37th Annual UCLA
Geriatric Medicine Update
Lost Angeles, CA
September 25, 2021

Jürgen Unützer, MD, MPH, MA
Including material c/o Randal Espinoza MD, MPH
Jürgen Unützer, MD, MPH, MA: Disclosures

- **Employment:** University of Washington
  - Professor & Chair, School of Medicine; Dept. of Psychiatry and Behavioral Sciences
  - Adjunct Professor, School of Public Health

- **Grant funding**
  - National Institute of Health
  - Center for Medicare and Medicaid Innovation (CMMI)
  - Archstone Foundation

- **Contracts**
  - Community Health Plan of Washington, Public Health of Seattle & King County

- **Advisor**
  - Substance Abuse and Mental Health Administration (CMHS)
  - World Health Organization

- **Royalties**
  - Up To Date: Chapter on Late-Life Depression

- **NO FINANCIAL RELATIONSHIPS THAT PRESENT A CONFLICT OF INTEREST FOR TODAY’s PRESENTATION**
- **I WILL NOT DISCUSS OFF LABEL OR INVESTIGATIONAL USE OF MEDICATIONS OR OTHER TREATMENTS.**
Major Depression in Late Life

• More than having a bad day, week, or month

• Pervasive depressed mood / sadness

• Loss of interest / pleasure
  Lack of energy, fatigue, poor sleep and appetite, physical slowing or agitation, poor concentration, physical symptoms (aches and pains), irritability, thoughts of guilt, and thoughts of suicide

• A miserable state that can last for months or even years
Step 1: Engaging Patients and Families

• Developing a shared understanding of the problem:
  – Cause, meaning, cultural / spiritual aspects
  – Potential solutions (what will help)
  – Biggest worry

• Instill hope:
  – “You don’t have to feel this way.”
  – “We have several good treatment options”
Treatments for Late-life Depression

• Antidepressant Medications
  – Over 30 FDA approved
  – All are effective in 40 - 50 % of patients if taken correctly
  – It often takes several trials to find effective treatment
  – Patients need support during this time

• Psychotherapy / Talk therapy
  – Multiple approaches

• Physical activity / exercise

• Other somatic treatments
  – Electroconvulsive Treatment (ECT), VNS, TMS

The ‘Cycle of Depression’

- **STRESSORS**
  - Medical illness
  - Family problems
  - Work problems

- **THOUGHTS & FEELINGS**
  - Negative thoughts
  - Low self esteem
  - Sadness
  - Hopelessness

- **DEPRESSION**

- **PHYSICAL PROBLEMS**
  - Poor sleep
  - Pain
  - Low energy
  - Poor concentration

- **BEHAVIOR**
  - Social withdrawal
  - Decreased activities
  - Decreased productivity
Choosing Antidepressants

• All FDA approved antidepressants are equally effective (~ 50 % have a substantial response)

• Considerations in selecting an antidepressant:
  – Prior treatment history in patient / family members.
  – Patient preferences
  – Expertise of prescribing provider
  – Side effect profile (sedating or activating)
  – Safety in overdose
  – Availability and costs
  – Drug-drug interactions
Serotonin Reuptake Inhibitors: First Choice

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose/day</th>
<th>Therapeutic Range/day*</th>
<th>Generic</th>
<th>CYP 450 effects</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine (Prozac®)</td>
<td>5-10mg Qam</td>
<td>10-20mg</td>
<td>Y</td>
<td>+++</td>
<td>+/++</td>
</tr>
<tr>
<td>Sertraline (Zoloft®)</td>
<td>12.5-25mg Qam</td>
<td>50-150mg</td>
<td>Y</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Paroxetine (Paxil®)</td>
<td>10mg Qhs</td>
<td>20-30mg</td>
<td>Y</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Citalopram (Celexa®)</td>
<td>10mg Qhs</td>
<td>20-40mg</td>
<td>Y</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Escitalopram (Lexapro®)</td>
<td>5-10mg Qam</td>
<td>10-20mg</td>
<td>Y</td>
<td>±</td>
<td>±</td>
</tr>
</tbody>
</table>

* Dosage for Major Depression

Espinoza R., Unützer, J. 2013; Mittman 1999; Solai 2001; Sommer 2003; Williams 2000
Adequate Medication Trials

• Bring the patient back regularly to assess progress:
  – Treatment adherence
    • “Are you taking medications”? 
    • “How are you taking them?”
    • Are you having side effects or concerns?
  – Treatment response
    • Use a scale such as the PHQ-9 to track symptoms

• Make sure the dose is high enough
  – Start low but make sure you achieve therapeutic doses.

