NACC UNIFORM DATA SET

Coding Guidebook

UDSv4.0, January 2025

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Revisions made to this Coding Guidebook since release (January 2025)

Date yyyy-mm-dd	Description	Form(s) affected	Question(s) affected
2026-07-09	Added Form D1c: Biological and Clinical Staging	D1c	
2026-01-12	Added instruction for participants with telephone-only visit.	B8	Q1
2025-06-26	Added information about missing codes for ADI state decile and ADI national perccentile.	A1	Q21, Q22
2025-03-25	Clarified intended interpretation of "Age of onset" questions.	A3	
2025-02-06	Added guidance to Form A1a regarding what to do in cases where participant marks feeling unsafe in home.	A1a	Q25a

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Coding Guidebook for **Form A1:** Participant Demographics

***INSTRUCTIONS**: This form may be completed by intake interviewer based on ADRC scheduling records, participant interview, medical records, and proxy co-participant report (according to what is deemed to be the most reliable source of information, except as indicated for specific questions that may be based on the participant's perceptions and experience which only they can provide accurate information for). This information can be collected by mail-in survey, electronic capture (web-based), phone or video interview, or during the in-person visit to accommodate and lessen participant visit burden.* Check only <u>one</u> box per question unless otherwise specified.

IVP	FVP	Section 1 — Demographics

1. **N.A.** What is your month and year of birth (MM / YYYY)? __ __ / __ __ __ __

2. **N.A.** In which country or region did you spend most of your childhood? ___ ___ ___ *(Enter three character code from Appendix 1)* *(If unknown, enter AX1)*

Common codes:
USA – United States; CAN – Canada; MEX – Mexico

If the participant self-administered this form, please verify the code entered is correct and matches a code provided on Appendix 1.

This question is designed to capture different early lifetime social determinants of health that might influence cogntiive test performance and/or include different dementia risk exposures. Please provide the answer that best captures these characteristics based on the participant's subjective experience.

3. **N.A.** What is your race and/or ethnicity? *(Check all that apply and enter additional details in the space below.)*

3a. ☐ 1 American Indian or Alaska Native (AIAN)
(SPECIFY, *for example, Navajo Nation, Blackfeet Tribe of the Blackfeet Indian Reservation of Montana, Native Village of Barrow Inupiat Traditional Government, Nome Eskimo Community, Aztec, Maya, etc.)***:** _____

3b. ☐ 1 Asian
- **3b1.** ☐ 1 Chinese
- **3b2.** ☐ 1 Asian Indian
- **3b3.** ☐ 1 Filipino
- **3b4.** ☐ 1 Vietnamese
- **3b5.** ☐ 1 Korean
- **3b6.** ☐ 1 Japanese
- **3b7.** ☐ 1 Other **(SPECIFY,** *for example, Pakistani, Hmong, Afghan, etc.)***:** _____

3c. ☐ 1 Black or African American
- **3c1.** ☐ 1 African American
- **3c2.** ☐ 1 Jamaican
- **3c3.** ☐ 1 Haitian
- **3c4.** ☐ 1 Nigerian
- **3c5.** ☐ 1 Ethiopian
- **3c6.** ☐ 1 Somali
- **3c7.** ☐ 1 Other **(SPECIFY,** *for example, Trinidadian and Tobagonian, Ghanian, Congolese, etc.)***:** _____

3d. ☐ 1 Hispanic or Latino
- **3d1.** ☐ 1 Mexican
- **3d2.** ☐ 1 Puerto Rican
- **3d3.** ☐ 1 Salvadoran
- **3d4.** ☐ 1 Cuban
- **3d5.** ☐ 1 Dominican
- **3d6.** ☐ 1 Guatemalan
- **3d7.** ☐ 1 Other **(SPECIFY,** *for example, Colombian, Honduran, Spaniard, etc.)***:** _____

3e. ☐ 1 Middle Eastern or North African
- **3e1.** ☐ 1 Lebanese
- **3e2.** ☐ 1 Iranian
- **3e3.** ☐ 1 Egyptian
- **3e4.** ☐ 1 Syrian
- **3e5.** ☐ 1 Iraqi
- **3e6.** ☐ 1 Israeli
- **3e7.** ☐ 1 Other **(SPECIFY,** *for example, Moroccan, Yemeni, Kurdish, etc.)***:** _____

3f. ☐ 1 Native Hawaiian or Pacific Islander
- **3f1.** ☐ 1 Native Hawaiian
- **3f2.** ☐ 1 Samoan
- **3f3.** ☐ 1 Chamorro
- **3f4.** ☐ 1 Tongan
- **3f5.** ☐ 1 Fijian
- **3f6.** ☐ 1 Marshallese
- **3f7.** ☐ 1 Other **(SPECIFY,** *for example, Chuukese, Palauan, Tahitian, etc.)***:** _____

3g. ☐ 1 White
- **3g1.** ☐ 1 English
- **3g2.** ☐ 1 German
- **3g3.** ☐ 1 Irish
- **3g4.** ☐ 1 Italian
- **3g5.** ☐ 1 Polish
- **3g6.** ☐ 1 Scottish
- **3g7.** ☐ 1 Other **(SPECIFY,** *for example, French, Swedish, Norwegian, etc.)***:** _____

3h. ☐ 1 Don't know

Ask the participant (or, if necessary for participants with dementia, the co-participant) what they consider the participant's race and ethnicity to be. The respondent should choose all that apply.

NOTE ON USING THESE NEW RACE/ETHNICITY OPTIONS FOR NIH RACIAL CATEGORIES

The Office of Management and Budget (OMB) introduced their new race/ethnicity question format in March 2024. Per OMB, "If detailed race and ethnicity data are collected in an interviewer-administered setting, the minimum categories [e.g., Asian, Hispanic, or Latino] should be asked first, treating each category as a yes/no question, followed by the detailed categories associated with the selected minimum categories [e.g., Chinese, Mexican]." The question that should be asked is as written, "What is your race and/or ethnicity?". You may need to drill down on the racial/ethnicity sub-categories for the more detailed information requested.

This question is focused on lineage. Please refer to the NIH OMB instructions.

NOTE ON FORM CLS (LINGUISTIC HISTORY FORM)

Complete the Linguistic History Form (Form CLS) if the participant or co-participant indicates that the participant is Hispanic/Latino and has not completed Form CLS at a previous visit.

Form CLS must be completed and submitted to NACC only **ONCE**. It may be completed along with any UDS Initial or Follow-up visit. Information to complete CLS may be obtained from the participant or a co-participant.

The next four questions ask about your gender identity, sex assigned at birth, sexual orientation, and intersex status. This information will be used to help us improve health, well-being, and quality of care. By gender identity, we mean the inner sense that you have of yourself as being a man, woman, or a different gender. Gender identity can be different from your sex assigned at birth or your sexual orientation, and it can change over time.

Sex, gender identity, and sexual orientation questions were derived from the following report:

National Academies of Sciences, Engineering and Medicine. 2022. Measuring Sex, Gender Identity, and Sexual Orientation. Washington, D.C.: The National Academies Press. https://doi.org/10.17226/26424

This information should come from self-report only. It should not be inferred by the co-participant and/or ADRC staff. Note that all quetions include an opt out for participants that are unsure and/or prefer not to answer. You should assure participants that the data collected is protected for both confidentiality and privacy. If the participant has a CDR over 1, the answers to these questions may not be reliable and a default answer of "Don't Know" may be most appropriate.

IVP | FVP | Section 1 — Demographics *continued...*

4. | **1.** Which term(s) best describes your current gender identity?
(Check all that apply)

- **a.** ☐ 1 Man
- **b.** ☐ 1 Woman
- **c.** ☐ 1 Transgender man
- **d.** ☐ 1 Transgender woman
- **e.** ☐ 1 Non-binary/genderqueer
- **f.** ☐ 1 Two-Spirit (if you are AIAN)
- **g.** ☐ 1 I use a different term **(SPECIFY):** _____
- **h.** ☐ 1 Don't know
- **i.** ☐ 1 Prefer not to answer

Ask the participant which term(s) best describe their gender identity. The participant should choose all that apply.

