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

CTF Behavioral Workgroup:

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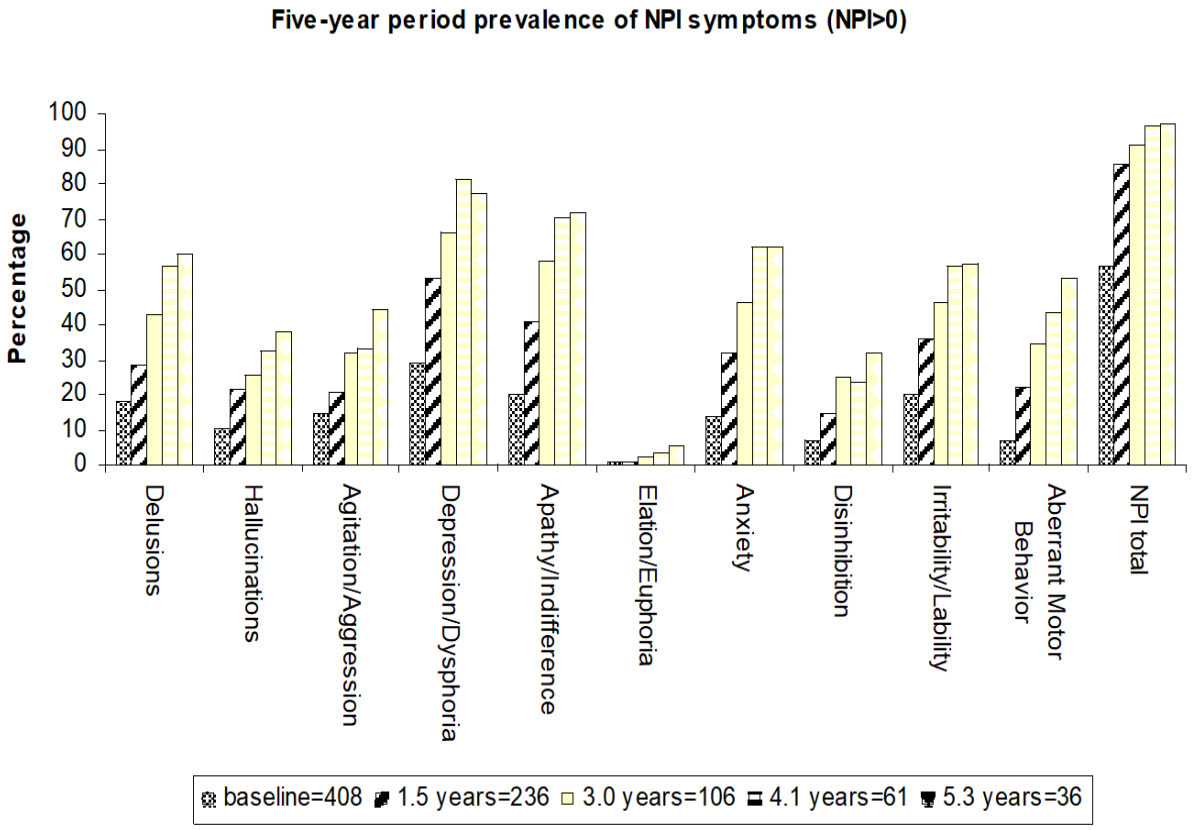
Why is the topic important?

