NACC-Clinical Task Force
Update on Expanded Documentation of Neuropsychiatric Symptoms in UDSv4

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Why is the topic important?

• Growing importance of NPS in early phases of cognitive disorders

• Strengthen existing UDS elements around NPS
  • Better capture in participants without dementia
    • Differentiate age of onset
  • Standardize diagnosis of DSM-5-TM disorders
    • Symptoms v. syndrome v. disorder
  • Incorporate diagnosis of Mild Behavioral Impairment (MBI)
NPS are UNIVERSAL in Dementia
Cache County Dementia Progression Study

NPS affect at least half with MCI
Cardiovascular Health Study

Table 3. Cumulative Prevalence of Individual NPI Symptoms From the Onset of the Cognitive Symptoms in the 2 Groups*

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>MCI (n = 320)</th>
<th>Dementia (n = 362)</th>
<th>( \chi^2 ) Test†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delusions</td>
<td>15 (4.7)</td>
<td>109 (30.1)</td>
<td>75.6</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>8 (2.5)</td>
<td>59 (16.3)</td>
<td>37.1</td>
</tr>
<tr>
<td>Agitation/aggression</td>
<td>47 (14.7)</td>
<td>145 (40.1)</td>
<td>54.4</td>
</tr>
<tr>
<td>Depression</td>
<td>84 (26.3)</td>
<td>158 (43.6)</td>
<td>23.0</td>
</tr>
<tr>
<td>Anxiety</td>
<td>33 (10.3)</td>
<td>92 (25.4)</td>
<td>27.9</td>
</tr>
<tr>
<td>Euphoria</td>
<td>4 (1.3)</td>
<td>11 (3.0)</td>
<td></td>
</tr>
<tr>
<td>Apathy</td>
<td>58 (18.1)</td>
<td>164 (45.3)</td>
<td>61.2</td>
</tr>
<tr>
<td>Disinhibition</td>
<td>13 (4.1)</td>
<td>66 (18.2)</td>
<td>33.7</td>
</tr>
<tr>
<td>Irritability</td>
<td>53 (16.6)</td>
<td>123 (34.0)</td>
<td>28.3</td>
</tr>
<tr>
<td>Aberrant motor behavior</td>
<td>13 (4.1)</td>
<td>62 (17.1)</td>
<td>31.2</td>
</tr>
<tr>
<td>Sleep</td>
<td>57 (17.8)</td>
<td>109 (30.1)</td>
<td>16.9</td>
</tr>
<tr>
<td>Eating</td>
<td>56 (17.5)</td>
<td>112 (30.9)</td>
<td>16.8</td>
</tr>
<tr>
<td>Any 1 NPI disturbance</td>
<td>139 (49.6)</td>
<td>233 (60.1)</td>
<td>88.8</td>
</tr>
</tbody>
</table>

* NPI indicates Neuropsychiatric Inventory; MCI, mild cognitive impairment. For any 1 NPI disturbance, the total number of symptoms for MCI was 280 and for dementia was 291.
† \( P < .001 \) for all symptoms except for euphoria \( (P = .03, \text{exact test}) \).
Over half with dementia develop NPS BEFORE cognitive diagnosis

Sequencing of NPS Presence with Cognitive Diagnosis in NACC (overall N=1,980)

Normal → MCI
NPS Before MCI: 55%

Normal → Dementia
NPS Before MCI 55%

Normal → Dementia (no MCI)
NPS Before Dementia 64%

Wise 2019
Neuropsychiatric Symptoms as Risk Factors for Progression From CIND to Dementia: The Cache County Study

M. E. Peters, M.D., P. R. Rosenberg, M.D., M. Steinberg, M.D., M. C. Norton, Ph.D., K. A. Welsb-Bahrer, Ph.D., K. M. Hayes, Ph.D., J. Breitner, M.D., M.P.H., J. T. Tosch, Ph.D., G. G. Lyketsos, M.D., M.H.S., and the Cache County Investigator Group

