OR 0.86 (0.6 to 1.24)	27 fewer per 1000 (from 83 fewer to 42 more)	⊕⊕⊕O MODERATE	IMPORTANT
Dropout rates <12 weeks (follow-up x-12 weeks)												
9	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[7]	none	-	25%[8]	OR 1.11 (0.71 to 1.74)	-	⊕⊕⊕O MODERATE	IMPORTANT
Dropout rates > 12 weeks												
6[5]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	25%[8]	OR 0.59 (0.39 to 0.88)	86 fewer per 1000 (from 23 fewer to 135 fewer)[4]	⊕⊕⊕⊕ HIGH	IMPORTANT

[1] Cuijpers 2009: Adding psychotherapy to pharmacotherapy in the treatment of depressive disorders in adults: A meta-analysis.
[2] Blinding of patients and not possible. Methodological quality of several of the included studies not optimal.
[3] Studies on adults with depression, not only older adults with severe depression. Subgroup analysis did not find significant differences in effect size based on patient groups, however, except for lower effect sized in patients with dysthymia.
[4] Dropout rate in control or intervention groups not stated.
[5] Pampallona Arch Gen Psych 2004
[6] Response rate not stated in review, 24% in control group in systematic review by Gensichen 2006.
[7] Wide confidence interval
[8] No absolute numbers or data on dropout rates given in review. Control group in systematic review of de Maat et al used here

Author(s): Flottorp, Aakhus
Date: 2013-08-25
Question: Should Antidepressants combined with psychotherapy vs psychotherapy alone be used for elderly patients with depression?
Settings: primary care
Bibliography: de Maat et al. Relative efficacy of psychotherapy and combined therapy in the treatment of depression: a meta-analysis. Eur Psychiatry 2007.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Antidepressants combined with psychotherapy**	**Psychotherapy alone**	**Relative (95% CI)**	**Absolute**		

Dropout rate (follow-up 8-20 weeks)												
7	randomised trials	no serious risk of bias[1]	no serious inconsistency	no serious indirectness	serious[2]	none	112/444 (25.2%)	112/459 (24.4%)	RR 1.03 (0.82 to 1.3)	7 more per 1000 (from 44 fewer to 73 more)	⊕⊕⊕O MODERATE	IMPORTANT
Remission (follow-up 8-20 weeks)												
7	randomised trials	no serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	202/444 (45.5%)	158/459 (34.4%)	RR 1.32 (1.12 to 1.56)	110 more per 1000 (from 41 more to 193 more)	⊕⊕⊕⊕ HIGH	

[1] Risk of bias in included studies not reported, but we chose not to grade down.
[2] Wide CI, crossing 1 (line of no difference)

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References

[1] Cuijpers et al. The efficacy of psychotherapy and pharmacotherapy in treating depressive and anxiety disorders: a meta-analysis of direct comparisons. World Psychiatry 2013

[2] Pinquart M et al. Treatments for later-life depressive conditions: a meta-analytic comparison of pharmacotherapy and psychotherapy. Am J Psychiatry 2006;163:1493-501.

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[4] Cuijpers P, Dekker J, Hollon SD, Andersson G. Adding psychotherapy to pharmacotherapy in the treatment of depressive disorders in adults: a meta-analysis. J Clin Psychiatry 2009;70:1219-29.

[5] Pampallona S, Bollini P, Tibaldi G, Kupelnick B, Munizza C. Combined pharmacotherapy and psychological treatment for depression: a systematic review. Arch Gen Psychiatry 2004;61:714-9.

[6] de Maat SM, Dekker J, Schoevers RA, de JF. Relative efficacy of psychotherapy and combined therapy in the treatment of depression: a meta-analysis. Eur Psychiatry 2007;22:1-8.

[7] Gensichen J, Beyer M, Muth C, Gerlach FM, Von KM, Ormel J. Case management to improve major depression in primary health care: a systematic review. Psychol Med 2006;36:7-14.

[8] Spijker J et al. Psychotherapy, antidepressants, and their combination for chronic major depressive disorder: a systematic review. Can J Psychiatry 2013;58:386-92.

[9] Keller et al. A comparison of nefazodone, the cognitive behavioral-analysis system of psychotherapy, and their combination for the treatment of chronic depression. N Engl J Med 2000;342:1462-70.

[10] Cuijpers P et al. Psychotherapy for chronic major depression and dysthymia: a meta-analysis. Clin Psychol Rev 2010;30:51-62.

Definitions for ratings of the certainty of the evidence (GRADE)

Ratings	Definitions	Implications
⨁⨁⨁⨁ High	This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different* is low.	This evidence provides a very good basis for making a decision about whether to implement the intervention. Impact evaluation and monitoring of the impact are unlikely to be needed if it is implemented.
⨁⨁⨁◯ Moderate	This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different[4] is moderate.	This evidence provides a good basis for making a decision about whether to implement the intervention. Monitoring of the impact is likely to be needed and impact evaluation may be warranted if it is implemented.
⨁⨁◯◯ Low	This research provides some indication of the likely effect. However, the likelihood that it will be substantially different[4] is high.	This evidence provides some basis for making a decision about whether to implement the intervention. Impact evaluation is likely to be warranted if it is implemented.
⨁◯◯◯ Very Low	This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different[4] is very high.	This evidence does not provide a good basis for making a decision about whether to implement the intervention. Impact evaluation is very likely to be warranted if it is implemented.

*Substantially different: large enough difference that it might have an effect on a decision

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