

Treatment of Geriatric Depression

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Rural Family Practice
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Objectives

- a) To discuss optimal psychosocial antidepressant therapy in the elderly
- b) To discuss optimal pharmacologic antidepressant therapy in the elderly

Disclosures

- No industry sponsorships

The Context
Prevalence of Depression >65

- 16.5% in the community
- 7.9-25% minor depression hospitalized seniors
- 10-44.5% major depression hospitalized seniors
- 29% of those in primary care
- Fewer than 20% of seniors with depression are being treated

The Context
Differences in Seniors

- In depressed older adults, depressed mood may be less commonly reported
- Somatic symptoms are more prominent
 - loss of appetite, lack of energy, irritability, sleeplessness, worrying, and aches and pains

The Context
Differences in Seniors

- Elderly depressed people are also more likely to have psychotic delusions than younger people
- Cognitive impairment more apparent, including executive dysfunction

The Context
Consequences of Late-life Depression

- Increased use of medical resources
- Decreased adherence to prescription medication for chronic illness
- Increased mortality
- Evidence for worsening prognosis of cardiac events

The Context
Elders at Higher Risk

- Socially isolated
- Persistent complaints of memory difficulties
- Chronic disabling illness, recent major physical illness (e.g., within 3 months)
- Persistent sleep difficulties

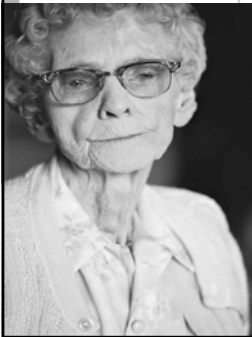
The Context
Elders at Higher Risk

- Significant somatic concerns or recent onset of anxiety
- Refusal to eat or neglect of personal care
- Recurrent or prolonged hospitalization
- Diagnosis of dementia, Parkinson Disease or stroke
- Recent placement in a nursing/LTC home

The Context Elders at Higher Risk

- Recently bereaved with unusual symptoms (active SI, guilt not related to the deceased, psychomotor retardation, mood congruent delusions, marked functional impairment after two months of loss, reaction that seems out of proportion with the loss)
- Bereaved individuals, 3 to 6 months after the loss

Patient Case: Mrs. M.



- 82 year old recently widowed, five grandchildren
- No psychiatric history
- Husband, John, of 50 years died one month ago and now lives alone
- Persistent sadness for 3/52, with initial insomnia, appetite loss, poor concentration, decreased energy

Patient Case: Mrs. M.

- History of HTN
- Recurrent UTI
- Stopped going to church and other activities she used to do with John
- No suicidal ideation; no psychosis; no worthlessness



Patient Case: Mrs. M.

Dx: Bereavement

WHAT WOULD YOU DO AT THIS POINT?

WHO WOULD START AN ANTIDEPRESSANT THIS VISIT?

**Optimizing Psychosocial Therapy:
Reminiscence and life review**

- involve going back over one's life and remembering particular days and events.
- reminiscence tends to be more about remembering pleasant events spontaneously
- life review therapy is more structured and involves an evaluation of one's life

Quality of evidence: I

Review of effectiveness: A meta-analysis of 23 studies

Conclusion: Well supported as effective treatments for depression in older people.

Optimizing Psychosocial Therapy: Cognitive-Behavior therapy

- **Description:** an active, time-limited therapy that aims to change the thinking and behavior that cause or maintain depression
- **Quality of evidence:** I
- **Review of effectiveness:** Five RCTs
- **Conclusion:** CBT has shown to be an effective treatment for depressed older people, although stroke patients may not benefit

Conclusions on the effectiveness of treatments for late-life depression: Psychological treatments

Treatment	Evidence level	Conclusion
Cognitive behaviour therapy	I	Sound evidence of effectiveness, but not for stroke patients
Dialectical behaviour therapy	II	Evidence of effectiveness as adjunct to antidepressant medication
Interpersonal therapy	II	Some evidence of effectiveness
Problem-solving therapy	II	Some evidence of effectiveness
Psychodynamic psychotherapy	II	Sound evidence of effectiveness
Reminiscence and life review	I	Sound evidence of effectiveness
Bibliotherapy	II	Sound evidence of effectiveness for mild to moderate depression

Patient Case Mrs. M.'s next visit...



- 6 weeks goes by
- Still low mood
- Isolating and more anxious than usual
- Insomnia and weight loss
- Low energy
- Passive suicidal ideation

WHAT IS YOUR TREATMENT CHOICE?