Objectives: To examine the association of neuropsychiatric symptoms (NPS) severity with risk of transition to Alzheimer's dementia, Alzheimer disease (AD), and vascular dementia (VaD). Design: Survival analysis of time to dementia, AD, or VaD onset. Setting: Population-based study. Participants: 2309 participants diagnosed with cognitive impairment, no dementia (CIND) from the Cache County Study of Memory Health and Aging were followed for a mean of 3.3 years. Measurements: The Neuropsychiatric Inventory (NPI) was used to quantify the presence, frequency, and severity of NPS. Observed statistics, t-tests, and Cox proportional hazards were used to assess associations. Results: The conversion rate from CIND to all dementia was 12.3% per year, with risk factors including an APOE ε4 allele, lower Mini-Mental State Examination, lower 3MS, and higher GDS sum-of-boxes. The presence of at least one NPI was a risk factor for all dementia diagnoses, as was the presence of NPS with mild severity. Nighttime behaviors were a risk factor for all-cause dementia and AD, whereas hallucinations were a risk factor for VaD. Conclusions: These data confirm that NPS are risk factors for conversion from CIND to dementia. Of special interest is that even NPS of mild severity are a risk for all-cause dementia or AD. (Ann J Geriatric Psychiatry 2012; 20:315-9)

Keywords: agitation, anxiety, Cache County, CIND, dementia, depression, MCI, NPS, NPI

The Association of Neuropsychiatric Symptoms in MCI with Incident Dementia and Alzheimer Disease

Paul B. Rosenberg, M.D., Michelle M. Mielke, Ph.D., Brian S. Appleby, M.D., Esther S. Oh, M.D., Younas E. Goda, M.D., Constantinie G. Lyketsos, M.D., M.H.S.

Objectives: Individuals with mild cognitive impairment (MCI) are at high risk of developing dementia and/or Alzheimer disease (AD). Among persons with MCI, depression and anxiety have been associated with an increased risk of incident dementia. We examined whether neuropsychiatric symptoms in MCI increased the risk of incident dementia (all causes) and incident AD. Design: Longitudinal cohort study followed annually (median: 1.58 years). Setting: National Alzheimer's Coordinating Center-database combining clinical data from 29 Alzheimer's Disease Centers. Participants: A total of 1,021 participants with MCI. Measurements: 1) Progression to dementia (all causes or AD); 2) Neuropsychiatric Inventory Questionnaire (NPI-Q); 3) Geriatric Depression Scale (GDS). Results: Clinical Dementia Rating Global Score and Sum of Boxes, and Mini-Mental State Examination (MMSE) association of outcomes with risk of incident dementia or AD was evaluated with hazard ratios (HR) determined by Cox proportional-hazard models adjusted for age, ethnicity, Clinical Dementia Rating Global Score, and MMSE score. Results: A total of 572 participants (26.9%) progressed to dementia and 454 (22.4%) to AD. Baseline GDS ≥ 9 was associated with an increased risk of incident dementia (HR: 1.67; 95% CI: 1.17-2.40) and AD (HR: 1.45; 95% CI: 1.14-1.84). Baseline NPI ≥ 6 was associated with an increased risk of incident dementia (HR: 1.17; 95% CI: 1.12-1.68) and AD (HR: 1.33; 95% CI: 1.09-1.61). Conclusions: Neuropsychiatric symptoms in MCI are associated with significantly increased risk of incident dementia and AD. Neuropsychiatric symptoms may be among the earliest symptoms of pre-clinical stage of AD and targeting them therapeutically might delay transition to dementia. (Ann J Geriatric Psychiatry 2013; 21:055-069)

Keywords: Alzheimer disease, dementia, depression, longitudinal study, mild cognitive impairment, neuropsychiatric symptoms

Baseline Neuropsychiatric Symptoms and the Risk of Incident Mild Cognitive Impairment: A Population-Based Study

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M. Mielke, Ph.D.
Knopman, M.D.
H. Christensen, B.Sc.
I. Pankratz, Ph.D.
F. Boeve, M.D.
G. Ocher, M.D.
G. Angalos, M.D.
J. K. Petersen, M.D., Ph.D.
R. Rocca, M.D., M.P.H.

Objectives: The authors conducted a prospective cohort study to estimate the risk of incident mild cognitive impairment (MCI) in cognitively normal elderly (aged 70-80 years) individuals with or without neuropsychiatric symptoms at baseline. The research was conducted in the setting of the population-based Mayo Clinic Study of Aging.