- 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

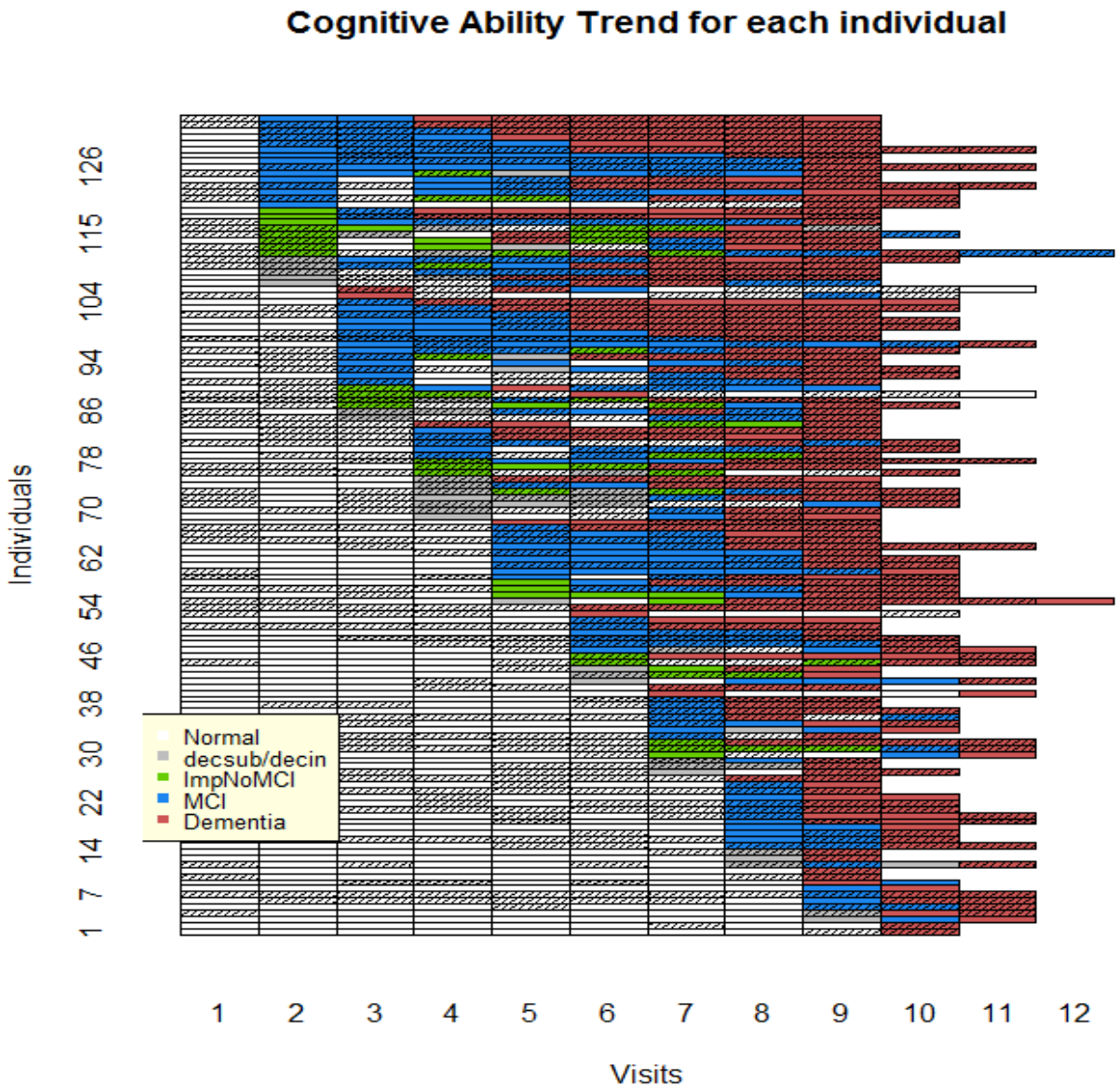
Table 3. Cumulative Prevalence of Individual NPI Symptoms From the Onset of the Cognitive Symptoms in the 2 Groups*

Symptoms	No. (%) MCI (n = 320)	No. (%) Dementia (n = 362)	χ^2 Test†
Delusions	15 (4.7)	109 (30.1)	75.6
Hallucinations	8 (2.5)	59 (16.3)	37.1
Agitation/aggression	47 (14.7)	145 (40.1)	54.4
Depression	84 (26.3)	158 (43.6)	23.0
Anxiety	33 (10.3)	92 (25.4)	27.9
Euphoria	4 (1.3)	11 (3.0)	
Apathy	58 (18.1)	164 (45.3)	61.2
Disinhibition	13 (4.1)	66 (18.2)	33.7
Irritability	53 (16.6)	123 (34.0)	28.3
Aberrant motor behavior	13 (4.1)	62 (17.1)	31.2
Sleep	57 (17.8)	109 (30.1)	16.9
Eating	56 (17.5)	112 (30.9)	16.8
Any 1 NPI disturbance	139 (49.6)	233 (80.1)	88.8

*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 ($P = .09$, exact test).