• Address side effects or other concerns
  – e.g., temporarily lower dose, change timing
Is the Patient at Maximum* Daily Therapeutic Dose?

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine (Prozac)</td>
<td>40 mg</td>
</tr>
<tr>
<td>Citalopram (Celexa)</td>
<td>20 mg</td>
</tr>
<tr>
<td>Escitalopram (Lexapro)</td>
<td>20 mg</td>
</tr>
<tr>
<td>Sertraline (Zoloft)</td>
<td>200 mg</td>
</tr>
<tr>
<td>Venlafaxine (Effexor)</td>
<td>300 mg</td>
</tr>
<tr>
<td>Desvenlafaxine (Pristiq)</td>
<td>100 mg</td>
</tr>
<tr>
<td>Duloxetine (Cymbalta)</td>
<td>60 mg</td>
</tr>
<tr>
<td>Bupropion (Wellbutrin)</td>
<td>450 mg</td>
</tr>
<tr>
<td>Mirtazapine (Remeron)</td>
<td>45 mg</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>125 mg (check serum level)</td>
</tr>
<tr>
<td>Desipramine</td>
<td>200 mg (check serum level)</td>
</tr>
</tbody>
</table>

* Start all meds low but consider to effective or maximum dose as tolerated over 4-12 wks.
# Adverse Effect Profiles of SRIs

SRIs: serotonergic; variably anticholinergic, antihistaminergic or antidopaminergic

<table>
<thead>
<tr>
<th>Common</th>
<th>Less Common</th>
</tr>
</thead>
<tbody>
<tr>
<td>• nausea</td>
<td>• Weight loss / gain</td>
</tr>
<tr>
<td>• loose stools</td>
<td>• Hyponatremia (SIADH)</td>
</tr>
<tr>
<td>• restlessness</td>
<td>• Sinus bradycardia</td>
</tr>
<tr>
<td>• akathisia</td>
<td>• Cardiac arrhythmia</td>
</tr>
<tr>
<td>• insomnia</td>
<td>• Bleeding (anti-platelet effect)</td>
</tr>
<tr>
<td>• headache</td>
<td>• Parkinsonism</td>
</tr>
<tr>
<td>• sexual dysfunction</td>
<td>• Serotonin Syndrome</td>
</tr>
</tbody>
</table>

Copyright © 2017 University of Washington
What if Patients Don’t Improve?

Is the diagnosis correct?

- **Comorbid anxiety** *(excessive worry, panic attacks, posttraumatic stress disorder):* SSRIs often appropriate Rx; cognitive behavioral therapy or exposure based therapy for PTSD

- **Bipolar depression** *(manic symptoms: no sleep, excess energy / irritability):* use mood stabilizers – not antidepressants: lithium, valproate, lamotrigine, quetiapine

- **Psychotic depression:** add antipsychotic *(e.g., risperidone, olanzapine, quetiapine);* consider ECT

- **Cognitive impairment / dementia:** MMSE or MOCA; work-up for treatable causes

- **Medical conditions:** hypothyroidism, sleep apnea, pain, neurological, neurodegenerative disease, vascular disease, chronic inflammation

- **Medications:** steroids, interferon, hormones

- **Withdrawal:** stimulants, anxiolytics, alcohol, opiates
What Else Can We Try?

• No response
  – Switch to antidepressant from a different class
• Partial response
  – Augment antidepressant
• Psychotherapy / Talk Therapy
• Behavioral Activation / Physical Activity
• Electroconvulsive therapy or other neuromodulation therapy
• PSYCHIATRY CONSULT
Psychiatry Consult

