Bipolar Disorder in Later Life

Martha Sajatovic, MD
Professor of Psychiatry and of Neurology
Willard Brown Chair in Neurological Outcomes
Case Western Reserve University
School of Medicine
Cleveland, Ohio
Disclosure

• The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration).
  – The off-label use of antidepressants, Omega-3, and Vitamin D for the treatment of bipolar disorder will be discussed.

• Applicable CME staff have no relationships to disclose relating to the subject matter of this activity.
• This activity has been independently reviewed for balance.
Old Age: Coming at you!!

- Number of people aged ≥ 60 doubled since 1980
- Number of people aged ≥ 80 will ↑ 4 × to 395 million by 2050
- By 2020, adults aged ≥ 65 will outnumber children < age 5
- By 2050, elderly will outnumber all children < age 14
- Majority of older people live in low- or middle-income countries. This number will increase to 80% by 2050

Why Care about Older Age Bipolar Disorder?

- Demographic changes (more elderly, living longer)
- Limited systematic data (high risk group to study)
- Late- vs early-onset (they look and behave differently)
- Cognitive impairment / Dementia risk (↑ costs)
- Medical and neurologic comorbidity (↑ costs)
- Health care planning (↑ costs)
Estimated Prevalence of Major Psychiatric Disorders in Younger vs Older Americans from 1970–2030

Symptom Domains of Bipolar Disorder

- **Manic Mood and Behavior**
  - Euphoria
  - Grandiosity
  - Pressured speech
  - Impulsivity
  - Excessive libido
  - Recklessness
  - Social intrusiveness
  - Diminished need for sleep

- **Dysphoric Mood and Behavior**
  - Depression
  - Anxiety
  - Irritability
  - Hostility
  - Violence or suicide

- **Psychotic Symptoms**
  - Delusions
  - Hallucinations

- **Cognitive Symptoms**
  - Racing thoughts
  - Distractibility
  - Disorganization
  - Inattentiveness

Bipolarity and Aging

- 9% geropsychiatric inpatients, 6% of outpatients have BD
- In community: 0.1% to 1.0% of elderly
- 1.6% individuals aged 55 to 64 and 0.5% aged ≥ 65 on MDQ
- HMO administrative data base: 0.25% of individuals aged ≥ 65 have BD

In summary: BD (I and II) affects 0.5% to 1.0% of population age > 60. NUMBERS SLIGHTLY LESS COMPARED TO YOUNGER INDIVIDUALS
Geriatric Bipolar Disorder Occurs in Varying Circumstances

• Those who have been ill for many years—“early onset”
• Onset later in life (especially after age 50)
• Illness associated with medical conditions (secondary mania)
• Newly diagnosed individuals with a mood disorder history
• As in younger patients, geriatric BD is often mis/under-diagnosed and is complicated by comorbidity

Early- vs Late-Onset Bipolar Disorder

**Age of onset of first manic/hypomanic episode qualifiers**

**Early-onset BD (EOBD)**
- 1st manic/hypomanic episode < age 50 (40?) years

**Late-onset BD (LOBD)**
- 1st manic/hypomanic episode ≥ age 50 years
- Task force recommends consideration of ≥ 40 years to be defined as LOBD
- LOBD includes individuals who have had prior depressive episodes, but no manic/hypomanic episode until age ≥ 50 (40?) years

**Older-Age Bipolar Disorder (OABD)**
- Solid consensus that OABD are ≥ age 60 years
- Task force recommends consideration of individuals ≥ 50 years as OABD given known ↓ life-span and ↑ medical burden in BD.

**Neuroprogression in OABD: A Controversial Concept**
- OABD with progressive cognitive and functional decline
- Whether this actually is specific to OABD is controversial
- May be determined by multiple factors such as comorbidity (esp. vascular disease) and treatment (esp. lithium)

Bipolar Disorder in Older Adults

• If first onset of mania occurs after age 60
  – Less likely to be associated with a family history of BD
  – More likely to be associated with medical or neurological conditions
    • CNS cause (stroke, frontotemporal dementia)
    • Right hemispheric events
    • Some medications may cause late-onset mania

• Differentiating between frontal disinhibition and BD mania can be a challenge, as many symptoms are overlapping

• BD mania characterized by elevated mood and decreased need for sleep rather than disturbed sleep which may be more common in dementia