WOULD YOU REFER TO A GERIATRIC PSYCHIATRIST?

Optimizing Therapy Pharmacologic

- In general, more than half of older adults treated with antidepressants experience at least a 50 percent reduction in depressive symptoms
- We still have little data to guide the choice and specific timing (algorithms) for interventions for any given individual

Optimizing Therapy Pharmacologic

- **Quality of evidence:** I
- **Review of effectiveness:** Antidepressants have been well tested for use in older people. A recent review of 17 RCTs concluded that three classes of antidepressants (TCAs, SSRIs and MAOIs) are effective for treating older people, even those who are hospitalized with severe physical illnesses
- **Conclusion:** Antidepressants have sound evidence of effectiveness for use in depressed older people.

Optimizing Therapy Pharmacologic


- No difference in tolerability between SSRIs and tricyclics on the basis of rates of discontinuation due to side effects, clinically significant differences may still be present
- For example, common reasons for discontinuing SSRIs include sleep disturbance, GI distress, anxiety, headaches, and weight loss
- Common complications of tricyclic agents (amitriptyline, imipramine, and doxepin) include more worrisome side effects, such as postural hypotension and arrhythmia

Optimizing Therapy Major Depression, Non-psychotic

- Number Needed to Treat
 - 4 for TCAs
 - 4 for citalopram
 - 8-32 for fluoxetine

Optimizing Therapy Pharmacologic

DOGGIE PROZAC



ELI LILLY
SETTING THE SAME HIGH STANDARDS OF
INTEGRITY FOR DOGS

<http://www.docstoc.com/docs/4026024/Antidepressants-for-the-Geriatric-Population-Preferred-Antidepressant-Citalopram-Celexa-Escitalopram>

Optimizing Therapy
Pharmacologic: Preferred Antidepressants

- Citalopram 10-40 mg/day; initial dose 10 mg daily with food; increase by 10 mg q3/52; helpful for anxiety; low risk of CYP450 interactions; caution with hyponatremia/GIB/sexual dysfunction
- Escitalopram
- Sertraline
- Bupropion IR/SR

Optimizing Therapy
Pharmacologic: Preferred Antidepressants

- Mirtazapine
- Duloxetine
- Venlafaxine
- Desvenlafaxine

Optimizing Therapy
Pharmacologic: Accepted Antidepressants

- Paroxetine: anticholinergic; inhibits CP450-2D6; may cause GI distress, discontinuation syndrome
- Imipramine
- Desipramine
- Phenelzine
- Tranylcypromine
- Selegiline

Optimizing Therapy
Pharmacologic: Not recommended
Antidepressants

- Fluoxetine (inhibits CP450-2D6 – metoprolol, codenine, risperidone, trazodone); stimulating, insomnia, sexual dysfunction
- Amitriptyline/doxepin: highly anticholinergic/antihistaminic; caution with urinary retention, glaucoma, or cardiac conduction problems; multiple drug interactions; very sedating; lethal in overdose

Optimizing Therapy
Pharmacologic: Suicide

- Little is known about the efficacy of interventions in preventing suicidal behaviors among older adults, even though the rate of suicide among older adults is greater than in any other age group
- An evidence-based review of the literature suggests that the only supported preventive intervention for late-life suicide is the identification and effective treatment of depression

Optimizing Therapy
Pharmacologic: Medical Comorbidity

- Select ADPs less likely to interact with the medications already prescribed for concurrent medical conditions
- Similar fall risk compared to TCAs but insignificant blood pressure effects
- Older adults have greater risk of hyponatremia due to renal changes in aging
- Dementia, cardiovascular disease, diabetes and Parkinson disease will worsen with highly anticholinergic tricyclic ADP

Optimizing Therapy
Pharmacologic: Medical Comorbidity

- Cochrane meta-analysis of treatment in adults of all ages with physical illness (DM, cancer, HIV, Parkinson disease, MI) found NNT of 4, similar to treatment in a general older population
- Fluoxetine in patients with co-morbid medical illness in a geriatric unit improved as well or better than those with less significant illness

Optimizing Therapy
Pharmacologic: Medical Comorbidity



- Escitalopram, citalopram and sertraline effective in medically compromised individuals (post-stroke depression and dementia) with favorable safety and drug interaction profile