Methods: A stratification of normal cognitive aging, mild cognitive impairment, and dementia was adjudicated by an expert consensus panel based on published criteria. Hazard ratios and 95% confidence intervals were computed using Cox proportional hazards models, with age as a time variable. Baseline Neuropsychiatric Inventory Questionnaire data set was available for 1507 cognitively normal persons who underwent at least one follow-up visit.

Results: The cohort was followed to incident mild cognitive impairment (MCI) or censoring variables (N=179) for a median of 5 years. Aplification (hazard ratio=1.36, 95% CI=1.09-1.70) anxiety (hazard ratio=2.36, 95% CI=1.49-3.41), and depression (hazard ratio=1.37, 95% CI=1.28-2.39), irritability (hazard ratio=1.03, 95% CI=1.21-2.56), and depression (hazard ratio=1.29, 95% CI=1.03-1.60) significantly increased the risk of incident mild cognitive impairment.

Conclusions: This study suggests that mild cognitive impairment in cognitively normal elderly had non-neuropsychiatric psychiatric baseline. These baseline psychiatric symptoms were more likely to occur as biomarkers (genetic and environmental) in increasing the risk of incident mild cognitive impairment.

(Am J Psychiatry 2014; 1 }
Neuropsychiatric symptoms as early manifestations of emergent dementia: Provisional diagnostic criteria for mild behavioral impairment

Zabihoo Isahaghi, Eric E. Smith, Yonas Gedo, David Saltz, Henry Brosdy, Gwenn Smith, Luis Agiza-Orta, Rob Sweet, David Miller, Constantine G. Lyketsos,
for the ISTAART Neuropsychiatric Symptoms Professional Interest Area

1. Changes in behavior or personality observed by patient, informant, or clinician, starting later in life (age ≥ 50 years) and persisting at least intermittently for ≥ 6 months. These represent clear change from the person’s usual behavior or personality as evidenced by at least one of the following:
   a. Decreased motivation (e.g., apathy, aspontaneity, indifference)
   b. Affective dysregulation (e.g., anxiety, dysphoria, changeability, euphoria, irritability)
   c. Impulse dyscontrol (e.g., agitation, disinhibition, gambling, obsessiveness, behavioral perseveration, stimulus bind)
   d. Social inappropriateness (e.g., lack of empathy, loss of insight, loss of social graces or tact, rigidity, exaggeration of previous personality traits)
   e. Abnormal perception or thought content (e.g., delusions, hallucinations)

2. Behaviors are of sufficient severity to produce at least minimal impairment in at least one of the following areas:
   a. Interpersonal relationships
   b. Other aspects of social functioning
   c. Ability to perform in the workplace

   The patient should generally maintain his/her independence of function in daily life, with minimal aids or assistance.

3. Although comorbid conditions may be present, the behavioral or personality changes are not attributable to another current psychiatric disorder (e.g., generalized anxiety disorder, major depression, manic or psychotic disorders), traumatic or general medical causes, or the physiological effects of a substance or medication.

4. The patient does not meet criteria for a dementia syndrome (e.g., Alzheimer’s disease, frontotemporal dementia, dementia with Lewy bodies, vascular dementia, other dementia). MCI can be concurrently diagnosed with MBI.

Abbreviations: ISTAART, International Society to Advance Alzheimer’s Research and Treatment; MBI, mild behavioral impairment; MCI, mild cognitive impairment.
Mild Behavioral Impairment (MBI) faster conversion to dementia than MCI alone

REPLICATIONS IN LARGE MCI COHORTS
• MBI v. no MBI/psych: ORs 2.13 to 8.07
  • USA, NACC
  • French
  • Japanese

REPLICATION IN A LARGE SCD COHORT
• MBI v. no MBI: OR 8.15
  • Canadian

Taragano 2018
McGirr 2022; Chen 2021; Matsuoka 2019; Ismail 2021
Current approach in UDS

• Symptom capture on NPI-Q and GDS
• Psychiatric symptoms potentially captured on B9
• Contribution of any (DSM-defined?) psychiatric disorders to cognitive changes marked on D1

• No clear approach for categorization of patients with recent onset, mainly behavioral changes
• No place to differentiate longstanding psychiatric disorders from recent onset
Example Case 1