CNS = central nervous system.
Bipolar Mania in Older Adults

- Manic symptoms often milder
- May present with mixed mania, dysphoric, or agitated states
- More likely to have
  - Irritability
  - Treatment resistance (if new onset)
  - Higher rate of mortality

Bipolar Depression in Older Adults

• Depressed or irritable mood
• Sleep, appetite, and activity level disturbance
• Cognitive impairment may lead to a dementia-like presentation
• In older adult individuals with BD, depression usually precedes mania by an average of 20 years

Cumulative Comorbidity in Late-Life Bipolar Disorder

• Norm is 3 to 4 chronic medical conditions
• Two-thirds of BD elders have HTN, one-third have DM
• Need to consider that BD elder research samples represent “healthier” survivors (“survivor effect”)
• Medical comorbidity data in BD elderly is limited and controlled/longitudinal analyses are needed

HTN = hypertension; DM = diabetes mellitus.
Summarizing OABD Symptoms

- Mania less common, overall lower disability than depression
- Psychosis may be less severe
- Depressive severity is similar between younger and older patients
- More episodes = worse outcome
- ↑ recurrence risk for each mood episode—this may be particularly pronounced for late-onset patients

OABD = older age bipolar disorder.
Why Does Having Bipolar Disorder Increase Cardiometabolic Risk?

• Lifestyle (smoking, isolation/inactivity)
• Iatrogenic effects (almost all BD drugs cause weight gain)
• Common factors that increase BD and cardiometabolic risk—BD is likely a multisystem disorder

Medical Complexity Causes Earlier Death in Bipolar Disorder

Standardized mortality ratios in BD
- 2.5 for men
- 2.7 for women (values > 1.0 indicate greater risk than general population)
- Most frequent cause of death
  - Cardiovascular disease 31%
  - Suicide 19%
  - Cancer 14%
  - Lifestyle issues such as smoking, diet, and substance abuse likely contribute
- Each 1-unit increase in BMI decreases BD treatment response by > 7%
- BD with obesity/caridiometabolic syndrome ↑ risk for suicide

BMI = body mass index.
Case Study

**Background**: Marie is a 62-year-old woman with BD maintained on lithium 1200 mg/day for 15 years. She has done well with this including excellent performance at her job—an insurance company clerk.

**A new problem**: 6 months ago Marie noticed a mild hand tremor that caused embarrassment and interfered with her clerical work. Her clinician checked basic labs and told her all looked OK except for “very mild elevation in kidney functioning,” but did not recommend further evaluation. Worried about the tremor and labs, Marie reduced her lithium to 900 mg/day. Tremor resolved.

**In last several weeks**: Increasingly irritable at home, a couple of inappropriate (and uncharacteristic) comments to a coworker in the employee lounge.

**Now**: Concerned husband accompanies her to the clinician’s office.
Case Study (cont’d)

Medical History
• 18 kg overweight
• Type 2 DM, last HgbA1c = 7.8%
• Hx HTN (last BP on β-blocker 130/90)
• Serum Creatinine 1.1, BUN 24
• Smokes ½ pack of cigarettes/day

BP = blood pressure; BUN = blood urea nitrogen.
What is the next best step for Marie’s clinician?

1. Increase the lithium back to 1200 mg/day and recheck serum levels
2. Stop lithium and switch to divalproex
3. Have her husband check her medication pillbox daily and report missing doses to you
4. Add divalproex and see her in 3 days for follow-up
5. Tell her to stop smoking
# Approved Agents for Bipolar Disorder

<table>
<thead>
<tr>
<th>Acute Mania</th>
<th>Acute Depression</th>
<th>Longer-Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year</td>
<td>Drug</td>
<td>Year</td>
</tr>
<tr>
<td>1970</td>
<td>Lithium</td>
<td>2003</td>
</tr>
<tr>
<td>2000</td>
<td>Olanzapine*</td>
<td>2003</td>
</tr>
<tr>
<td>2003</td>
<td>Risperidone*</td>
<td>2005</td>
</tr>
<tr>
<td>2004</td>
<td>Quetiapine, XR (2008)*</td>
<td>2008</td>
</tr>
<tr>
<td>2004</td>
<td>Ziprasidone</td>
<td>2009</td>
</tr>
<tr>
<td>2004</td>
<td>Aripiprazole*</td>
<td>2009</td>
</tr>
<tr>
<td>2004</td>
<td>Carbamazepine ERC</td>
<td>2017</td>
</tr>
<tr>
<td>2009</td>
<td>Asenapine</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>Cariprazine</td>
<td></td>
</tr>
</tbody>
</table>