Transgender: An umbrella term for people whose gender identity and/or expression is different from cultural expectation based on the sex they were assigned at birth. Being transgender does not imply any specific sexual orientation. Therefore, transgender people may identify as straight, gay, lesbian, bisexual, etc. [hrc.org/resources/glossary-of-terms]. A transgender man was assigned female at birth. A transgender woman was assigned male at birth.

Non-binary / genderqueer: Description for a person who does not identify exclusively as a man or a woman. Non-binary people may identify as being both a man and woman, somewhere in between, or as falling completely outside these categories. While many also identify as transgender, not all non-binary people do. Non-binary can also be used as an umbrella term encompassing identities such as agender, bigender, genderqueer, or gender-fluid. [hrc.org/resources/glossary-of-terms]

Two-spirit: A term used within some American Indian (AI) and Alaska Native (AN) communities to refer to a person who identifies as having both a male and a female essence or spirit. The term encompasses sexual, cultural, gender, and spiritual identities. Non-indigenous people should not use this term. [pflag.org/glossary]

5. | **N.A.** What sex were you assigned at birth, on your original birth certificate?

- ☐ 1 Male
- ☐ 2 Female
- ☐ 9 Don't know
- ☐ 8 Prefer not to answer

6. | **N.A.** Have you ever been diagnosed by a medical doctor or other health professional with an intersex condition or a "Difference of Sex Development (DSD)" or were you born with (or developed naturally in puberty) genitals, reproductive organs, and/or chromosomal patterns that do not fit standard definitions of male or female?

- ☐ 0 No
- ☐ 1 Yes
- ☐ 9 Don't know
- ☐ 8 Prefer not to answer

IVP	FVP	Section 1 — Demographics	*continued...*

7.	**2.**	Which term(s) best describes your sexual orientation? *(Check all that apply)*	**a.** ☐ 1 Lesbian or gay **b.** ☐ 1 Straight/heterosexual **c.** ☐ 1 Bisexual **d.** ☐ 1 Two-Spirit (if you are AIAN) **e.** ☐ 1 I use a different term **(SPECIFY,** *e.g., asexual, queer, questioning*): _____ **f.** ☐ 1 Don't know **g.** ☐ 1 Prefer not to answer

Ask the participant which term(s) best describe their sexual orientation. The participant should choose all that apply.

Two-spirit: A term used within some American Indian (AI) and Alaska Native (AN) communities to refer to a person who identifies as having both a male and a female essence or spirit. The term encompasses sexual, cultural, gender, and spiritual identities. Non-indigenous people should not use this term. [pflag.org/glossary]

8.	**N.A.**	What is your primary language? *(Primary language is defined as the predominant language you have used throughout your life. Please take into consideration first language learned and used as well as the length of use.)*	☐ 1 English ☐ 2 Spanish ☐ 3 Chinese dialect ☐ 8 Other **(SPECIFY):** _____ ☐ 9 Don't know

Record the language that the participant (or co-participant) considers to be the participant's main language that they speak and write best, even if they speak more than one and or consider their primary language different from their first language.

9.	**N.A.**	Are you left- or right-handed (*for example, which hand would normally be used for writing*)?	☐ 1 Left-handed ☐ 2 Right-handed ☐ 3 Ambidextrous ☐ 9 Don't know

If the participant describes themselves as ambidextrous, check the box that describes the hand used for writing rather than the hand used for other activites as this question focuses on language dominance over bilateral manual dexterity. If the participant writes with both hands, then they could be considered ambidextrous.

10a.	**N.A.**	How many years of education have you completed? **(99 = Unknown)** ___ ___ ___

This question refers to completed years of education, rather than achieved educational levels. Enter the total number of years of education completed. Total years should include trade school and/or other formal profesional training and not be restricted to classical education (i.e., grammar, middle, junior high, high school and classic college attendance). If the participant has attended formal education on a part-time basis over an extended period of time, please report standard years for level obtained rather than using whole years for part-time attendance.

Examples: If the participant attended school for eight years, enter "08". If the participant completed 17.5 years of school, enter "17", regardless of degrees attempted or earned. If the participant attended to school for 25 years to earn a PhD, enter "25".

If the participant or co-participant is unable or unwilling to answer the question, enter "99".

10b.	**N.A.**	What is your highest achieved level of education?	☐ 1 Less than high school ☐ 2 High school or GED ☐ 3 Some college ☐ 4 Bachelor's degree ☐ 5 Master's degree ☐ 6 Doctorate ☐ 9 Don't know

This question refers to achieved educational levels; do not select a level attempted but not completed.

Example: If the participant earned a bachelor's degree but did not complete an attempted master's degree, enter **4 = Bachelor's degree.**

11.	**3.**	What is your <u>current</u> marital status?	☐ 1 Married ☐ 2 Widowed ☐ 3 Divorced ☐ 4 Separated ☐ 5 Never married (or marriage was annulled) ☐ 6 Living with a domestic partner that you are not married to ☐ 9 Don't know

IVP	FVP	Section 1 — Demographics *continued...*	
12.	4.	What is your living situation?	☐ 1 Live alone ☐ 2 Live with one other person: a spouse or partner ☐ 3 Live with one other person: a relative, friend, or roommate ☐ 4 Live with caregiver who is not spouse/partner, relative, or friend ☐ 5 Live with a group *(related or not related)* in a private residence ☐ 6 Live in group home *(e.g., assisted living, nursing home, convent)* ☐ 9 Don't know

"Caregiver" applies to a person who provides assistance with another person's social or health needs, and may include help with activities of daily living, emotional support, and/or help with managing a chronic disease or disability.

13.	5.	What is your primary type of residence?	☐ 1 Single– or multi–family private residence (apartment, condo, house) ☐ 2 Retirement community or independent group living ☐ 3 Assisted living, adult family home, or boarding home ☐ 4 Skilled nursing facility, nursing home, hospital, or hospice ☐ 5 Do not have housing *(e.g., staying with others, in a hotel, in a shelter, living outside on the street, on a beach, in a car, or in a park)* ☐ 9 Don't know

Please choose the answer that is the best fit.

14.	6.	What are the first three digits of the ZIP code of your primary residence? *(For example, if your ZIP code is 12345, enter 123.)*	___ ___ ___ *(If unknown, leave blank)*
15.	N.A.	Have you ever served on active duty in the U.S. Armed Forces, military Reserves, or National Guard?	☐ 0 No (**IF NO, SKIP TO QUESTION 17**) ☐ 1 Yes ☐ 9 Don't know

Active duty does not include training in the Reserves or National Guard, but DOES include activation, for example, for the Persian Gulf War.

16.	7.	Have you ever obtained medical care or prescription drugs from a Veterans Affairs (VA) facility?	☐ 0 No ☐ 1 Yes ☐ 9 Don't know

Section 2 — Memory

17.	8.	How much time in total do you spend each week exercising or engaged in physically strenuous activities that cause increases in your breathing or heart rate for at least 10 minutes continuously? *(Include activity at work, traveling to and from places, fitness activities, and recreational activities.)*	☐ 1 None ☐ 2 1 hour or less ☐ 3 2.5 hours or less ☐ 4 More than 2.5 hours ☐ 8 Prefer not to answer ☐ 9 Don't know

The following three questions are intended to capture subjective cognitive impairment in the memory domain. These questions refer to memory only and not behavior, motor, or other non-memory symptoms. These questions should only be answered by the participant.

Select "Don't know/Prefer not to answer" for IVP Q18-20 (FVP Q9-11) if the co-participant is completing this form on behalf of the participant.

18.	9.	Do you feel like your memory is becoming worse?	☐ 0 No ☐ 1 Yes, but this does not worry me ☐ 2 Yes, and this worries me ☐ 9 Don't know / Prefer not to answer

This should be answered in relation to the participant's previous memory abilities.

19.	10.	About how often do you have trouble remembering things?	☐ 1 Never ☐ 2 Rarely ☐ 3 Sometimes ☐ 4 Often ☐ 5 Very often ☐ 9 Don't know / Prefer not to answer

20. **11.** Compared to 10 years ago, would you say that your memory is much worse, a little worse, the same, a little better, or much better?

- ☐ 1 Much better
- ☐ 2 A little better
- ☐ 3 The same
- ☐ 4 A little worse
- ☐ 5 Much worse
- ☐ 9 Don't know / Prefer not to answer

For ADRC use only:

The next two questions use the Area Deprivation Index (ADI) lookup at *https://www.neighborhoodatlas.medicine.wisc.edu/mapping*. Enter the participant's state and full address.