- 65 yo man
- No prior history of psychiatric illness
- 3 years of behavior changes
- Losing interest in hobbies/activities (men’s group, church…)
  - More blunt/inappropriate at social gatherings
  - Challenging people, insulting them, calling them stupid, saying things like “fat people won’t be able to survive after the rebellion anyway”)
- Endorsing different political ideas from past interests
- Preoccupied with “survivalist” ideas
  - Buying a lot of equipment (camping, nonperishable food, etc, more than he needs, multiples of everything)
  - Eschews family gatherings to go to survivalist meetings
- Denies feeling anxious, depressed
- No evidence of delusional thinking
- No cognitive complaints, normal cognitive testing
- Still working, able to perform all household tasks
Planned changes

• Approach chosen to limit departure from current format and approach to UDS forms
• Add questions/checkboxes to D1 form to allow diagnosis of recent onset (last few years) behavioral changes
  • Diagnosis of mild behavioral impairment (MBI) for symptoms not meeting DSM criteria for specific psychiatric disorder
    • Criteria for MBI provided
    • Designation of category of MBI (ISTAART)
  • Diagnosis of "behaviorally impaired not MBI" for recent onset syndromes meeting DSM-V criteria
    • Specific diagnosis marked on D1 form
  • Specific symptoms, with age of onset, marked on B9 form
# Use of forms for Case 1

## Section 1 – Level of Impairment – Normal Cognition/MCI and MBI/Dementia

2. **Does the participant have:**
   - 1) Normal cognition *(global CDR=0 and/or neuropsychological testing within normal range)*?
     - AND
   - 2) Normal behavior *(i.e., the participant does not exhibit behavior sufficient to diagnose MBI or dementia due to FTLD or LBD and/or FTLD behavior and language domains=0)*?
     - 0 No *(CONTINUE TO QUESTION 3)*
     - 1 Yes *(END FORM HERE)*

3. **Does the participant meet criteria for dementia?**
   - 0 No *(CONTINUE TO QUESTION 4)*
   - 1 Yes *(SKIP TO QUESTION 5a)*

4. **Does the participant meet criteria for MCI (amnestic or non-amnestic)?**
   - 0 No *(SKIP TO QUESTION 6)*
   - 1 Yes *(CONTINUE TO QUESTION 5a)*
### Mild Behavioral Impairment (MBI) Core Clinical Criteria

- Participant, co-participant, or clinician identifies a change in the participant's affect, motivation, thought content, behavior, or personality that is clearly different from their usual affect, motivation, thought content, behavior, or personality
- Symptoms have been present at least intermittently for the last six months or longer
- Late onset (i.e., age > ~50)

<table>
<thead>
<tr>
<th>Not explained by delirium or psychiatric disorder meeting DSM criteria (including new onset, persistence or recurrence of longstanding). If recent onset, mark below as “behaviorally impaired, not MBI”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms interfere with at least one of these: Work, interpersonal relationships, social activities</td>
</tr>
<tr>
<td>Largely preserved independence in other functional abilities (no change from prior manner/level of functioning, or uses minimal aids or assistance)</td>
</tr>
</tbody>
</table>

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#### 7. Does the participant meet criteria for MBI?

- □ 0  No (SKIP TO QUESTION 8)  
  - ✓  Yes (CONTINUE TO QUESTION 7a)

#### 7a. MBI affected domains

Select one or more affected domains

Note: if “Yes” is indicated in any domain below, the participant should have a corresponding symptom checked on Form B9 — Clinician Judgment of Symptoms, either from among the specific symptoms denoted there, or in “other”

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>7a1. Motivation</td>
<td>□ 0</td>
<td>✓ 1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Apathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7a2. Affective Regulation</td>
<td>□ 0</td>
<td>✓ 1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Anxiety, irritability, depression, euphoria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7a3. Impulse Control</td>
<td>□ 0</td>
<td>✓ 1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Obsessions/compulsions, personality change, substance abuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7a4. Social appropriateness</td>
<td>□ 0</td>
<td>✓ 1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Disinhibition, personality change, loss of empathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7a5. Thought Content/Perception</td>
<td>□ 0</td>
<td>✓ 1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Delusions, hallucinations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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#### 8. Behaviorally impaired, not MBI