- Physical illnesses or treatments causes psychiatric symptoms
- Psychiatric illness complicates management of medical problems
- Psychosocial / psychological contributors to depression
- Differentiating affective from cognitive disorders
- Psychiatric complications such as:
  - Psychotic depression, bipolar depression
  - Treatment-resistant depression
  - Suicidal depression
  - Catatonia
- Psychotherapy
- Complex psychopharmacology
- Consideration of inpatient psychiatric hospitalization
- Evaluation for neuromodulation therapy (e.g., ECT)
<table>
<thead>
<tr>
<th><strong>“Dual Action” and Atypical Antidepressants</strong></th>
<th>Starting Dosage (mg)</th>
<th>Range* (mg)</th>
<th>Treatment Resistance</th>
<th>Drug Interactions</th>
<th>Potential SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venlafaxine (Effexor XR®)</td>
<td>37.5 Qam</td>
<td>75-225</td>
<td>Yes</td>
<td>Minimal</td>
<td>↑DBP, ↑BP ↓Na, Nausea</td>
</tr>
<tr>
<td>Desvenlafaxine (Pristiq®)</td>
<td>50 Qam</td>
<td>50-100</td>
<td>Unknown</td>
<td>Minimal</td>
<td>↑DBP, ↑BP ↓Na, Nausea</td>
</tr>
<tr>
<td>Mirtazapine (Remeron®)</td>
<td>7.5-15 Qhs</td>
<td>30-45</td>
<td>Yes</td>
<td>Minimal</td>
<td>Sedation, ↑wt Dry mouth</td>
</tr>
<tr>
<td>Duloxetine (Cymbalta®)</td>
<td>20 Qam</td>
<td>20-60</td>
<td>Unknown</td>
<td>Minimal</td>
<td>↑DBP, ↑BP ↓Na, Nausea</td>
</tr>
<tr>
<td>Nefazodone (^Serzone®)</td>
<td>50-100 BID</td>
<td>300-600</td>
<td>Unknown</td>
<td>Probable (3A4 inhibition)</td>
<td>↑liver enzymes? Sedation</td>
</tr>
<tr>
<td>Trazodone (Desyrel®)</td>
<td>25-50 Qhs</td>
<td>300-600</td>
<td>Unknown</td>
<td>Minimal</td>
<td>↓BP, sedation, priapism</td>
</tr>
<tr>
<td>Bupropion (Wellbutrin XL, SR®)</td>
<td>50-75 BID</td>
<td>100-450</td>
<td>Possible</td>
<td>Minimal</td>
<td>↑DBP, ↑BP Seizures</td>
</tr>
<tr>
<td>Vilazodone (Viibryd®)</td>
<td>10 Qam</td>
<td>10-40</td>
<td>Unknown</td>
<td>Minimal</td>
<td>GI upset, insomnia</td>
</tr>
<tr>
<td>Levomilnacipran ER (Fetzima®)</td>
<td>20 Qam</td>
<td>40-120</td>
<td>Unknown</td>
<td>Unlikley</td>
<td>GI distress, ↑BP, ↑HR,constipation</td>
</tr>
<tr>
<td>Vortioxetine (Brintellix ®)</td>
<td>5mg Qam</td>
<td>5-20mg</td>
<td>Unknown</td>
<td>Possible</td>
<td>HA, dizziness, GI upset, constipation</td>
</tr>
</tbody>
</table>

* Dosage for Major Depression; ^ Brand not available
# Tricyclic, Psychostimulant, and MAOI Antidepressants in Late-life Depression

<table>
<thead>
<tr>
<th>Drug</th>
<th>Drug Class</th>
<th>Starting Dose (mg)</th>
<th>Therapeutic Range (total)</th>
<th>Concerns and Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nortriptyline (Pamelor®)</td>
<td>TCA</td>
<td>10 Qhs</td>
<td>25 – 150 Qhs or divided dose</td>
<td>Follow EKG; α-cholin. SEs; lethal in OD</td>
</tr>
<tr>
<td>Desipramine (Norpramine®)</td>
<td>TCA</td>
<td>10 Qam</td>
<td>25-200 Qam or divided dose</td>
<td>Follow EKG; α-cholin. SEs; lethal in OD</td>
</tr>
<tr>
<td>Dextroamphetamine (Dexedrine®)</td>
<td>Psychostimulant</td>
<td>2.5 Qam</td>
<td>5-60 Bid to qid</td>
<td>HTN, anorexia, arrhythmias;</td>
</tr>
<tr>
<td>Methylphenidate (Ritalin®)</td>
<td>Psychostimulant</td>
<td>2.5 Qam</td>
<td>5-60 Bid to qid</td>
<td>HTN, anorexia, arrhythmias;</td>
</tr>
<tr>
<td>Modafinil (Provigil®)</td>
<td>Psychostimulant</td>
<td>50 Qam</td>
<td>50-400 Qam-bid</td>
<td>HTN, anorexia, arrhythmias;</td>
</tr>
<tr>
<td>Phenelzine (Nardil®)</td>
<td>MAOI</td>
<td>15 Qam</td>
<td>30-60 Bid to tid</td>
<td>MAOI diet; drug-drug interactions</td>
</tr>
<tr>
<td>Selegilene (Emsam® patch)</td>
<td>MAOI</td>
<td>6 Qam</td>
<td>6-12 qday (24-hr patch)</td>
<td>Diet at dose ≥ 9mg; drug-drug interaction</td>
</tr>
</tbody>
</table>