Enter the participant's state at https://www.neighborhoodatlas.medicine.wisc.edu/mapping. After the state map loads, enter the participant's full address (including a minimum of street address and city) in the lower right and click "search." A box will pop up with the state decile and national percentile. Enter these values in for the following two questions.

Occassionally, ADI percentiles will be missing. According to the Neighborhood Atlas FAQ:

When a census block group has less than 100 people, less than 30 housing units, more than 33% of the population living in group quarters, or census data labeled as N/A or missing in the core component variables, the ADI rank is replaced with a code describing the suppression reason. Three possible codes will appear in the ADI field: "PH" for suppression due to low population and/or housing, "GQ" for suppression due to a high group quarters population, and "PH-GQ" for suppression due to both types of suppression criteria. A code of "QDI" designates block groups without an ADI due to Questionable Data Integrity, stemming from missing data in the source ACS data.

ADI state decile and national percentile must be looked up at each visit, even if the participant has not moved, since these values can change over time.

21. **12.** ADI state-only decile
(If unknown, leave blank. For special codes, enter 884 for "PH", 885 for "GQ", 886 for "PH-GQ", and 887 for "QDI".) ___ ___ ___

22. **13.** ADI national percentile:
(If unknown, leave blank. For special codes, enter 884 for "PH", 885 for "GQ", 886 for "PH-GQ", and 887 for "QDI".) ___ ___ ___

23. **N.A.** Participant's primary occupation throughout their working life
(See Appendix 2 for codes): ___ ___ ___
(If unknown, leave blank)

Choose the occupation code that best fits the participant's primary occupation throughout their working life. Please use the participant's judgement as to what their primary occupation was in cases where they may have had several different occupations. If a close fit cannot be found among the available options, use the header "#00" codes, e.g. 500=Skilled Manual Employees.

For participants who worked inside the home and were not formally employed, use 713=Homemaker.

24. **N.A.** ADRC enrollment type:

- ☐ 1 Participant is supported primarily by ADRC funding *(Clinical Core, Satellite Core, or other ADRC Core or project)*
- ☐ 2 Participant is supported primarily by a non-ADRC study *(e.g., R01, including non-ADRC grants supporting FTLD Module participation)*

If the participant is engaged in more than one study, please answer in relation to the study that is funding the UDS form completion. If co-funded equally, please select 1 = ADRC funding.

25. **N.A.** Principal referral source

- ☐ 1 Self
- ☐ 2 Non-professional personal contact who is not a current or previous ADRC participant *(e.g., spouse/partner, relative, friend, coworker)*
- ☐ 3 Current or previous ADRC participant **(END FORM HERE)**
- ☐ 4 ADRC clinician, staff, or investigator **(END FORM HERE)**
- ☐ 5 Non-ADRC healthcare professional *(e.g., clinician, nurse, social worker)* **(END FORM HERE)**
- ☐ 6 Other research study clinician/staff/investigator *(non-ADRC; e.g., ADNI, Women's Health Initiative, LEADS, ALL-FTD)* **(END FORM HERE)**
- ☐ 8 Other **(SPECIFY):** _____ **(END FORM HERE)**
- ☐ 9 Unknown **(END FORM HERE)**

Select **1=Self** if the participant decided to enroll in the ADRC on their own initiative (e.g., after seeing an advertisement, media appeal, website, news article, or learning about the ADRC's research through a community event). ADRC clinician, staff or investigator includes members of all ADRC cores and should not be restricted to clinical core staff.

Many participants may have been recruited through multiple contacts. Please use the participants report of the primary referral source responsible for ultimate engagement which may nor necessarily be the last contact prior to enrollment, but rather the most influential.

26. **N.A.** If the referral source was self-referral or a nonprofessional contact, how did the referral source learn of the ADRC?

(choose most relevant option)

Community outreach event

- ☐ 1 ADRC sponsored event
- ☐ 2 Event sponsored by an external organization *(e.g., Alzheimer's Association event, institution sponsored venue, community health fair, professional conference)*

Other ADRC outreach

- ☐ 3 Newsletter *(mailed or digital)*
- ☐ 4 Study flyer/brochure *(mailed or digital)*
- ☐ 5 Center website
- ☐ 6 Center social media **(SPECIFY):** _____
- ☐ 7 Center registry **(SPECIFY):** _____

Other registries, websites, organizations, or media promotions

- ☐ 8 Website **(SPECIFY):** _____
- ☐ 9 Media **(SPECIFY):** _____
- ☐ 10 Registry **(SPECIFY):** _____
- ☐ 88 Other **(SPECIFY):** _____
- ☐ 99 Unknown

Participants may have learned of the ADRC through multiple sources. Please use the participants report of the primary referral source responsible for ultimate engagement which may not necessarily be the last contact prior to enrollment, but rather the most influential.

Appendix 1: Birth Country*

Code	Country	Code	Country	Code	Country
AFG	Afghanistan	CHN	China	GRL	Greenland
XQZ	Akrotiri	CXR	Christmas Island	GRD	Grenada
ALB	Albania	CPT	Clipperton Island	GLP	Guadeloupe
DZA	Algeria	CCK	Cocos (Keeling) Islands	GUM	Guam
ASM	American Samoa	COL	Colombia	AX2	Guantanamo Bay Naval Base
AND	Andorra	COM	Comoros	GTM	Guatemala
AGO	Angola	COG	Congo (Brazzaville)	GGY	Guernsey
AIA	Anguilla	COD	Congo (Kinshasa)	GIN	Guinea
ATA	Antarctica	COK	Cook Islands	GNB	Guinea-Bissau
ATG	Antigua and Barbuda	XCS	Coral Sea Islands	GUY	Guyana
ARG	Argentina	CRI	Costa Rica	HTI	Haiti
ARM	Armenia	CIV	Cote D'Ivoire	HMD	Heard Island and McDonald Islands
ABW	Aruba	HRV	Croatia	HND	Honduras
XAC	Ashmore and Cartier Islands	CUB	Cuba	HKG	Hong Kong
AUS	Australia	CUW	Curacao	XHO	Howland Island
AUT	Austria	CYP	Cyprus	HUN	Hungary
AZE	Azerbaijan	CZE	Czechia	ISL	Iceland
BHS	The Bahamas	DNK	Denmark	IND	India
BHR	Bahrain	XXD	Dhekelia	IDN	Indonesia
XBK	Baker Island	DGA	Diego Garcia	IRN	Iran
BGD	Bangladesh	DJI	Djibouti	IRQ	Iraq
BRB	Barbados	DMA	Dominica	IRL	Ireland
XBI	Bassas da India	DOM	Dominican Republic	IMN	Isle of Man
BLR	Belarus	ECU	Ecuador	ISR	Israel
BEL	Belgium	EGY	Egypt	ITA	Italy
BLZ	Belize	SLV	El Salvador	JAM	Jamaica
BEN	Benin	GNQ	Equatorial Guinea	XJM	Jan Mayen
BMU	Bermuda	ERI	Eritrea	JPN	Japan
BTN	Bhutan	EST	Estonia	XJV	Jarvis Island
BOL	Bolivia	SWZ	Eswatini	JEY	Jersey
BES	Bonaire, Sint Eustatius, and Saba	ETH	Ethiopia	XJA	Johnston Atoll
BIH	Bosnia and Herzegovina	XEU	Europa Island	JOR	Jordan
BWA	Botswana	FLK	Falkland Islands (Islas Malvinas)	XJN	Juan de Nova Island
BVT	Bouvet Island	FRO	Faroe Islands	KAZ	Kazakhstan
BRA	Brazil	FJI	Fiji	KEN	Kenya
IOT	British Indian Ocean Territory	FIN	Finland	XKR	Kingman Reef
BRN	Brunei	FRA	France	KIR	Kiribati
BGR	Bulgaria	GUF	French Guiana	PRK	North Korea
BFA	Burkina Faso	PYF	French Polynesia	KOR	South Korea
MMR	Burma	ATF	French Southern and Antarctic Lands	XKS	Kosovo
BDI	Burundi	GAB	Gabon	KWT	Kuwait
CPV	Cabo Verde	GMB	The Gambia	KGZ	Kyrgyzstan
KHM	Cambodia	XGZ	Gaza Strip	LAO	Laos
CMR	Cameroon	GEO	Georgia	LVA	Latvia
CAN	Canada	DEU	Germany	LBN	Lebanon
CYM	Cayman Islands	GHA	Ghana	LSO	Lesotho
CAF	Central African Republic	GIB	Gibraltar	LBR	Liberia
TCD	Chad	XGL	Glorioso Islands	LBY	Libya
CHL	Chile	GRC	Greece	LIE	Liechtenstein