*Adjunctive and monotherapy. LAI = long-acting injectable.
Other Treatments: Beyond Traditional Mood Stabilizers and Antipsychotics

- Antidepressants
- Other medication treatments (Omega-3, Vitamin D, etc.)
- Electroconvulsive therapy
- Psychotherapeutic/Psychosocial Approaches
- Enhancing treatment adherence
What Do International Guidelines Say about OABD Treatment?

- 35 guidelines from 6 continents and 19 countries published 2005–2015
- Most guidelines have no separate section on OABD
- General principles for medication similar to younger adults
- Caution for side effects due to somatic comorbidity and concomitant medications
- Therapeutic lithium serum levels are suggested to be lower, but not informed by specific research evidence

Adverse Drug Reactions as a Function of Increasing Age

ADR = adverse drug reaction.
What are the Best Treatments for OABD?

- Efficacy data suggest OABD have fairly similar BD symptom response to younger patients
- Tolerability is often rate-limiting
- Still need to determine the best way to use lithium and other drugs in OABD
- Some drugs might be “neuroprotective”

9-Week RCT of Lithium vs Divalproex in Late-Life Type I Bipolar Mania

RCT = randomized controlled trial; Li = lithium; DV = divalproex.
YMRS Scores: 3-Week Completers

YMRS = Young Mania Rating Scale.
Safety and Tolerability of Lithium

• Associated with significant adverse effects
  – Weight gain, GI disturbances
  – Cognitive slowing
  – Neurotoxic effects with minor overdose
  – Thyroid toxicity
  – Diabetes insipidus
  – Narrow therapeutic index
  – Need for therapeutic drug monitoring

GI = gastrointestinal.
Lithium Treatment in Older Adults

- Baseline screening: Renal function, electrolytes, thyroid function, fasting blood glucose, EKG
- Begin with low dose—300 mg/day. Usual dose not exceeding 900 mg/day
- Evaluate concomitant medications, specially those that alter sodium excretion: Diuretics, NSAIDs, ACE inhibitors
- Target serum concentrations:
  - Low: 0.4–0.7 mEq/L
  - High: ≥ 0.8 mEq/L

EKG = electrocardiogram; NSAID = nonsteroidal anti-inflammatory drug; ACE = angiotensin-converting-enzyme.
Rate of Dementia Related to Number of Lithium Prescriptions

Incidence of Delirium with New Users of Lithium or Divalproex (Older Adults)


Adjusted Survival Curves

- Lithium (n=2442)
- Divalproex (n=2918)
- Benztropine (n=4870)

Hazard Ratio (95% CI)
- Lithium: 1.00 (reference)
- Divalproex: 1.36 (0.94–1.97)
- Benztropine: 1.88 (1.35–2.62)
**Hospitalization for Lithium Toxicity and Use of Other Medications** (May Increase Li Levels and/or Reduce Renal Clearance)

<table>
<thead>
<tr>
<th></th>
<th>Cases (n=413)</th>
<th>Controls (n=1651)</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazide diuretics</td>
<td>3.9%</td>
<td>2.2%</td>
<td>1.8 (1.0–3.3)</td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>13.1%</td>
<td>4.3%</td>
<td>3.4 (2.3–5.0)</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>15.3%</td>
<td>6.7%</td>
<td>2.5 (1.8–3.5)</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>15.3%</td>
<td>11.3%</td>
<td>1.4 (1.0–1.9)</td>
</tr>
</tbody>
</table>

Serum Levels Do Not Always Correlate with Brain Levels

• Cross-sectional evaluation of 26 patients with BD (10 patients age > 50)
• Assessment of brain lithium, serum lithium, cognition. Serum and brain levels were correlated in group as a whole, but not for older patients
• In older patients higher brain lithium was associated with frontal lobe dysfunction and higher depression ratings

Conclusion: Relationship between brain and serum lithium not predictable and elevated brain lithium may cause toxicity. **TREAT THE PATIENT, NOT THE LEVEL!**