- □ 1
Use of forms for Case 1

• Use form B9 to denote specific symptoms
  • Apathy
  • Disinhibition
  • Personality change
  • Obsessions/compulsions
Example Case 2

- 60 yo man, works as a college professor of sociology
- 18 months of behavior changes
  - Decided to start five businesses at once
    - combined ice-cream store and clothing store, a ride-share company ("like Uber, but way better"), high-end Italian restaurant...
  - Stayed up in the middle of the night writing business plans
  - Used family savings to lease space (didn’t discuss)
  - Says he feels very energized, better than he’s felt in years, because of these new ideas
  - Thinks he’s so good at this, he might be “the one”
  - Gets angry when people tell him he should slow down
- 6 months ago, got into altercation with police after harassing developer that owns local shopping mall
  - Admitted to psychiatric unit, treated with lithium
  - Improved over few weeks
  - No longer thinking about these ideas
- Currently no cognitive complaints, normal cognitive testing
- Now back to work at college, functioning normally
Planned changes

• Approach chosen to limit departure from current format and approach to UDS forms
• Add questions/checkboxes to D1 form to allow diagnosis of recent onset (last few years) behavioral changes
  • Diagnosis of mild behavioral impairment (MBI) for symptoms not meeting DSM criteria for specific psychiatric disorder
    • Criteria for MBI provided
    • Designation of category of MBI (ISTAART)
  • Diagnosis of "behaviorally impaired not MBI" for recent onset syndromes meeting DSM-V criteria
    • Specific diagnosis marked on D1 form
  • Specific symptoms, with age of onset, marked on B9 form
Use of forms for Case 2

### Section 1 – Level of Impairment – Normal Cognition/MCI and MBI/Dementia

2. Does the participant have:
   1) Normal cognition *(global CDR=0 and/or neuropsychological testing within normal range)*?

   *AND*

   2) Normal behavior *(i.e., the participant does not exhibit behavior sufficient to diagnose MBI or dementia due to FTLD or LBD and/or FTLD behavior and language domains=0)*?

   - [x] No  **(CONTINUE TO QUESTION 3)**  [ ] Yes  **(END FORM HERE)**

3. Does the participant meet criteria for dementia?

   - [x] No  **(CONTINUE TO QUESTION 4)**  [ ] Yes  **(SKIP TO QUESTION 5a)**

4. Does the participant meet criteria for MCI (amnestic or non-amnestic)?

   - [x] No  **(SKIP TO QUESTION 6)**  [ ] Yes  **(CONTINUE TO QUESTION 5a)**
### Mild Behavioral Impairment (MBI) Core Clinical Criteria

- Participant, co-participant, or clinician identifies a change in the participant’s affect, motivation, thought content, behavior, or personality that is clearly different from their usual affect, motivation, thought content, behavior, or personality
- Symptoms have been present at least intermittently for the last six months or longer
- Late onset (i.e., age > ~50)
- Not explained by delirium or psychiatric disorder meeting DSM criteria (including new onset, persistence or recurrence of longstanding). If recent onset, mark below as *behaviorally impaired, not MBI*
- Symptoms interfere with at least one of these: Work, interpersonal relationships, Social activities
- Largely preserved independence in other functional abilities (no change from prior manner/level of functioning, or uses minimal aids or assistance)

#### 7. Does the participant meet criteria for MBI?

- **No (SKIP TO QUESTION 8)**
- **Yes (CONTINUE TO QUESTION 7a)**

#### 7a. MBI affected domains

Select one or more affected domains

*Note: If “Yes” is indicated in any domain below, the participant should have a corresponding symptom checked on Form B9 — Clinician Judgment of Symptoms, either from among the specific symptoms denoted there, or in “other”*