*Codes were developed by the U.S. Government and endorsed by the Federal Geographic Data Committee.
https://www.fgdc.gov/standards/news/GENC

Appendix 1: Birth Country*

Code	Country	Code	Country	Code	Country
LTU	Lithuania	PRY	Paraguay	TWN	Taiwan
LUX	Luxembourg	PER	Peru	TJK	Tajikistan
MAC	Macau	PHL	Philippines	TZA	Tanzania
MDG	Madagascar	PCN	Pitcairn Islands	THA	Thailand
MWI	Malawi	POL	Poland	TLS	Timor-Leste
MYS	Malaysia	PRT	Portugal	TGO	Togo
MDV	Maldives	PRI	Puerto Rico	TKL	Tokelau
MLI	Mali	QAT	Qatar	TON	Tonga
MLT	Malta	REU	Reunion	TTO	Trinidad and Tobago
MHL	Marshall Islands	ROU	Romania	XTR	Tromelin Island
MTQ	Martinique	RUS	Russia	TUN	Tunisia
MRT	Mauritania	RWA	Rwanda	TUR	Turkey
MUS	Mauritius	BLM	Saint Barthelemy	TKM	Turkmenistan
MYT	Mayotte	SHN	Saint Helena, Ascension, and Tristan da Cunha	TCA	Turks and Caicos Islands
MEX	Mexico	KNA	Saint Kitts and Nevis	TUV	Tuvalu
FSM	Federated States of Micronesia	LCA	Saint Lucia	UGA	Uganda
XMW	Midway Islands	MAF	Saint Martin	UKR	Ukraine
MDA	Moldova	SPM	Saint Pierre and Miquelon	ARE	United Arab Emirates
MCO	Monaco	VCT	Saint Vincent and the Grenadines	GBR	United Kingdom
MNG	Mongolia	WSM	Samoa	USA	United States
MNE	Montenegro	SMR	San Marino	AX1	Unknown
MSR	Montserrat	STP	Sao Tome and Principe	URY	Uruguay
MAR	Morocco	SAU	Saudi Arabia	UZB	Uzbekistan
MOZ	Mozambique	SEN	Senegal	VUT	Vanuatu
NAM	Namibia	SRB	Serbia	VAT	Vatican City
NRU	Nauru	SYC	Seychelles	VEN	Venezuela
XNV	Navassa Island	SLE	Sierra Leone	VNM	Vietnam
NPL	Nepal	SGP	Singapore	VGB	British Virgin Islands
NLD	Netherlands	SXM	Sint Maarten	VIR	U.S. Virgin Islands
NCL	New Caledonia	SVK	Slovakia	XWK	Wake Island
NZL	New Zealand	SVN	Slovenia	WLF	Wallis and Futuna
NIC	Nicaragua	SLB	Soloman Islands	XWB	West Bank
NER	Niger	SOM	Somalia	ESH	Western Sahara
NGA	Nigeria	ZAF	South Africa	YEM	Yemen
NIU	Niue	SGS	South Georgia and South Sandwich Islands	ZMB	Zambia
NFK	Norfolk Island	SSD	South Sudan	ZWE	Zimbabwe
MKD	North Macedonia	ESP	Spain		
MNP	Northern Mariana Islands	XSP	Spratly Islands		
NOR	Norway	LKA	Sri Lanka		
OMN	Oman	SDN	Sudan		
PAK	Pakistan	SUR	Suriname		
PLW	Palau	XSV	Svalbard		
XPL	Palmyra Atoll	SWE	Sweden		
PAN	Panama	CHE	Switzerland		
PNG	Papua New Guinea	SYR	Syria		
XPR	Paracel Islands				

*Codes were developed by the U.S. Government and endorsed by the Federal Geographic Data Committee.
https://www.fgdc.gov/standards/news/GENC

Appendix 2: NACC Occupation Codes

Code	Occupation	Code	Occupation	Code	Occupation	Code	Occupation
100	Major professionals/ Higher Executives/ Proprietors of Large Concerns	200	Lesser Professionals/ Business Managers of Medium-sized Businesses	300	Administrative Personnel/Small Business Owners/ Minor Professionals	400	Clerical and Sales Workers/Technicians/ Owners of Little Businesses
101	Actuaries	201	Accountants	301	Actors	401	Bank tellers
102	Architects	202	Advertising executives	302	Administrative assistants	402	Bill collectors
103	Bank officers	203	Authors	303	Advertising agents	403	Bookkeepers
104	Certified public accountants	204	Branch managers	304	Artists	404	Claims examiners
105	Chief executives (CEO, CFO, COO)	205	Building contractors	305	Bakers	405	Drafters
106	Clergy (professionally trained)	206	Business managers	306	Beauty shop owners	406	Driving teachers
107	Commissioned officers in the military	207	Chiropractors	307	Chefs	407	Factory supervisors
108	Dentists	208	Computer programmer	308	Chief clerks	408	Small farm owners / farmers
109	Economists	209	Computer specialists	309	Clergy (not professionally trained)	409	Flower shop workers
110	Engineers (Masters level and above)	210	Database developer	310	Court reporters	410	Human resources workers
111	Financial managers	211	Editors	311	Credit managers	411	Laboratory technicians
112	Federal government officials	212	Engineers (no advanced degree)	312	Dental hygienists	412	Newsstand operators
113	Large business owners	213	Executive managers	313	Department store man-agers	413	Post office clerks
114	Lawyers / judges	214	Industrial farm owners	314	Deputy sheriffs	414	Railroad conductors
115	Mathematicians	215	Furniture business owners	315	Dietitians / Nutritionists	415	Railroad train engineers
116	Major contractors	216	Jewelers	316	Dispatchers	416	Receptionists
117	Orthodontist	217	Labor relations consultant	317	Florists	417	Route managers
118	Physicians	218	Librarians	318	Funeral directors	418	Sales clerks
119	Professor / University teachers	219	Manufacturing owners	319	Insurance agents	419	Secretaries / stenographers
120	Psychologists	220	Medium business owners	320	Laboratory assistants	420	Shipping clerks
121	Research scientists	221	Musicians / composers	321	Landscape planners	421	Tailors
122	Urban and regional planners	222	Nurses	322	Noncommissioned officers in the military (at or above rank of master sergeant / C.P.O.)	422	Tax clerks
123	Veterinarians	223	Office manager	323	Morticians	423	Telephone company workers
124	VP of large business	224	Opticians	324	Newspaper / TV reporters	424	Telephone operators
		225	Personnel managers	325	Photographers	425	Timekeepers
		226	Pharmacists	326	Piano teachers	426	Toll collectors
		227	Pilots	327	Radio / TV announcers	427	Tower operators
		228	Police chief / sheriff	328	Real estate agents	428	Truck dispatchers
		229	Postmaster	329	Restaurant owners	429	Typists
		230	Production managers (TV / radio)	330	Sales representatives	430	Utility workers
		231	Public administration officials	331	Service managers	431	Warehouse clerks
		232	Public health officers	332	Small business owners	432	Window store trimmers
		233	Purchasing managers	333	Store managers		
		234	Real estate brokers	334	Surveyors		
		235	Research assistants	335	Title searchers		
		236	Sales engineers	336	Tool designers		
		237	Sales managers	337	Traffic managers		
		238	Social workers	338	Travel agents		
		239	State / Local government officials	339	Yard masters (railroad)		
		240	Teachers (Elementary & high school)				