Safety and Tolerability of Valproate

- GI disturbances
- Sedation, tremor
- Weight gain
- Alopecia
- Transaminase elevations
- Hepatic failure
- Thrombocytopenia

Relevant Interactions for Valproate

- Valproate may increase concentrations of:
  - Amitriptyline
  - Carbamazepine-epoxide
  - Clomipramine
  - Diazepam
  - Lamotrigine
  - Nortriptyline
  - Phenobarbital

- Serum valproate levels may be decreased by:
  - Carbamazepine
  - Lamotrigine
  - Phenytoin

Use of Valproate in OABD

- Screening: Liver enzymes, complete blood count with platelets
- Typical starting dose = 125–250 mg/day with gradual titration
- Usual daily dose of 500–1000 mg/day
- Therapeutic range for classic mania in the elderly: 65–90 mcg/mL
- Monitor for hepatic auto-induction/decrease in serum levels

### Therapeutic Plasma Concentrations

<table>
<thead>
<tr>
<th>Medication</th>
<th>Plasma Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>Acute Mania: 0.8–1.2 mEq/L</td>
</tr>
<tr>
<td></td>
<td>Maintenance: 0.6–1.0 mEq/L</td>
</tr>
<tr>
<td></td>
<td>Elderly: 0.4–1.0 mEq/L</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>6–12 mg/L</td>
</tr>
<tr>
<td></td>
<td>Elderly 4–12 mg/L</td>
</tr>
<tr>
<td>Valproic Acid</td>
<td>Acute Mania: 45–125 mg/L</td>
</tr>
<tr>
<td></td>
<td>Elderly: 25–100 mg/L</td>
</tr>
</tbody>
</table>

FDA Advisory for Antipsychotic Drugs Used for Treatment of Behavioral Disorders in Elderly Patients

• Antipsychotic drugs used “off-label” to treat behavioral disorders in elderly patients with dementia have shown a 1.6 to 1.7 × higher death rate associated with their use compared to patients receiving a placebo.
• All antipsychotics affected.
• Death causes varied—most heart-related (heart failure, sudden death) or infections (pneumonia).

• IMPLICATIONS FOR FDA ADVISORY FOR NON-DEMENTED ELDERLY WITH SERIOUS MENTAL ILLNESS ARE NOT CLEAR—ANTIPSYCHOTICS ARE STILL NOTED AS FIRST-LINE TREATMENT FOR INDIVIDUALS WITH BIPOLAR DISORDER AND OTHER PRIMARY PSYCHOTIC ILLNESSES (SCHIZOPHRENIA).
CGI-BP Scores at Baseline and Endpoint for Younger (< age 55) and Older (≥ age 55) Bipolar Manic Patients Receiving Quetiapine or Placebo

CGI-BP = Clinical Global Impressions Scale for use in bipolar illness.
Asenapine in Elderly Patients with Bipolar Mania

- Prospective uncontrolled trial of 11 patients with bipolar I mania, mean age: 67.8 years
- Asenapine 10 mg/BID monotherapy for 4 weeks
- Assessed on YMRS from baseline to week 4
- 1 patient developed rash, 1 patient with peripheral edema; Both resolved with Tx termination
- Mild sedation in 3 patients
- Mean improvement in YMRS at week 4 was -21.4 ± 12.9
- 7/11 (63.6%) remitted with YMRS ≤ 12

### Lurasidone in Acute Bipolar Depression: Baseline Characteristics

**Table:**

<table>
<thead>
<tr>
<th></th>
<th>Monotherapy</th>
<th>Adjunctive Therapy with Li / VPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>**Lurasidone (combined doses)**a (n=56)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>32.1</td>
<td>48.1</td>
</tr>
<tr>
<td>Age, years, mean (SD)</td>
<td>59.8 (4.2)</td>
<td>60.1 (4.5)</td>
</tr>
<tr>
<td>Duration of current episode, weeks, mean (SD)</td>
<td>11.3 (8.5)</td>
<td>9.6 (5.6)</td>
</tr>
<tr>
<td>White (%)</td>
<td>89.3</td>
<td>85.2</td>
</tr>
<tr>
<td>≥ 2 Prior hospitalizations for depression (%)</td>
<td>50.0</td>
<td>44.4</td>
</tr>
<tr>
<td>Adjunctive treatment (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lithium</td>
<td>---</td>
<td>42.3</td>
</tr>
<tr>
<td>Valproate</td>
<td>---</td>
<td>57.7</td>
</tr>
<tr>
<td>MADRS score, mean (SD)</td>
<td>30.4 (4.7)</td>
<td>29.7 (4.8)</td>
</tr>
<tr>
<td>CGI-BP-Severity of Depression, mean (SD)</td>
<td>4.6 (0.7)</td>
<td>4.4 (0.6)</td>
</tr>
</tbody>
</table>