Steinberg 2008; Lyketsos 2002

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

NPS in CIND/MCI

faster conversion to dementia

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

M. E. Peters, M.D., P. B. Rosenberg, M.D., M. Steinberg, M.D., M. C. Norton, Ph.D., K. A. Welsh-Bohmer, Ph.D., K. M. Hayden, Ph.D., J. Breitner, M.D., M.P.H., J. T. Tschanz, Ph.D., C. G. Lyketsos, M.D., M.H.S., and the Cache County Investigato

Objectives: *To examine the association of neuropsychiatric symptom (NPS) severity with risk of transition to all-cause dementia, Alzheimer disease (AD), and vascular dementia (VaD).* **Design:** *Survival analysis of time to dementia, AD, or VaD onset.* **Setting:** *Population-based study.* **Participants:** *230 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. Chi-squared statistics, t-tests, and Cox proportional hazard ratios were used to assess associations.* **Results:** *The conversion rate from CIND to all-cause dementia was 12% per year, with risk factors including an* APOE *ε4 allele, lower Mini-Mental State Examination, lower 3MS, and higher CDR sum-of-boxes. The presence of at least one NPS was a risk factor for all-cause dementia, as was the presence of NPS with mild severity. Nighttime behaviors were a risk factor for all-cause dementia and of 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.* (Am J Geriatr Psychiatry 2012; 00:1–9)

Key Words: 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., Yonas E. Geda, M.D., Constantine 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-cause) 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 1,821 participants with MCI.* **Measurements:** *1) Progression to dementia (all-cause) or AD, 2) Neuropsychiatric Inventory Questionnaire (NPI-Q), 3) Geriatric Depression Scale (GDS), 4) Clinical Dementia Rating Global Score and Sum of Boxes, and 5) Mini-Mental State Examination (MMSE). The association of covariates with risk of incident dementia or AD was evaluated with hazard ratios (HR) determined by Cox proportional-hazards models adjusted for age, ethnicity, Clinical Dementia Rating Global Score and Sum of Boxes, and MMSE.* **Results:** *A total of 527 participants (28.9%) progressed to dementia and 454 (24.9%) to AD. Baseline GDS > 0 was associated with an increased risk of incident dementia (HR: 1.47, 95% CI: 1.17–1.84) and AD (HR: 1.45, 95% CI: 1.14–1.83). Baseline NPI > 0 was associated with an increased risk of incident dementia (HR: 1.37, 95% CI: 1.12–1.66) and AD (HR: 1.35, 95% CI: 1.09–1.66).* **Conclusions:** *Neuropsychiatric symptoms in MCI are associated with significantly an increased risk of incident dementia and AD. Neuropsychiatric symptoms may be among the earliest symptoms of preclinical stages of AD and targeting them therapeutically might delay transition to dementia.* (Am J Geriatr Psychiatry 2013; 21:685–695)

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

NPS in unimpaired

faster conversion to MCI

Article

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

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. Rocca, M.D., M.P.H.

Objective: The authors conducted a prospective cohort study to estimate the risk of incident mild cognitive impairment in cognitively normal elderly (aged ≥70 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.

Method: A classification 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 model, with age as a time scale. Baseline Neuropsychiatric Inventory Questionnaire data were available for 1,587 cognitively normal persons who underwent at least one follow-up visit.