Appendix 2: NACC Occupation Codes

Code	Occupation	Code	Occupation	Code	Occupation	Code	Occupation
500	Skilled Manual Employees	500	Skilled Manual Employees (cont.)	600	Machine Operators/ Semiskilled Employees	700	Unskilled Employees
501	Auto body repairers	538	Piano tuners	601	Apprentices (electrician / printers / etc.)	701	Amusement park workers
502	Barbers	539	Plumbers	602	Assembly line workers	702	Cafeteria workers
503	Boiler repairers	540	Police officers	603	Bartenders	703	Car cleaners
504	Bookbinders	541	Postal workers	604	Building superintendents	704	Child care workers (private household)
505	Brewers	542	Printers	605	Bus drivers	705	Construction laborers
506	Cabinet makers	543	Radio / TV maintenance	606	Cab / taxi drivers	706	Dairy workers
507	Carpenters	544	Railroad brake operators	607	Cashiers	707	Deck hands
508	Cement layers / finishers	545	Repair people	608	Child care workers (not private household)	708	Farm laborers
509	Checkers / examiners / inspectors	546	Seamstresses / seamsters	609	Cooks (short order)	709	Fishers
510	Cheese makers	547	Sheet metal workers	610	Corrections workers	710	Freight handlers
511	Construction forepeople	548	Ship smiths	611	Delivery people	711	Garbage collectors
512	Die makers	549	Shoe repairers	612	Dry cleaning pressers	712	Grave diggers
513	Electricians	550	Steelworkers	613	Elevator operators	713	Homemakers
514	Engravers	551	Tile layers	614	Enlisted military personnel (other than noncommissioned officers)	714	House cleaners
515	Exterminators	552	Tool makers	615	Factory machine operators	715	Janitors
516	Firefighters	553	Upholsterers	616	Factory workers	716	Junk / recycle sorters
517	Gardeners / landscapers	554	Utility line workers	617	Foundry workers	717	Laundry workers
518	Glassblowers	555	Weavers	618	Garage and gas station assistants	718	Messengers
519	Glaziers	556	Welders	619	Greenhouse workers	719	Peddlers
520	Gun smiths			620	Guards / security watch people	720	Porters
521	Hair stylists			621	Machine operators	721	Roofing laborers
522	Heavy equipment operators			622	Meat cutters / packers	722	Shoe shiners
523	Home repairs			623	Meter readers	723	Stagehands
524	Iron workers			624	Nursing aides / attendants	724	Stock handlers
525	Kitchen workers / cooks			625	Oil delivery people	725	Street cleaners
526	Locksmiths			626	Practical nurses	726	Unemployed
527	Machinists			627	Pump operators	727	Unskilled factory workers
528	Mail carriers			628	Receivers / checkers	728	Unspecified laborers
529	Maintenance forepeople			629	Servers (waiters / waitresses)	729	Window cleaners
530	Masons			630	Signal operators (railroad)	730	Woodchoppers
531	Mechanics			631	Truck drivers	731	Worked while incarcerated
532	Millwrights			632	Wood workers		
533	Noncommissioned officers in the military (below rank of master sergeant / C.P.O.)			633	Wrappers (stores / factories)		
534	Painters						
535	Paperhangers						
536	Patrolmen						
537	Piano builders						

Coding Guidebook for **Form A1a:** Social Determinants of Health

Frequently Asked Questions

Q: The participant has cognitive impairment (or a CDR>1). Should I give the A1a form to them?
A: No, the A1a form should only be given to those participants who are cognitively unimpaired enough to provide reliable and accurate responses (generally, CDR<1).

Q: The participant came to the visit with a co-participant. Can I have the co-participant fill the A1a form out for the participant?
A: No, the A1a form is for the participant to fill out as it asks about experiences and perceptions that only the participant would know.

Q: The participant does not feel comfortable filling out forms on their own, can the A1a form be administered by staff?
A: The A1a form should be self-administered by the participant. The form can be sent to the participant before the UDS visit (via email or electronically). However, if the participant is unable to fill out the form due to low literacy or some other reason, a staff member who is comfortable asking these personal (non-medical) questions, may administer the form.

Q: What happens if the participant does not want to answer the questions or feels the questions are too personal?
A: We have added "Prefer not to answer" to every question. The participant does not have to answer any question that they feel is intrusive.

Q: What do I tell a participant who wants to know why we are asking these kinds of questions?
A: We have added additional instructions to the form to explain why these questions are important. Please inform the participant that we are collecting all types of information that we think is important for brain health. Some information, like the questions on the A1a form, are important to understand the context in which people live, or the experiences that they have on a daily basis. We know that these social factors are important for health, but they have rarely been examined in regards to brain health. This is an important opportunity to collect data on an aspect of human experience that we know little about.

INSTRUCTIONS: *The following questions are designed to assess your current and past life experiences. These questions will help us understand how certain experiences affect your health. You do not have to answer any question that makes you feel uncomfortable.*

IVP	FVP	Section 1 — Transportation	
		In this section we are trying to understand the extent to which lack of reliable and consistent transportation is a barrier to accomplishing important activities, such as going to the doctor for appointments, going grocery shopping, or picking up medications (these are only examples).	
1.	1.	Do you or someone in your household currently own a car?	☐ 0 No ☐ 1 Yes ☐ 8 Prefer not to answer
2.	2.	Do you have consistent access to transportation?	☐ 0 No ☐ 1 Yes ☐ 8 Prefer not to answer
		To get to the places they need to go, people might walk, bike, take a bus, train or taxi, drive a car, or get a ride. The next three questions are trying to assess whether or not you have had recent issues with transportation.	
3.	3.	In the past 30 days, how often were you **not** able to leave the house when you wanted to because of a problem with transportation?	☐ 1 Often ☐ 2 Sometimes ☐ 3 Never ☐ 8 Prefer not to answer
4.	4.	In the past 30 days, how often did you worry about whether or not you would be able to get somewhere because of a problem with transportation?	☐ 1 Often ☐ 2 Sometimes ☐ 3 Never ☐ 8 Prefer not to answer
5.	5.	In the past 30 days, how often has a lack of transportation kept you from medical appointments or from doing things needed for daily living?	☐ 1 Often ☐ 2 Sometimes ☐ 3 Never ☐ 8 Prefer not to answer

Section 2 — Financial security

These next set of questions are designed to assess your current and past financial situation. If you do not feel comfortable with any question in this section, you can respond **Prefer not to answer**.

6. Which of these income groups represents your household income for the past year? Include income from all sources such as wages, salaries, social security or retirement benefits, help from relatives, rent from property, and so forth.

This information will be kept confidential and will not be shared in a way that identifies you with any other person, organization or government entity.

- ☐ 1 $0 - $14,999
- ☐ 2 $15,000 – $29,999
- ☐ 3 $30,000 – $74,999
- ☐ 4 $75,000 and over
- ☐ 8 Prefer not to answer
- ☐ 9 Don't know

7. How satisfied are you with your current personal financial condition?

- ☐ 1 Completely satisfied
- ☐ 2 Satisfied
- ☐ 3 Somewhat satisfied
- ☐ 4 Not very satisfied
- ☐ 5 Not at all satisfied
- ☐ 8 Prefer not to answer

8. How difficult is it for you to meet monthly payments on your bills?

- ☐ 1 Not at all
- ☐ 2 Slightly
- ☐ 3 Moderately
- ☐ 4 Very
- ☐ 5 Extremely
- ☐ 8 Prefer not to answer

9. If you have had financial problems that lasted twelve months or longer, how upsetting has it been to you?

- ☐ 1 No financial problems for twelve months or longer
- ☐ 2 Yes, financial problems for twelve months or longer, but not upsetting to me
- ☐ 3 Yes, financial problems for twelve months or longer, and somewhat upsetting to me
- ☐ 4 Yes, financial problems for twelve months or longer, and very upsetting to me
- ☐ 8 Prefer not to answer

10. At any time, did you ever eat less than you felt you should because there wasn't enough money to buy food?

- ☐ 0 No
- ☐ 1 Yes
- ☐ 8 Prefer not to answer

11. In the last 12 months, did you ever eat less than you felt you should because there wasn't enough money to buy food?

- ☐ 0 No
- ☐ 1 Yes
- ☐ 8 Prefer not to answer

12. At any time, have you ended up taking less medication than was prescribed for you because of the cost?

- ☐ 0 No
- ☐ 1 Yes
- ☐ 8 Prefer not to answer

13. In the last 12 months, have you ended up taking less medication than was prescribed for you because of the cost?

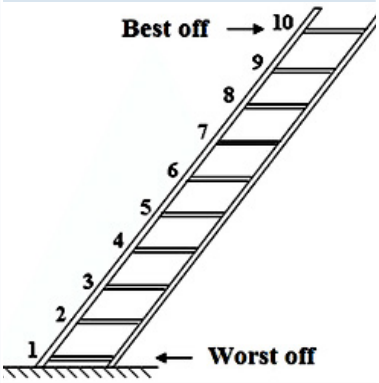
- ☐ 0 No
- ☐ 1 Yes
- ☐ 8 Prefer not to answer

14. This is a picture of a ladder with 10 steps. Each step represents a level of status as far as money, education, and jobs. The highest step is step 10. This represents people with the most money, the most education, and the best jobs. Step 1 is the lowest step. This step represents people with the least money, least education, and the worst jobs or no job. Steps in between (2 through 9) represent those people who fall somewhere between those who are best off and those who are worst off.