Optimizing Therapy
Pharmacologic: Medical Comorbidity

- TCA side effects include
 - postural hypotension (resulting in falls and fractures)
 - cardiac conduction abnormalities
 - delirium
 - worsened cognitive function
 - acute urinary retention
 - dry mouth
 - constipation

Optimizing Therapy
Pharmacologic: Medical Comorbidity

- EKG and postural BP should be done when starting or increasing TCA
- Nortriptyline and desipramine are less anticholinergic
- Blood monitoring of TCA is recommended given toxicity risk and some patients are slow metabolizers

Optimizing Therapy
Pharmacologic: Medical Comorbidity


- Newer agents with lower anticholinergic properties and less potential to cause postural hypotension or cardiac conduction problems (SSRI, bupropion, mirtazapine, venlafaxine, duloxetine) are usually recommended for treatment in medically ill patients

Optimizing Therapy
Pharmacologic: Minor Depression

- Evidence-based reviews of interventions for geriatric depression primarily address major depression
- Little attention to the treatment of associated conditions such as minor depression or suicidal behaviors
- Results of randomized placebo-controlled studies of SSRIs in the treatment of older adults with minor depression suggest only modest benefits

Optimizing Therapy

Pharmacologic: Medical Comorbidity




- Remission may be impeded by undiagnosed or poorly controlled physical or mental disorders
- Reassessment for
 - Anxiety
 - Cognitive changes
 - Medical issues
 - Substance abuse (alcohol, BZD, pain killers)

Conclusions on the effectiveness of treatments for late-life depression: Medical treatments

Treatment	Evidence level	Conclusion
Antidepressant medication	I	Sound evidence of effectiveness
Electroconvulsive therapy	I	Sound evidence of effectiveness, but only appropriate in extreme circumstances
Oestrogen	II	No effect found
Testosterone	III-3	No convincing evidence
Transcranial magnetic stimulation	II	No convincing evidence

Optimizing Therapy

When to refer to the psychiatrist...




If patients have

- Psychotic depression
- Bipolar disorder
- Depression with suicidal ideation or intent
- Also consider for
 - Co-morbid substance abuse
 - Major depressive episode, severe
 - Co-morbid dementia



Patient Case: Mrs. T.

- 72 year old widow with periods of depression throughout her life
- No clear periods of euthymia
- Baseline general anxiety for many years
- Guilt over first husband's suicide 30 years ago



Patient Case: Mrs. T.

- Son found father's body and he is on antidepressants
- Seasonal major depressive symptoms brought on by anniversary of husband's death

Patient Case: Mrs. T.

Provisional Dx:

1. Major Depressive Disorder
2. Dysthymic Disorder
3. R/O GAD

Patient Case: Mrs. T.

Management

1. Due to insomnia, mirtazapine was chosen reaching 30 mg QHS
2. Start counselling

**Optimizing Therapy
Non-psychotic MDE**

- Data suggest non-pharmacological care to study subjects on placebo (regular monitoring, encouragement, and instilling hope) can be effective in less severe depression
- reinforces the need to include supportive psychotherapeutic interventions in the treatment of depressed elderly

**Optimizing Therapy
Pharmacologic**

- A recent meta-analysis of antidepressant studies that included all age groups found that antidepressants offer only a 20 percent (2 points) greater reduction in scores on the Hamilton Rating Scale for Depression compared with placebo
- This suggests that placebo medication combined with visits by the prescribing physician may account for 80 percent of the effect of antidepressants

**Patient Case:
Mrs. T.'s next visit...**

- Significant improvement in mood and anxiety at three months
- Residual symptoms, including annual stressors of anniversary of his death

**WHAT NOW?
HOW LONG DO YOU TREAT?
WHAT ELSE CAN BE DONE?**

**Optimizing Therapy
How Long Do You Treat?**

- What is remission?
 - When patient and family members describe patients as being "back to his/her normal self"
 - In many cases, more than one intervention needed. Therefore, monitor responses to treatment and consider addition of targeted interventions

Optimizing Therapy How Long Do You Treat?

- Remission of depressive symptoms is the most appropriate goal of therapy

Optimizing Therapy How Long Do You Treat?

- *Is remission of depressive symptoms in primary care a realistic goal? A meta-analysis.*
- Remission rates in primary care studies of depression are at least as high as for those in psychiatric settings
- It is a realistic goal for family physicians to target remission of symptoms as an optimal outcome for treatment of depression

Optimizing Therapy How Long Do You Treat?