Results: The cohort was followed to incident mild cognitive impairment (N=365) or censoring variables (N=179) for a median of 5 years. Agitation (hazard ratio=3.06, 95% CI=1.89–4.93), apathy (hazard ratio=2.26, 95% CI=1.49–3.41), anxiety (hazard ratio=1.87, 95% CI=1.28–2.73), irritability (haza 95% CI=1.31–2.58), and depre ratio=1.63, 95% CI=1.23–2.16), tially, increased risk for later impairment. Delusion and hal not. A secondary analysis, lim cance by the small number o ipants, showed that euphoria, and nighttime behaviors we predictors of nonamnestic n impairment but not amnestic impairment. By contrast, de dicted amnestic mild cognitiv (hazard ratio=1.74, 95% CI=1 not nonamnestic mild cognitiv

Conclusions: An increased mild cognitive impairment v in community-dwelling elder had nonpsychotic psychiatric baseline. These baseline psyc toms were of similar or great as biomarkers (genetic and s in increasing the risk of incid nitive impairment.

ELSEVIER

Alzheimer's & Dementia ■ (2015) 1-8

Alzheimer's & Dementia

Perspective

Neuropsychiatric symptoms as early manifestations of emergent dementia: Provisional diagnostic criteria for mild behavioral impairment

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ISTAART research diagnostic criteria for MBI

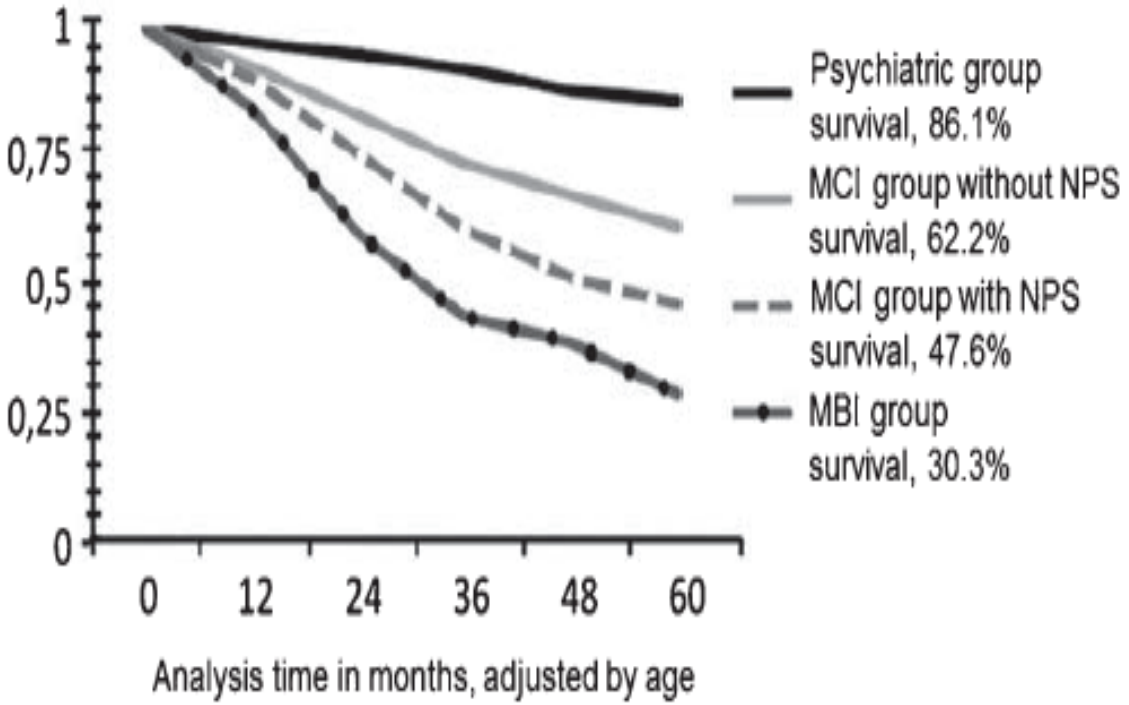
1. Changes in behavior or personality observed by patient, informant, or clinician, starting later in life (age ≥50 years) and persisting at least intermittently for ≥6 months. These represent clear change from the person's usual behavior or personality as evidenced by at least one of the following:
   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)**

Section 1 – Level of Impairment – *Normal Cognition/MCI and MBI/Dementia* *continued...*

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?