Where would you place yourself on this ladder compared to others in your community (or neighborhood)? The closer you are to step 10 the better off you think you are. Please mark the number where you would place yourself.

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
10 9 8 7 6 5 4 3 2 1

☐ 88 Prefer not to answer



IVP	FVP	Section 2 — Financial security *continued...*	
15.	15.	What was your mother's (or primary person who raised you up until age 18) highest level of education completed at the time they were raising you?	☐ 1 Never attended school or only attended kindergarten ☐ 2 Grades 1 through 8 (elementary) ☐ 3 Grades 9 through 11 (some high school) ☐ 4 Grade 12 or GED (high school graduate) ☐ 5 College 1 year to 3 years (some college) ☐ 6 College 4 years or more (college graduate) ☐ 8 Prefer not to answer/Not applicable ☐ 9 Do not know

Section 3 — Social connections, activities, and environment

These next set of questions are designed to learn what you think about your social connections, the types of activities you spend your time on, and how you view your home and neighborhood.

Following are some statements to learn how you describe yourself in general. For each statement, select the number that most closely represents your opinion.

16.	16.	I experience a general sense of emptiness	☐ 1 Strongly disagree ☐ 2 Disagree ☐ 3 Neither disagree or agree ☐ 4 Agree ☐ 5 Strongly agree ☐ 8 Prefer not to answer
17.	17.	I miss having people around	☐ 1 Strongly disagree ☐ 2 Disagree ☐ 3 Neither disagree or agree ☐ 4 Agree ☐ 5 Strongly agree ☐ 8 Prefer not to answer
18.	18.	I feel like I don't have enough friends	☐ 1 Strongly disagree ☐ 2 Disagree ☐ 3 Neither disagree or agree ☐ 4 Agree ☐ 5 Strongly agree ☐ 8 Prefer not to answer
19.	19.	I often feel abandoned	☐ 1 Strongly disagree ☐ 2 Disagree ☐ 3 Neither disagree or agree ☐ 4 Agree ☐ 5 Strongly agree ☐ 8 Prefer not to answer
20.	20.	I miss having a really close friend	☐ 1 Strongly disagree ☐ 2 Disagree ☐ 3 Neither disagree or agree ☐ 4 Agree ☐ 5 Strongly agree ☐ 8 Prefer not to answer

The next four questions are about how you spend your time.

21.	21.	If your parents are still alive, how often do you have contact with them (including mother, father, mother-in-law, and father-in-law) either in person, by phone, mail, or email (e.g., any online interaction)?	☐ 0 Parents not living ☐ 1 Once a year or less ☐ 2 Several times a year ☐ 3 Several times a month ☐ 4 Several times a week ☐ 5 Everyday or almost everyday ☐ 8 Prefer not to answer

IVP	FVP	Section 3 — Social connections, activities, and environment *continued...*	
22.	22.	If you have children, how often do you have contact with your children (including child[ren]-in-law and stepchild[ren]) either in person, by phone, mail, or email (e.g., any online interaction)?	☐ 0 Do not have children ☐ 1 Once a year or less ☐ 2 Several times a year ☐ 3 Several times a month ☐ 4 Several times a week ☐ 5 Everyday or almost everyday ☐ 8 Prefer not to answer
23.	23.	How often do you have contact with close friends either in person, by phone, mail, or email (e.g., any online interaction)?	☐ 0 Do not have close friends ☐ 1 Once a year or less ☐ 2 Several times a year ☐ 3 Several times a month ☐ 4 Several times a week ☐ 5 Everyday or almost everyday ☐ 8 Prefer not to answer
24.	24.	How often do you participate in activities outside the home (e.g., religious activities, educational activities, volunteer work, paid work, or activities with groups or organizations)?	☐ 0 Do not participate in activities outside the home ☐ 1 Once a year or less ☐ 2 Several times a year ☐ 3 Several times a month ☐ 4 Several times a week ☐ 5 Everyday or almost everyday ☐ 8 Prefer not to answer

This next set of questions is about how safe you feel in different contexts.

25.	25.	How safe do you feel in your home and community (or neighborhood)?	
25a.	25a.	Home	☐ 1 Very safe ☐ 2 Mostly safe ☐ 3 Unsafe at times ☐ 4 Very unsafe ☐ 8 Prefer not to answer

If a participant reports that they feel unsafe or very unsafe in their home, please refer to your local ADRC's safetly practices, or seek guidance from your IRB and/or state laws for how to proceed with safety concerns.

25b.	25b.	Community (or neighborhood)	☐ 1 Very safe ☐ 2 Mostly safe ☐ 3 Unsafe at times ☐ 4 Very unsafe ☐ 8 Prefer not to answer

IVP	FVP	Section 4 — Experiences with the healthcare system	

These next five questions are about your experiences with the healthcare system over the past year. In answering the questions, please think about your regular medical doctors (not the doctors you see for this research study).

26.	26.	In the past year, how often did you delay seeking medical attention for a problem that was bothering you?	☐ 1 All of the time ☐ 2 Most of the time ☐ 3 Sometimes ☐ 4 None or almost none of the time ☐ 5 Not applicable ☐ 8 Prefer not to answer
27.	27.	In the past year, how often did you experience challenges in filling a prescription?	☐ 1 All of the time ☐ 2 Most of the time ☐ 3 Sometimes ☐ 4 None or almost none of the time ☐ 5 Not applicable ☐ 8 Prefer not to answer

IVP	FVP	Section 4 — Experiences with the healthcare system *continued...*	
28.	28.	In the past year, how often did you miss a follow-up medical appointment that was scheduled?	☐ 1 All of the time ☐ 2 Most of the time ☐ 3 Sometimes ☐ 4 None or almost none of the time ☐ 5 Not applicable ☐ 8 Prefer not to answer
29.	29.	In the past year, how often did you follow a doctor's advice or treatment plan when it was given?	☐ 1 All of the time ☐ 2 Most of the time ☐ 3 Sometimes ☐ 4 None or almost none of the time ☐ 5 Not applicable ☐ 8 Prefer not to answer
30.	30.	Overall, which of these describes your health insurance, access to healthcare services, and access to medications?	☐ 1 Not available to any extent ☐ 2 Below the level of my needs ☐ 3 Able to meet my needs ☐ 4 Exceeds my needs ☐ 8 Prefer not to answer

Section 5 — Experiences of Discrimination

Research has shown that experiences of unfair treatment in daily life, for any reason, can negatively affect health. Please answer the following questions about whether you have experienced unfair treatment in the following ways.