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>7a1. Motivation</strong></td>
<td>□ 0</td>
<td>□ 1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Apathy</td>
<td>□ 0</td>
<td>□ 1</td>
</tr>
<tr>
<td><strong>7a2. Affective Regulation</strong></td>
<td>□ 0</td>
<td>□ 1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Anxiety, irritability, depression, euphoria</td>
<td>□ 0</td>
<td>□ 1</td>
</tr>
<tr>
<td><strong>7a3. Impulse Control</strong></td>
<td>□ 0</td>
<td>□ 1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Obsessions/compulsions, personality change, substance abuse</td>
<td>□ 0</td>
<td>□ 1</td>
</tr>
<tr>
<td><strong>7a4. Social appropriateness</strong></td>
<td>□ 0</td>
<td>□ 1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Disinhibition, personality change, loss of empathy</td>
<td>□ 0</td>
<td>□ 1</td>
</tr>
<tr>
<td><strong>7a5. Thought Content/Perception</strong></td>
<td>□ 0</td>
<td>□ 1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Delusions, hallucinations</td>
<td>□ 0</td>
<td>□ 1</td>
</tr>
</tbody>
</table>

#### 8. Behaviorally impaired, not MBI
Use of forms for Case 2

- Use form B9 to denote specific symptoms
  - Euphoria (added for UDS-4)
  - Irritability
  - Delusions (chosen one)
  - Obsessions, compulsions

- Age of onset for all at 58
**Section 3 – Primary or Contributing Non-neurodegenerative or Non-CVD Conditions**

**Must be filled out for all participants with cognitive or behavioral impairment (i.e., MCI, MRI, Dementia, etc.).**

Indicate whether a given condition is a primary, contributing, or non-contributing cause of the observed impairment, based on the clinician’s best judgment. Select one or more syndrome from questions (below) as **Present**; all others will default to **Absent** in the NACC database. **Only one diagnosis should be selected as 1 = Primary.**

**For participants with normal cognition:** If a new diagnosis has been made during the evaluation, ensure that it is recorded in Form A5: Participant Health History.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Present</th>
<th>Primary</th>
<th>Contributing</th>
<th>Non-contributing</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. Major depressive disorder (DSM-5-TR criteria)</td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>11b. If Present, select one:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Untreated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated with medication and/or counseling</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Bipolar disorder (DSM-5-TR criteria)</td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>13. Schizophrenia or other psychosis disorder (DSM-5-TR criteria)</td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>14. Anxiety disorder (DSM-5-TR criteria)</td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>If Present, specify:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14b. Generalized Anxiety Disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14c. Panic Disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14d. Obsessive-compulsive disorder (OCD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14e. Other (specify):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Post-traumatic stress disorder (PTSD) (DSM-5-TR criteria)</td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Developmental neuropsychiatric disorders (e.g., autism spectrum disorder (ASD), attention-deficit hyperactivity disorder (ADHD), dyslexia)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16. Other psychiatric disorder (DSM-5-TR criteria)</td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>17. Delirium (DSM-5-TR criteria)</td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>18. Delirium (DSM-5-TR criteria)</td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
Example Case 3

• 70 yo man
• History of depression since early adulthood
  • Several bouts of major depressive episodes in past, one with hospitalization
• Currently depressed for the last two years
  • Working with therapist and psychiatrist
  • On sertraline
  • Has been difficult to treat
### Use of forms for Case 2

#### Section 1 – Level of Impairment – Normal Cognition/MCI and MBI/Dementia

2. Does the participant have:
   - Normal cognition (global CDR=0 and/or neuropsychological testing within normal range)?
     - AND
   - Normal behavior (i.e., the participant does not exhibit behavior sufficient to diagnose MBI or dementia due to FTLD or LBD and/or FTLD behavior and language domains=0)?
     - No *(CONTINUE TO QUESTION 3)*
     - Yes *(END FORM HERE)*

3. Does the participant meet criteria for dementia?
   - No *(CONTINUE TO QUESTION 4)*
   - Yes *(SKIP TO QUESTION 5a)*

4. Does the participant meet criteria for MCI (amnestic or non-amnestic)?
   - No *(SKIP TO QUESTION 6)*
   - Yes *(CONTINUE TO QUESTION 5a)*
### Section 1 – Level of Impairment – Normal Cognition/MCI and MBI/Dementia