Antidepressant Augmentation

- Most strategies not tested in large RCTs in LLD
- Concern about polypharmacy, side-effects
- Data from trials with adult populations support:
  - Lithium
  - T3 or T4
  - Psychostimulants (e.g., Methylphenidate)
  - Atypical antipsychotics FDA approved for TRD
    - Quetiapine
    - Aripiprazole
    - Olanzapine + fluoxetine
    - Same concerns as for use in dementia?
  - Experimental
    - Ketamine for TRD
    - Supplements: O3FA; Methylfolate-NAC; Vit D3; SAM-e?

Psychotherapy: “Help You Make Change”

• Orientation
  - Cognitive-behavioral
  - Interpersonal
  - Problem-solving
  - Dialectical-behavioral
  - Bereavement/Grief Therapy
  - Psychodynamic Therapy
  - Supportive Therapy
  - Reminiscence and life review
  - Bibliotherapy

• Modality
  - Individual
  - Couple
  - Family
  - Group

• Practitioners
  - Psychiatrists
  - Psychologists
  - Social Workers
  - Nurse therapists
  - MFTs

Physical Activity / Exercise

• Two main types
  – Cardiovascular fitness
  – Strength/resistance training

• Effect size comparable to psychotherapy or medications in select populations of older adults

• Motivation is key, but can also be the main obstacle

• May be most helpful in or for:
  – Sedentary or inactive lifestyles
  – Complaints of fatigue or insomnia
  – Recent cardiac event or history of CHF
  – Post-stroke or Vascular Depression
  – Minor or subsyndromal depression
  – Dementia syndromes with behavioral or depressive features
  – NH patients

Neuromodulation / Stimulation Therapy

• **ECT**: Electroconvulsive Therapy

• **VNS**: Vagus Nerve Stimulation

• **TMS**: Transcranial Magnetic Stimulation
  – rTMS, dTMS

• **Research**
  – **DBS**: Deep Brain Stimulation
  – **MST**: Magnetic Seizure Therapy
  – **tDCS**: Transcranial Direct Current Stimulation
ECT in Late-life Depression

**Advantages**

- Strong efficacy
- Good efficacy in TRD
- Rapid onset of action
- Good safety profile
  - Very low mortality
  - Low morbidity
- Absence of med SE
- Older adults may respond better than younger.

**Disadvantages**

- Repeated brief general anesthesia
- Cognitive / memory effects
- Treatment side effects
  - Fall risk, Headache
- High rate of relapse without maintenance treatment
- Cost
- Stigma / fear

Electroconvulsive Therapy in Late-life Depression

• Indications

  – Serious, life-threatening mood disorders
    • Catatonia
    • Suicidal depression
    • Psychotic depression
  – Medication treatment failures
  – Chronic depression with significant psychosocial, functional, cognitive impairment
  – Some dementia syndromes
    • Mood or psychotic features

ECT in Late-life Depression

• Treatments can be inpatient or outpatient depending on severity of illness
  – Index series is comprised of between 6 – 12 treatments
  – Usually done 2-3 times per week for 2-4 weeks

• New techniques or reduced frequency of treatments can help reduce cognitive side effects

• If patient shows a positive acute response to an index series, a maintenance plan must be instituted:
  – Meds: combination (TCA or VFX + lithium)
  – Maintenance ECT: treatments at reduced frequency
  – ECT + meds

Transcranial Magnetic Stimulation: rTMS/dTMS for Major Depression

- First FDA approved in 2008
- Labeling:
  - Major Depressive Disorder
  - Failure of 1 antidepressant trial at or above the minimal effective dose and duration in current index episode
- Outpatient procedure: ~ 20-30 sessions
  - No pre-op required
  - No anesthesia or sedation
  - Return to normal activities upon completion
  - Contraindications: implanted metallic devices or non-removable metal objects near head, implants controlled by physiological signals (pacemakers, ICDs)
dTMS/rTMS

Brainsway, Inc

Neuronetics TMS Therapy System
How Good is Current Depression Care?