31.	31.	In your day-to-day life how often are you treated with less courtesy or respect than other people?	☐ 1 Almost every day ☐ 2 At least once a week ☐ 3 A few times a month ☐ 4 A few times a year ☐ 5 Less than once a year ☐ 6 Never ☐ 8 Prefer not to answer
32.	32.	In your day-to-day life how often do you receive poorer service than other people at restaurants or stores?	☐ 1 Almost every day ☐ 2 At least once a week ☐ 3 A few times a month ☐ 4 A few times a year ☐ 5 Less than once a year ☐ 6 Never ☐ 8 Prefer not to answer
33.	33.	In your day-to-day life how often do people act as if they think you are not smart?	☐ 1 Almost every day ☐ 2 At least once a week ☐ 3 A few times a month ☐ 4 A few times a year ☐ 5 Less than once a year ☐ 6 Never ☐ 8 Prefer not to answer
34.	34.	In your day-to-day life how often do people act as if they are afraid of you?	☐ 1 Almost every day ☐ 2 At least once a week ☐ 3 A few times a month ☐ 4 A few times a year ☐ 5 Less than once a year ☐ 6 Never ☐ 8 Prefer not to answer
35.	35.	In your day-to-day life how often are you threatened or harassed?	☐ 1 Almost every day ☐ 2 At least once a week ☐ 3 A few times a month ☐ 4 A few times a year ☐ 5 Less than once a year ☐ 6 Never ☐ 8 Prefer not to answer

IVP	FVP	Section 5 — Experiences of Discrimination *continued...*	
36.	**36.**	How frequently do you receive poorer service or treatment from doctors or in hospitals compared to other people?	☐ 1 All of the time ☐ 2 Most of the time ☐ 3 Sometimes ☐ 4 None or almost none of the time ☐ 5 Not applicable ☐ 8 Prefer not to answer
37.	**37.**	When reflecting on the day-to-day experiences in questions 33 to 38, what do you think are the main reasons for these experiences? *(Check all that apply)*	**39a1.** ☐ 1 My ancestry or national origins **39a2.** ☐ 1 My gender **39a3.** ☐ 1 My race **39a4.** ☐ 1 My age **39a5.** ☐ 1 My religion **39a6.** ☐ 1 My height **39a7.** ☐ 1 My weight **39a8.** ☐ 1 Some other aspect of my physical appearance **39a9.** ☐ 1 My sexual orientation **39a10.** ☐ 1 My education or income level **39a11.** ☐ 1 A physical disability **39a12.** ☐ 1 My shade of skin color **39a13.** ☐ 1 Other **39a14.** ☐ 1 Not applicable - I do not have these experiences in my day-to-day life **(END FORM HERE)** **39a15.** ☐ 1 Prefer not to answer
38.	**38.**	When you have had day-to-day experiences like those in questions 33 to 38, would you say they have been very stressful, moderately stressful, or not stressful?	☐ 1 Very stressful ☐ 2 Moderately stressful ☐ 3 Not stressful ☐ 9 Don't know ☐ 8 Prefer not to answer

Coding Guidebook for **Form A2:** Co-participant Demographics

INSTRUCTIONS: *This form is to be completed by intake interviewer based on co-participant's report. This form should not be provided directly to the co-participant. Check only one box per question.*

IVP	FVP	Section 1 — Co–participant's Relationship to Participant		
N.A.	1.	Is this a new co-participant *(i.e., one who was not a co-participant at any past UDS visit)*?	☐ 0 No	☐ 1 Yes
1.	2.	What is the co-participant's relationship to the participant?	☐ 1 Spouse, partner, or companion *(include ex-spouse, ex-partner, fiancé(e), boyfriend, girlfriend)* ☐ 2 Child *(by blood or through marriage or adoption)* ☐ 3 Sibling *(by blood or through marriage or adoption)* ☐ 4 Other relative *(by blood or through marriage or adoption)* ☐ 5 Friend, neighbor, or someone known through family, friends, work, or community *(e.g., church)* ☐ 6 Paid caregiver, health care provider, or clinician	
2.	3.	How long has the co-participant known the participant? *(If the co-participant has known the participant for less than 1 year, use 0.)*	___ ___ ___	Years (**999 = Unknown**)
		If the exact number of years is unknown, ask the co-participant to estimate it. If the co-participant is not able to estimate the number of years he/she has known the participant, enter **999=Unknown**.		
3.	4.	Does the co-participant live with the participant?	☐ 0 No	☐ 1 Yes **(SKIP TO QUESTION 5/6)**
		Select **1=Yes** if the co-participant currently lives with the participant at least part of the time.		
4.	5.	What is the primary mode of contact with the participant?	☐ 1 In-person ☐ 2 Telephone ☐ 3 Video conferencing	☐ 4 Texting or email ☐ 5 Social media platforms ☐ 6 Other **(SPECIFY):** _____
4a1.	5a1.	What is the approximate frequency of types of contact?	☐ 1 Daily ☐ 2 At least three times per week ☐ 3 Weekly	☐ 4 At least three times per month ☐ 5 Monthly ☐ 6 Less than once a month
4a2.	5a2.	What is the average amount of time spent in contact with the participant during each encounter? *(Please include an average of all encounter types.)*	☐ 1 Less than 5 minutes *(appropriate for texting or email and may be applicable to other modes of contact as well)*	☐ 2 5-15 minutes ☐ 3 15-30 minutes ☐ 4 30-60 minutes ☐ 5 Longer than one hour
5.	6.	Is there a question about the co-participant's reliability?	☐ 0 No	☐ 1 Yes
		The co-participant's reliability should be based on a consensus opinion from the staff that interacted with the co-participant. This question would best be filled out after the UDS assessments have been completed, when a better judgment can be made about the co-participant's reliability. If there is any reason to doubt the reliability of the co-participant, select **1=Yes**.		
		Section 2 — Co–participant's Judgment of Participant's Memory		
		*Ask the next three questions **directly to the co-participant**.*		
6.	7.	Do you feel like the participant's memory is becoming worse?	☐ 0 No ☐ 1 Yes, but this does not worry me ☐ 2 Yes, and this worries me ☐ 9 Unknown	
7.	8.	About how often does the participant have trouble remembering things?	☐ 1 Never ☐ 2 Rarely ☐ 3 Sometimes	☐ 4 Often ☐ 5 Very Often ☐ 9 Unknown
8.	9.	Compared to 10 years ago, would you say that the participant's memory is much worse, a little worse, the same, a little better, or much better?	☐ 1 Much better ☐ 2 A little better ☐ 3 The same	☐ 4 A little worse ☐ 5 Much worse ☐ 9 Unknown
		If the co-participant has not known the participant for at least 10 years, select **9 = Unknown**.		

Coding Guidebook for **Form A3:** Participant Family History

INSTRUCTIONS: *This form is to be completed by a clinician with experience in evaluating participants with neurological and psychiatric diagnoses. Estimates are allowed if exact birth year or age at death is unknown.*

INSTRUCTIONS FOR SECTIONS 1–3:

For biological parents, full siblings, and biological children with no neurological or psychiatric problem, provide the birth month, birth year, and age at death, enter **00 = No known neurological/psychiatric diagnosis** in the primary diagnosis column, and leave the rest of the row blank.

For biological parents, full siblings, and biological children with an unknown neurological or psychiatric condition (clinician cannot determine specific neurological or psychiatric condition based on all available information), provide the birth year, and age at death, enter **99=Unknown** in the primary diagnosis column, and leave the subsequent items in the row blank.

If multiple neurological problems exist for a parent, sibling, or child, enter the code for the neurological/psychiatric condition that corresponds to the primary diagnosis in the primary diagnosis column, and then enter the code for the neurological/psychiatric condition that corresponds to the secondary diagnosis in the secondary diagnosis column.

When entering a code for the primary diagnosis ("Primary Dx") and secondary diagnosis ("Secondary DX") columns, select the most specific diagnosis that is known.

If the method of evaluation is unknown, select **1=Participant/family report**. See Appendix (page 5) for descriptions of the methods of evaluation.

"Age of onset" refers to the age at which the first cognitive, behavioral, or motor symptoms were noted, not the age at which diagnosis was made. If the participant and/or co-participant is unwilling or unable to answer, enter **999=Unknown**. If the primary diagnosis is a congenital condition, or present since birth, enter an age of onset of "0".

Birth year for parents, siblings, and children should be consistent across forms:

- Uniform Data Set (UDS) Initial Visit Form A3 or UDS Follow-up Visit Form A3 (if applicable),
- FTLD Module Initial Visit Form A3a or FTLD Module Follow-up Visit Form A3a (if applicable), and
- Any previously submitted FTLD Module Initial Visit Form A3F and Follow-up Visit Form A3F (if applicable).

IVP / FVP — Section 1 – Biological parents

N.A. **1.** Since the last UDS visit, is new information available concerning the status of the participant's biological mother or father?

☐ 1 No **(SKIP TO QUESTION 2)**
☐ 2 Yes **(COMPLETE QUESTIONS 1a-1b)**

For any parent with a neurological or psychiatric diagnosis, the entire row must be filled out.