☐0 No **(SKIP TO QUESTION 8)** ☒1 Yes **(CONTINUE TO QUESTION 7a)**

7a. MBI affected domains

Select one or more affected domains

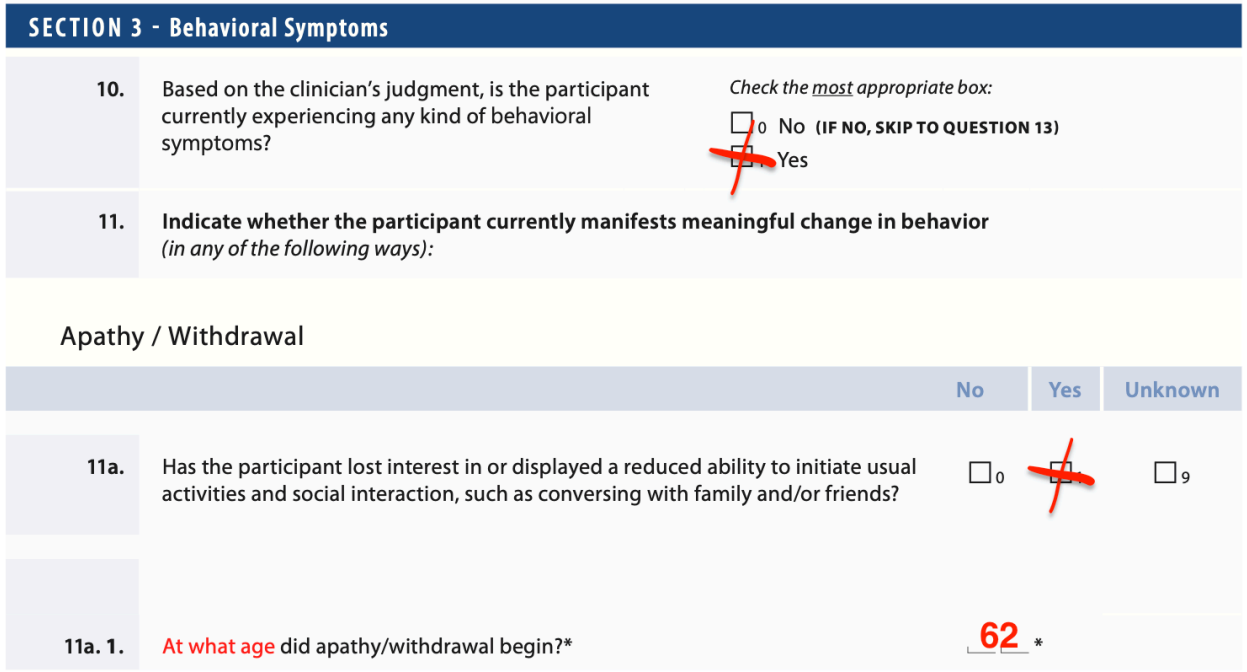
Note: If "Yes" is indicated in any domain below, the participant should have a corresponding symptom checked on Form B9 — Clinician Judgment of Symptoms, either from among the specific symptoms denoted there, or in "other"

		No	Yes
7a1.	Motivation *Potential Form B9 symptoms: Apathy*	☐0	☒1
7a2.	Affective Regulation *Potential Form B9 symptoms: Anxiety, irritability, depression, euphoria*	☐0	☐1
7a3.	Impulse Control *Potential Form B9 symptoms: Obsessions/compulsions, personality change, substance abuse*	☐0	☒1
7a4.	Social appropriateness *Potential Form B9 symptoms: Disinhibition, personality change, loss of empathy*	☐0	☒1
7a5.	Thought Content/Perception *Potential Form B9 symptoms: Delusions, hallucinations*	☐0	☐1