- Fewer than 2/10 see a psychiatrist or psychologist
- 5/10 receive treatment in primary care
- The ‘2-minute mental health visit’ : Ming Tai-Seale; JAGS 2008.
- 4-5 million older adults receive an antidepressant Rx, but only 20% improve
- Few get effective psychotherapy

"Of course you feel great. These things are loaded with antidepressants.”
2/3 of PCPs report poor access to mental health services for their patients.

"We couldn’t get a psychiatrist, but perhaps you’d like to talk about your skin. Dr. Perry here is a dermatologist."

Cunningham PJ, Health Affairs, 2009;28(3)490-501
How Do We Get Effective Treatment To More People?
IMPACT Collaborative Care

Primary Care Practice
- Primary Care Physician
- Patient
- Mental Health Care Manager
- Psychiatric Consultant

Outcome Measures
- PHQ-9

Treatment Protocols
- Problem Solving Treatment (PST)
- Behavioral Activation (BA)
- Motivational Interviewing (MI)
- Medications

Population Registry

Psychiatric Consultation

Copyright © 2017 University of Washington
IMPACT Doubles Effectiveness of Care for Depression

50% or greater improvement in depression at 12 months

Unützer et al., JAMA 2002; Psych Clinics North America 2004
IMPACT improves physical function

SF-12 Physical Function Component Summary Score (PCS-12)

Callahan et al., JAGS 2005; 53:367-373
IMPACT reduces health care costs
ROI: $ 6.5 saved / $ 1 invested

<table>
<thead>
<tr>
<th>Cost Category</th>
<th>4-year costs in $</th>
<th>Intervention group cost in $</th>
<th>Usual care group cost in $</th>
<th>Difference in $</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMPACT program cost</td>
<td>522</td>
<td>0</td>
<td>0</td>
<td>522</td>
</tr>
<tr>
<td>Outpatient mental health costs</td>
<td>661</td>
<td>558</td>
<td>767</td>
<td>-210</td>
</tr>
<tr>
<td>Pharmacy costs</td>
<td>7,284</td>
<td>6,942</td>
<td>7,636</td>
<td>-694</td>
</tr>
<tr>
<td>Other outpatient costs</td>
<td>14,306</td>
<td>14,160</td>
<td>14,456</td>
<td>-296</td>
</tr>
<tr>
<td>Inpatient medical costs</td>
<td>8,452</td>
<td>7,179</td>
<td>9,757</td>
<td>-2578</td>
</tr>
<tr>
<td>Inpatient mental health / substance abuse costs</td>
<td>114</td>
<td>61</td>
<td>169</td>
<td>-108</td>
</tr>
<tr>
<td>Total health care cost</td>
<td>31,082</td>
<td>29,422</td>
<td>32,785</td>
<td>-$3363</td>
</tr>
</tbody>
</table>

IMPACT: Summary

- Less depression
  - IMPACT more than doubles effectiveness of usual care
- Less physical pain
- Better functioning
- Higher quality of life
- Greater patient and provider satisfaction
- More cost-effective

“I got my life back”
Collaborative Care Billing Codes

<table>
<thead>
<tr>
<th>CPT</th>
<th>Description</th>
<th>Payment/Pt (Non-Facilities)</th>
<th>Payment/Pt (Fac) Hospitals and Facilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>99492</td>
<td>Initial psych care mgmt, 70 min/month - CoCM</td>
<td>$161.28</td>
<td>$90.36</td>
</tr>
<tr>
<td>99493</td>
<td>Subsequent psych care mgmt, 60 min/month - CoCM</td>
<td>$128.88</td>
<td>$81.72</td>
</tr>
<tr>
<td>99494</td>
<td>Initial/subsequent psych care mgmt, additional 30 min CoCM</td>
<td>$66.60</td>
<td>$43.56</td>
</tr>
<tr>
<td>99484</td>
<td>Care mgmt. services, min 20 min – General BHI Services</td>
<td>$48.60</td>
<td>$32.76</td>
</tr>
</tbody>
</table>

*Please note actual payment rates may vary. Check with your billing/finance department.

http://aims.uw.edu
Thank you.

Jurgen Unutzer, MD, MPH, MA
unutzer@uw.edu