- Not as under-treated as earlier studies suggest, but rates of adequate treatment are not encouraging
- Optimal dosing does not always occur
- Adequate doses reached for 79% of SSRIs and 31% of TCAs



**SO...
START LOW
GO SLOW,
BUT GO!**

**Optimizing Therapy
National Guidelines for Seniors' Mental
Health, May 2006**

- Minor Depressive Disorder
 - Of less than 4 weeks' duration should be treated with supportive psychotherapies or psychosocial interventions
 - Pharmacological treatment or evidence-based psychotherapy if symptoms persist more than 4 weeks after psychosocial interventions initiated

**Optimizing Therapy
National Guidelines for Seniors' Mental
Health, May 2006**

- Dysthymic Disorder
 - Should be treated with pharmacologic therapy with or without psychotherapy, with periodic reassessment to measure response
 - Psychotherapy may be used alone with periodic reassessment to measure response

**Optimizing Therapy
National Guidelines for Seniors' Mental
Health, May 2006**

- Major Depressive Disorder, single or recurrent episode, mild to moderate in severity (unipolar depression)
 - Antidepressants
 - Psychotherapy
 - Antidepressants plus psychotherapy

**Optimizing Therapy
National Guidelines for Seniors' Mental
Health, May 2006**

- Major Depressive Disorder, single or recurrent episode, severe without psychosis
 - Should be offered a combination of antidepressants and concurrent psychotherapy when appropriate services are available and there is no contra-indication to either treatment
 - consider ECT if adequate trials of antidepressants combined with psychotherapy ineffective or if health is deteriorating rapidly

**Optimizing Therapy
National Guidelines for Seniors' Mental
Health, May 2006**

- Major Depressive Disorder, single or recurrent episode, severe with psychosis
 - If there is no contra-indications to its use, offer ECT when available. Alternatively, combination of antidepressant plus antipsychotic medicine. If not effective (poorly tolerated, no improvement in at least some of the symptoms within 4-8 weeks of treatment, or lack of remission despite optimization of dose and duration of treatment over 8-12 weeks, ECT needs to be offered
 - ECT offered if severe health consequences (suicide, metabolic derangement) are imminent

Patient Case: Mrs. T.'s next visit...

- No further improvement with mirtazapine 45 mg HS for 4/52
- Combine with venlafaxine 37.5 mg PO AM
- Combine with psychotherapy (CBT focus – journal, closure letter; IPT – family-oriented)

Conclusions

1. Depression is not uncommon in older adults
2. There are effective pharmacologic and psychosocial therapies in older adults, although studies are very limited
3. A combination of pharmacologic and psychosocial therapies is likely more effective than either alone in treating and preventing depression
4. Pharmacodynamic/kinetic changes, comorbid psychiatric and medical issues need consideration but should not prevent treatment of depression

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Potential Cytochrome P450 Interactions Involving Antidepressants

(Cupps and Tracy, 1998; Devane *et al.*, 2004; Nemeroff *et al.*, 1996)

Isoenzyme	Substrate of Isoenzyme	Moderate to Strong Inhibition of Isoenzyme	Inducer of Isoenzyme
CYP2D6	Fluoxetine Paroxetine Venlafaxine Nortriptyline Desipramine Amiripryline Fluvoxamine	Fluoxetine Paroxetine Bupropion	None known
CYP 3A4	Sertraline Venlafaxine Amiripryline Citalopram Escitalopram	Fluvoxamine Fluoxetine (metabolite) Sertraline Desipramine	St. John's Wort Carbamazepine Phenytoin Phenobarbital Dexamethasone
CYP 1A2	Amiripryline	Fluvoxamine	Phenytoin Phenobarbital Charcoal-broil meat