		Present
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



SECTION 3 - Behavioral Symptoms

10. Based on the clinician's judgment, is the participant currently experiencing any kind of behavioral symptoms?

Check the most appropriate box:

☐ 0 No **(IF NO, SKIP TO QUESTION 13)**

☐ 1 Yes

11. **Indicate whether the participant currently manifests meaningful change in behavior** *(in any of the following ways):*

Apathy / Withdrawal

		No	Yes	Unknown
11a.	Has the participant lost interest in or displayed a reduced ability to initiate usual activities and social interaction, such as conversing with family and/or friends?	☐ 0	☐ 1	☐ 9
11a. 1.	At what age did apathy/withdrawal begin?*		62 *	

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)?*

☒ 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)**

Section 1 – Level of Impairment – *Normal Cognition/MCI and MBI/Dementia* *continued...*

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?

☒ 0 No **(SKIP TO QUESTION 8)** ☐ 1 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"

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

		Present
8.	Behaviorally impaired, not MBI	☒ 1

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, 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 » *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.

Condition		Present		Primary	Contributing	Non-contributing
11.	Major depressive disorder (DSM-5-TR criteria)	☐1	11a.	☐1	☐2	☐3
11b.	If **Present**, *select one*:					
	Untreated ☐0					
	Treated with medication and/or counseling ☐1					
12.	Bipolar disorder (DSM-5-TR criteria)	☐1	12a.	☐1	☐2	☐3
13.	Schizophrenia or other psychosis disorder (DSM-5-TR criteria)	☐1	13a.	☐1	☐2	☐3
14.	Anxiety disorder (DSM-5-TR criteria)	☐1	14a.	☐1	☐2	☐3
	If **Present**, *specify*:					
14b.	Generalized Anxiety Disorder ☐1					
14c.	Panic Disorder ☐1					
14d.	Obsessive-compulsive disorder (OCD) ☐1					
14e.	Other (specify) : _____					
15.	Post-traumatic stress disorder (PTSD) (DSM-5-TR criteria)	☐1	15a.	☐1	☐2	☐3
16.	Developmental neuropsychiatric disorders (e.g., autism spectrum disorder (ASD), attention-deficit hyperactivity disorder (ADHD), dyslexia)	☐1	16a.	☐1	☐2	☐3
17.	Other psychiatric disorder (DSM-5-TR criteria)	☐1	17a.	☐1	☐2	☐3
18.	Delirium (DSM-5-TR criteria)	☐1	18a.	☐1	☐2	☐3

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:

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)**

Section 1 – Level of Impairment – *Normal Cognition/MCI and MBI/Dementia* *continued...*

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?

☒ 0 No **(SKIP TO QUESTION 8)** ☐ 1 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"

		No	Yes
7a1.	Motivation *Potential Form B9 symptoms: Apathy*	☐ 0	☐ 1
7a2.	Affective Regulation *Potential Form B9 symptoms: Anxiety, irritability, depression, euphoria*	☐ 0	☐ 1
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7a5.	Thought Content/Perception *Potential Form B9 symptoms: Delusions, hallucinations*	☐ 0	☐ 1

		Present
8.	Behaviorally impaired, not MBI	☒ 1

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 ›› *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.