#### Mild Behavioral Impairment (MBI) Core Clinical Criteria

- Participant, co-participant, or clinician identifies a change in the participant’s affect, motivation, thought content, behavior, or personality that is clearly different from their usual affect, motivation, thought content, behavior, or personality
- Symptoms have been present at least intermittently for the last six months or longer
- Late onset (i.e., age > ~50)
- Not explained by delirium or psychiatric disorder meeting DSM criteria (including new onset, persistence or recurrence of longstanding). If recent onset, mark below as "behaviorally impaired, not MBI"
- Symptoms interfere with at least one of these work, interpersonal relationships, social activities
- Largely preserved independence in other functional abilities (no change from prior manner/level of functioning, or uses minimal aids or assistance)

<table>
<thead>
<tr>
<th>7. Does the participant meet criteria for MBI?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No (SKIP TO QUESTION 8) □1 Yes (CONTINUE TO QUESTION 7a)</td>
</tr>
</tbody>
</table>

#### 7a. MBI affected domains

Select one or more affected domains

*Note: If “Yes” is indicated in any domain below, the participant should have a corresponding symptom checked on Form B9 — Clinician Judgment of Symptoms, either among the specific symptoms denoted there, or in “other”*

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>7a1. Motivation</td>
<td>□0</td>
<td>□1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Apathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7a2. Affective Regulation</td>
<td>□0</td>
<td>□1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Anxiety, irritability, depression, euphoria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7a3. Impulse Control</td>
<td>□0</td>
<td>□1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Obsessions/compulsions, personality change, substance abuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7a4. Social appropriateness</td>
<td>□0</td>
<td>□1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Disinhibition, personality change, loss of empathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7a5. Thought Content/Perception</td>
<td>□0</td>
<td>□1</td>
</tr>
<tr>
<td>Potential Form B9 symptoms: Delusions, hallucinations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

8. Behaviorally impaired, not MBI

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### Section 3 – Primary or Contributing Non-neurodegenerative or Non-CVD Conditions

Must be filled out for all participants with cognitive or behavioral impairment (i.e., MCI, MBI, Dementia, etc.). Indicate whether a given condition is a primary, contributing, or non-contributing cause of the observed impairment, based on the clinician’s best judgment. Select one or more syndrome from questions (below) as Present; all others will default to Absent in the NACC database. 

- **For participants with normal cognition:** If a new diagnosis has been made during the evaluation, ensure that it is recorded in Form A5: Participant Health History.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Present</th>
<th>Primary</th>
<th>Contributing</th>
<th>Non-contributing</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. Major depressive disorder (DSM-5-TR criteria)</td>
<td>☑️ 1</td>
<td>☑️ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
</tr>
<tr>
<td>11b. If Present, select one:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Untreated</td>
<td>☐ 0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated with medication and/or counseling</td>
<td>☑️ 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Bipolar disorder (DSM-5-TR criteria)</td>
<td>☐ 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Schizophrenia or other psychosis disorder (DSM-5-TR criteria)</td>
<td>☐ 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. Anxiety disorder (DSM-5-TR criteria)</td>
<td>☐ 1</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>If Present, specify:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14b. Generalized Anxiety Disorder</td>
<td>☑️ 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14c. Panic Disorder</td>
<td>☑️ 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14d. Obsessive-compulsive disorder (OCD)</td>
<td>☑️ 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14e. Other (specify):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Post-traumatic stress disorder (PTSD) (DSM-5-TR criteria)</td>
<td>☐ 1</td>
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<td></td>
</tr>
<tr>
<td>Developmental neuropsychiatric disorders (e.g., autism spectrum disorder (ASD), attention-deficit hyperactivity disorder (ADHD), dyslexia)</td>
<td>☐ 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16. Other psychiatric disorder (DSM-5-TR criteria)</td>
<td>☐ 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17. Delirium (DSM-5-TR criteria)</td>
<td>☐ 1</td>
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</tr>
</tbody>
</table>
Example Case 3

- Since the changes are not new, but result from a longstanding psychiatric illness, no specific symptoms are denoted on B9
Additional points

- Continue as now with NPI-Q, GDS

- ADD MBI-C (checklist) as optional symptom inventory
  - Useful as continuous measure of behavioral dysfunction
Thank you!

The CTF NPS/MBI Subgroup:
Rosen (lead), Lyketsos, Sano, Boeve, Rascovsky
also Burns, Schindler
Others that may have contributed to process by providing data analysis etc

10 min of Question time