**Note:**
- aCombined data shown for 2 fixed-flexible dosing arms (20–60 mg/day; 80–120 mg/day).
- MADRS = Montgomery-Åsberg Depression Rating Scale.
### Treatment-Emergent Adverse Events %
(incidence ≥ 5%)

<table>
<thead>
<tr>
<th></th>
<th>Monotherapy</th>
<th>Adjunctive Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lurasidone 20–60 mg/day (n=27)</td>
<td>Lurasidone 80–120 mg/day (n=31)</td>
</tr>
<tr>
<td>Nausea</td>
<td>18.5</td>
<td>9.7</td>
</tr>
<tr>
<td>Somnolence</td>
<td>11.1</td>
<td>0</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>7.4</td>
<td>0</td>
</tr>
<tr>
<td>Akathisia</td>
<td>0</td>
<td>9.7</td>
</tr>
<tr>
<td>Anxiety</td>
<td>7.4</td>
<td>0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7.4</td>
<td>0</td>
</tr>
<tr>
<td>Pruritus</td>
<td>7.4</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7.4</td>
<td>6.5</td>
</tr>
<tr>
<td>Insomnia</td>
<td>7.4</td>
<td>9.7</td>
</tr>
<tr>
<td>Muscle spasms</td>
<td>3.7</td>
<td>6.5</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0</td>
<td>6.5</td>
</tr>
<tr>
<td>Restlessness</td>
<td>0</td>
<td>6.5</td>
</tr>
<tr>
<td>Abnormal dreams</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tremor</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Monotherapy: Change in MADRS

-15 -10 -5 0
Baseline Week 1 Week 2 Week 3 Week 4 Week 5 Week 6

LS Mean Change from Baseline in MADRS Score

Lurasidone (combined doses), n=56
Placebo, n=27

* P<.05
** P<.01
Effect size = 0.81

Adjunctive Therapy: Change in MADRS


LS Mean Change from Baseline in MADRS Score

-15 -10 -5 0 5 10 15

Baseline Week 1 Week 2 Week 3 Week 4 Week 5 Week 6

Lurasidone (+ Li/VPA), n=26
Placebo (+ Li/VPA), n=27

Effect size = 0.26
Open-Label Lamotrigine in Older Adults with Type I or II Bipolar Depression

N=57. *P*<.01.
Neuroimaging Findings and Effects on Treatment

• Long-term lithium is associated with ↑ total gray matter
• Compared with BD individuals not treated with lithium, lithium treatment is associated with ↑ hippocampal volumes and ↓ white matter microstructural abnormalities
• Long-term antipsychotic use may have variable impact on white matter microstructure
• FA shows coherence of white matter tracts. ↑ FA = ↑ white matter structural integrity/brain health. Antipsychotic treatment is associated with ↓ FA in frontolimbic regions, but ↑ FA in fronto-occipital regions

FA = fractional anisotropy.
Adherence with Antipsychotic Medications among Older Adults with Bipolar Disorder