	Condition	Present		Primary	Contributing	Non-contributing
11.	Major depressive disorder (DSM-5-TR criteria)	☒ 1	11a.	☒ 1	☐ 2	☐ 3
11b.	If **Present**, *select one*:					
	Untreated ☐ 0					
	Treated with medication and/or counseling ☒ 1					
12.	Bipolar disorder (DSM-5-TR criteria)	☐ 1	12a.	☐ 1	☐ 2	☐ 3
13.	Schizophrenia or other psychosis disorder (DSM-5-TR criteria)	☐ 1	13a.	☐ 1	☐ 2	☐ 3
14.	Anxiety disorder (DSM-5-TR criteria)	☐ 1	14a.	☐ 1	☐ 2	☐ 3
	If **Present**, *specify*:					
14b.	Generalized Anxiety Disorder ☐ 1					
14c.	Panic Disorder ☐ 1					
14d.	Obsessive-compulsive disorder (OCD) ☐ 1					
14e.	Other (specify) : _____					
15.	Post-traumatic stress disorder (PTSD) (DSM-5-TR criteria)	☐ 1	15a.	☐ 1	☐ 2	☐ 3
16.	Developmental neuropsychiatric disorders (e.g., autism spectrum disorder (ASD), attention-deficit hyperactivity disorder (ADHD), dyslexia)	☐ 1	16a.	☐ 1	☐ 2	☐ 3
17.	Other psychiatric disorder (DSM-5-TR criteria)	☐ 1	17a.	☐ 1	☐ 2	☐ 3
18.	Delirium (DSM-5-TR criteria)	☐ 1	18a.	☐ 1	☐ 2	☐ 3

Example Case 3

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

SECTION 3 - Behavioral Symptoms

10.	Based on the clinician's judgment, is the participant currently experiencing any kind of behavioral symptoms?	*Check the most appropriate box:* ☒ 0 No **(IF NO, SKIP TO QUESTION 13)** ☐ 1 Yes
11.	**Indicate whether the participant currently manifests meaningful change in behavior relative to stable baseline prior to onset of current syndrome, and not explained by longstanding psychiatric disorder** *(in any of the following ways):*	

Additional points

- Continue as now with NPI-Q, GDS
- ADD MBI-C (checklist) as optional symptom inventory
  - Useful as continuous measure of behavioral dysfunction

Mild Behavioral Impairment Checklist (MBI-C)

Date: _____

Rated by: ☐ Clinician ☐ Informant ☐ Subject

Location: ☐ Clinic ☐ Research

Label

Circle "Yes" **only** if the behavior has been present for at least **6 months** (continuously, or on and off) and is a **change** from her/his longstanding pattern of behavior. Otherwise, circle "No".

Please rate severity: **1 = Mild** (noticeable, but not a significant change); **2 = Moderate** (significant, but not a dramatic change); **3 = Severe** (very marked or prominent, a dramatic change). If more than 1 item in a question, rate the most severe.

	YES	NO	SEVERITY
This domain describes interest, motivation, and drive			
Has the person lost interest in friends, family, or home activities?	Yes	No	1 2 3
Does the person lack curiosity in topics that would usually have attracted her/his interest?	Yes	No	1 2 3
Has the person become less spontaneous and active – for example, is she/he less likely to initiate or maintain conversation?	Yes	No	1 2 3
Has the person lost motivation to act on her/his obligations or interests?	Yes	No	1 2 3
Is the person less affectionate and/or lacking in emotions when compared to her/his usual self?	Yes	No	1 2 3
Does she/he no longer care about anything?	Yes	No	1 2 3
This domain describes mood or anxiety symptoms			
Has the person developed sadness or appear to be in low spirits? Does she/she have episodes of tearfulness?	Yes	No	1 2 3
Has the person become less able to experience pleasure?	Yes	No	1 2 3
Has the person become discouraged about their future or feel that she/he is a failure?	Yes	No	1 2 3
Does the person view herself/himself as a burden to family?	Yes	No	1 2 3
Has the person become more anxious or worried about things that are routine (e.g. events, visits, etc.)?	Yes	No	1 2 3
Does the person feel very tense, having developed an inability to relax, or shakiness, or symptoms of panic?	Yes	No	1 2 3
This domain describes the ability to delay gratification and control behavior, impulses, oral intake and/or changes in reward			
Has the person become agitated, aggressive, irritable, or temperamental?	Yes	No	1 2 3
Has she/he become unreasonably or uncharacteristically argumentative?	Yes	No	1 2 3
Has the person become more impulsive, seeming to act without considering things?	Yes	No	1 2 3
Does the person display sexually disinhibited or intrusive behaviour, such as touching (themselves/others), hugging, groping, etc., in a manner that is out of character or may cause offence?	Yes	No	1 2 3

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