Commonly Used Antidepressant Medications

Generic Name	Trade Name	Starting Dose (mg/day)	Average Dose	Max recom'd dose (CPS)	Comments/caution
SSRI					
Citalopram	Celexa	10	20-40	40 mg	
Escitalopram	Cipralax	5	10-20	20 mg	
Fluoxetine	Prozac	5	10-20	20 mg	*Max. dose used in studies; Long elimination 1/2 life; Several potential interactions
Fluvoxamine	Luvox	25-50	100-200	300 mg	Several potential interactions
Paroxetine	Paxil	5-10	20	50 mg	*Significant anticholinergic load & possible interactions
Sertraline	Zoloft	25	50-150	200 mg	
Other Agents					
Bupropion	Wellbutrin	100	100 mg BID	150 mg BID	May cause seizures
Mirtazapine	Remeron	15	30-45	45 mg	
Moclobemide	Manerix	150	150-300 BID	300 mg BID	Do not combine with MAO B inhibitors or Tricyclics
Venlafaxine	Effexor	37.5	75-225	375 mg	*For severe depression; May increase blood pressure
Tetracyclic Antidepressants					
Desipramine	Norpramin	10-25	50-150	300 mg	Anticholinergic properties; cardio-vascular side effects; Monitor blood levels
Nortriptyline	Aventyl	10-25	40-100	200 mg	Anticholinergic properties; cardio-vas blood levels

Treatments identified as being used for depression, but for which no evidence was found on depression in older people (aged ≥ 60 years)

Medicines and remedies

- Biotin, black cohosh (*Actaea racemosa* and *Cimicifuga racemosa*), borage (*Borago officinalis*), brahmi (*Bacopa monniera*), Californian poppy (*Eschscholtzia californica*), cat's claw (*Uncaria tomentosa*), catnip (*Nepeta cataria*), chamomile (*Anthemis nobilis*), chaste tree berry (*Vitex agnus castus*), Chinese medicinal mushrooms (reishi) (*Ganoderma lucidum*), choline, chromium, coenzyme Q10, cowslip (*Primula veris*), damiana (*Turnera aphrodisiaca*), dandelion (*Taraxacum officinale*), flax seeds (linseed) (*Linum usitatissimum*), γ -aminobutyric acid (GABA), ginkgo (*Ginkgo biloba*), ginseng (*Panax ginseng*), glutamine, hawthorn (*Crataegus oxyacantha*), homoeopathy, hops (*Humulus lupulus*), hyssop (*Hyssopus officinalis*), inositol, lecithin,

Treatments identified as being used for depression, but for which no evidence was found on depression in older people (aged ≥ 60 years)

Medicines and remedies

- lemon balm (*Melissa officinalis*), L-glutamine, L-tyrosine, melatonin, milk thistle (*Silybum marianum*), mistletoe (*Viscum album*), motherwort (*Leonurus cardiaca*), nettles (*Urtica dioica*), nicotinamide, oats (*Avena sativa*), para-aminobenzoic acid (PABA), pantothenic acid, peppermint (*Mentha piperita*), phenylalanine, potassium, rehmannia (*Rehmannia glutinosa*), S-adenosylmethionine (SAMe), schizandra (*Schizandra chinensis*), selenium, Siberian ginseng (*Eleutherococcus senticosus*), skullcap (*Scutellaria lateriflora*), spirulina (*Spirulina maxima*, *Spirulina platensis*), St Ignatius bean (*Ignatia amara*), taurine, tension tamer, tissue salts, vervain (*Verbena officinalis*), wild yam (*Dioscorea villosa*), wood betony (*Stachys officinalis*, *Betonica officinalis*), yeast, zinc, zizyphus (*Zizyphus spinosa*).

Treatments identified as being used for depression, but for which no evidence was found on depression in older people (aged ≥ 60 years)

Lifestyle and alternative treatments

- Acupuncture, air ionisation, alcohol (for relaxation), aromatherapy, adequate sleep, avoidance of certain foods (barley, rye, wheat, dairy foods), caffeine avoidance, dance and movement, distraction techniques, ketogenic diet, marijuana avoidance, meditation, pets, pleasant activities, relaxation therapy, sugar avoidance, t'ai chi, yoga.

Conclusions on the effectiveness of treatments for late-life depression: Lifestyle changes and alternative therapies

Treatment	Evidence level	Conclusion
Alcohol avoidance	V	No evidence
Exercise	II	Evidence of effectiveness
Fish oils	V	No convincing evidence
Light therapy	II	Evidence of effectiveness for people in hospitals or nursing homes
Massage therapy	III-3	No convincing evidence
Music therapy	V	No evidence
St John's wort	II	Evidence of effectiveness for mild to moderate depression
Vitamins		
Folate	II	Some evidence of effectiveness for patients with Alzheimer's disease
	III-3	No convincing evidence for patients without Alzheimer's disease
Other B vit.	II	No convincing evidence
Vit. C, D and E	V	No evidence*

Based on National Health and Medical Research Council levels of evidence, with the addition of "Level V" for even weaker types of evidence.

The End - Thank You!



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