<table>
<thead>
<tr>
<th></th>
<th>Fully adherent N (%)</th>
<th>Partially adherent N (%)</th>
<th>Non-adherent N (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>3360 (61.2)</td>
<td>1037 (18.9)</td>
<td>1096 (20.0)</td>
<td></td>
</tr>
<tr>
<td>Age (SD)</td>
<td>69.2 (6.9)</td>
<td>69.1 (7.0)</td>
<td>69.0 (7.3)</td>
<td>ns</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>2480 (73.8)</td>
<td>714 (68.9)</td>
<td>798 (72.8)</td>
<td>ns</td>
</tr>
<tr>
<td>Black</td>
<td>169 (5.0)</td>
<td>65 (6.3)</td>
<td>64 (5.8)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>110 (3.3)</td>
<td>46 (4.4)</td>
<td>30 (2.7)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never married</td>
<td>372 (11.1)</td>
<td>89 (8.7)</td>
<td>105 (9.6)</td>
<td>ns</td>
</tr>
<tr>
<td>Married</td>
<td>1679 (50.2)</td>
<td>505 (49.2)</td>
<td>511 (46.9)</td>
<td></td>
</tr>
<tr>
<td>Divorced/separated</td>
<td>973 (29.1)</td>
<td>331 (32.3)</td>
<td>385 (35.4)</td>
<td></td>
</tr>
<tr>
<td>Widowed</td>
<td>318 (9.5)</td>
<td>101 (9.8)</td>
<td>88 (8.1)</td>
<td></td>
</tr>
<tr>
<td>Substance use</td>
<td>380 (11.3)</td>
<td>140 (13.5)</td>
<td>198 (18.1)</td>
<td>P=.002</td>
</tr>
<tr>
<td>Homeless</td>
<td>113 (3.4)</td>
<td>56 (5.4)</td>
<td>76 (6.9)</td>
<td>P=.023</td>
</tr>
</tbody>
</table>
Married patients had YMRS higher by 2.7 ± 1.4 points ($P=0.05$)

SHORTER DURATION OF EPISODE
- Presence of family in the house or living nearby ($P=0.017$)
- Greater Instrumental Support ($P=0.0062$)

INCREASED SOCIAL INTERACTIONS (non-family)
- Lower severity of manic symptoms ($P=0.01$)
- Longer duration of episode ($P=0.0003$)
- Satisfaction with instrumental support NOT associated with severity or duration

GERI-BD = Acute Treatment of Late Life Mania study.
Targeted Training in Illness Management for Older Adults with Serious Mental Illness

• 12 group-format, weekly group sessions
• Nurse and Peer Educator codelivery
• Focus on active self-management
• Highly manualized with scripts/group exercises
• Positive results in Parkinson’s Disease, epilepsy, and stroke

Targeted Training in Illness Management Study Design

TTIM = targeted training in illness management; TAU = treatment as usual.
Targeted Training in Illness Management Study Findings

- One-third had BD and comorbid DM
- At baseline older patients had better control of DM than younger people, likely a survivor effect
- TTIM was associated with improved depression and functioning
- Similar improvement in global DM control between TTIM vs TAU, but better control in TTIM for those with baseline HbA1c ≤ 7.5

Lithium Use in OABD Delphi Exercise

- Expert panel on OABD, aging, psychopharmacology
- Key Questions
  - Appropriate place in BD armamentarium
  - Appropriate dose and dosing frequency
  - Biological monitoring
  - Drug interactions and comorbidity
- Delphi Process
  - Iterative surveys
  - Consensus
  - Increasingly specific questions
  - Expert-driven recommendations
- Serum levels of 0.4–0.8 mmol/l were recommended for ages 60–79
- Serum levels of 0.4–0.7 mmol/l were recommended for ages ≥ 80

A Minimum Dataset to Assess OABD

- International group of investigators performed a systematic literature review to identify articles on OABD published in the past 5 years
- Relevant articles were assessed delineating the types of clinical, cognitive, biomarker, and neuroimaging data usually collected
- Mostly clinical data and to a lesser extent cognitive data
- Little biomarker and neuroimaging data
- Types of data and data collection methods varied considerably

Symptoms, Functioning, and Other Key Domains Assessed in OABD Studies

• Most studies collected age, gender, and level of education
• Ethnicity and social support were less often noted
• Bipolar diagnosis typically confirmed with Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) or Mini International Neuropsychiatric Interview (MINI)
• Course and chronicity measures: Age of onset, number of previous mood episodes, hospitalization record
• Symptoms scales: YMRS, a mix of rater-administered depression scales, none specific to bipolar depression
• Few studies collected physical comorbidity
• Comorbidity measures most relevant to OABD: BP/HTN, diabetes, weight, cardiovascular status, and cumulative medical burden

Suggestions for Treatment of OABD

- Mood stabilizers with OABD evidence include: Lithium, valproate, olanzapine, quetiapine, lurasidone, lamotrigine
- Consider lithium at appropriate doses as a first-line agent
- Dose one-half to two-thirds of younger BD patients
- Be attentive to drug interactions/medical comorbidity
- Promote self-management/exercise and use of other behavioral modalities
- Recognize that illness may change over time