If the clinician cannot determine the primary neurological/psychiatric diagnosis after reviewing all available evidence, enter **99 = Unknown** in the **Primary diagnosis** column, and *skip the subsequent questions in the row*. For a parent with no neurological or psychiatric diagnosis, enter **00 = No known neurological/psychiatric diagnosis** in the **Primary diagnosis** column, and then *skip the subsequent questions in the row.* For a parent with a primary diagnosis but no secondary diagnosis, enter **88 = No secondary diagnosis** in the Secondary diagnosis column.

Provide information on biological parents below. If birth year is unknown, please provide an approximate year on the Initial Visit Form A3 and ensure that it is consistently reported on any Follow-up Visit Form A3, as applicable. If it is impossible for the participant and co-participant to estimate the birth year, enter **9999=Unknown**.

For any biological parent with a neurological or psychiatric condition, the entire row must be filled out. If the clinician cannot determine the primary neurological problem/psychiatric condition after reviewing all available evidence, enter **99 = Unknown** in the **Primary diagnosis** column, and then skip the subsequent questions in the row. For a biological parent with no neurological or psychiatric problem, enter **00=No known neurological illness** in the **Primary diagnosis** column, and then skip the subsequent questions in the row.

IVP	FVP		Birth year *(6666=provided at previous visit, 9999=Unknown)*	Age at death *(666=provided at previous visit, 888=N/A, 999 = Unknown)*	Primary dx*	Secondary dx*	Method of evaluation**	Age of onset of primary dx *(666=provided at previous visit, 999 = Unknown)*
					····· SEE LIST OF CODES ·····			
1a.	1a.	**Mother**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
1b.	1b.	**Father**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __

Codes

*DIAGNOSES

00 No known neurological/psychiatric diagnosis
01 Alzheimer's Disease
02 Lewy Body dementia (includes DLB and PDD)
03 Vascular dementia
04 Stroke
05 FTLD* without motor neuron disease
06 FTLD* with motor neuron disease
07 Motor Neuron Disease
08 Parkinson's Disease
09 Prion pathology
10 Psychiatric condition
11 Dementia of unknown etiology
12 Other
66 Provided at previous visit
88 No secondary diagnosis
99 Specific diagnosis unknown *(acceptable if method of evaluation is not by exam or autopsy)*

**METHOD OF EVALUATION

1 Participant/family report
2 Medical records
3 Exam
(co-enrolled family members)
4 Autopsy
(if autopsy report available)
6 Provided at previous visit

****FTLD includes:** bvFTD or FTD, PPA (any subtype), CBS or CBD, PSP*

***Abbreviations:** bvFTD = behavioral variant frontotemporal dementia, CBS = corticobasal syndrome, CBD = corticobasal degeneration, DLB = dementia with Lewy bodies, FTD = frontotemporal dementia, PDD = Parkinson's disease with dementia, PPA = primary progressive aphasia, PSP = progressive supranuclear palsy*

YEAR OF BIRTH FOR FULL SIBLINGS & BIOLOGICAL CHILDREN: If birth year is unknown, please provide an approximate year on **UDS Initial Visit Form A3** and **UDS Follow-up Visit Form A3** so that the sibling or child with unknown birth year ends up in correct birth order relative to the other siblings/children.

***Example:** A participant is the oldest of three children. The participant was born in 1940 and the middle sibling in 1943; the youngest sibling's birth year is unknown. An approximate birth year of 1944 or later should be assigned to the youngest sibling.*

Use that same birth year on **FTLD Module Form A3a**, *if applicable*, and across all UDS visits so that any new information on a particular sibling or child can be linked to previously submitted information. If it is impossible for the participant and co-participant to estimate the birth year, *enter* **9999=Unknown**.

IVP FVP Section 2 – Full siblings

Only full siblings should be listed.

N.A. **2.** Since the last UDS visit, is new information available concerning the status of the participant's full siblings?

☐ 1 No **(SKIP TO QUESTION 3)**
☐ 2 Yes **(COMPLETE QUESTIONS 2b-2u)**

2. **2.1** How many full siblings does the participant have?

___ ___ (77 = participant adopted or siblings unknown; 66 = provided at previous visit)

If participant has no full siblings, **SKIP TO QUESTION 3**; *otherwise, provide information on all full siblings.*

For any full sibling with a neurological or psychiatric diagnosis, the entire row must be filled out.

If the clinician cannot determine the primary neurological/psychiatric diagnosis after reviewing all available evidence, enter **99 = Unknown** in the **Primary diagnosis** column, and *skip the subsequent questions in the row*. For a full sibling with no neurological or psychiatric diagnosis, enter **00 = No known neurological/psychiatric diagnosis** in the **Primary diagnosis** column, and then *skip the subsequent questions in the row.* For a full sibling with a primary diagnosis but no secondary diagnosis, enter **88 = No secondary diagnosis** in the Secondary diagnosis column.

			Birth year *(6666=provided at previous visit, 9999=Unknown)*	Age at death *(666=provided at previous visit, 888=N/A, 999 = Unknown)*	Primary dx*	Secondary dx*	Method of evaluation**	Age of onset of primary dx *(666=provided at previous visit, 999 = Unknown)*
					····· SEE LIST OF CODES ·····			
2a.	2a.	**Sibling 1**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2b.	2b.	**Sibling 2**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2c.	2c.	**Sibling 3**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2d.	2d.	**Sibling 4**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2e.	2e.	**Sibling 5**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2f.	2f.	**Sibling 6**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2g.	2g.	**Sibling 7**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2h.	2h.	**Sibling 8**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2i.	2i.	**Sibling 9**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2j.	2j.	**Sibling 10**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2k.	2k.	**Sibling 11**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2l.	2l.	**Sibling 12**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2m.	2m.	**Sibling 13**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2n.	2n.	**Sibling 14**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2o.	2o.	**Sibling 15**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2p.	2p.	**Sibling 16**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2q.	2q.	**Sibling 17**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2r.	2r.	**Sibling 18**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2s.	2s.	**Sibling 19**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
2t.	2t.	**Sibling 20**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __

Section 3 – Biological children

IVP	FVP		
N.A.	3.	Since the last UDS visit, is new information available concerning the status of the participant's biological children?	☐1 No **(END FORM HERE)** ☐2 Yes **(COMPLETE QUESTIONS 3b-3p)**
3.	3.1	How many biological children does the participant have? ___ ___ (66 = provided at previous visit) If participant has no biological children, **END FORM HERE**; *otherwise, provide information on all biological children.*	

For any biological child with a neurological or psychiatric diagnosis, the entire row must be filled out.

If the clinician cannot determine the primary neurological/psychiatric diagnosis after reviewing all available evidence, enter **99 = Unknown** in the **Primary diagnosis** column, and *skip the subsequent questions in the row*. For a biological child with no neurological or psychiatric diagnosis, enter **00 = No known neurological/psychiatric diagnosis** in the **Primary diagnosis** column, and then *skip the subsequent questions in the row.* For a biological child with a primary diagnosis but no secondary diagnosis, enter **88 = No secondary diagnosis** in the Secondary diagnosis column.

			Birth year *(6666=provided at previous visit, 9999=Unknown)*	Age at death *(666=provided at previous visit, 888=N/A, 999 = Unknown)*	Primary dx*	Secondary dx*	Method of evaluation**	Age of onset of primary dx *(666=provided at previous visit, 999 = Unknown)*
					····· SEE LIST OF CODES ·····			
3a.	3a.	**Child 1**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
3b.	3b.	**Child 2**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
3c.	3c.	**Child 3**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
3d.	3d.	**Child 4**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
3e.	3e.	**Child 5**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
3f.	3f.	**Child 6**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
3g.	3g.	**Child 7**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
3h.	3h.	**Child 8**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
3i.	3i.	**Child 9**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
3j.	3j.	**Child 10**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
3k.	3k.	**Child 11**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
3l.	3l.	**Child 12**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
3m.	3m.	**Child 13**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
3n.	3n.	**Child 14**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __
3o.	3o.	**Child 15**	__ __ __ __	__ __ __	__ __	__ __	__	__ __ __

Appendix

1. **Participant/family report**

   Family report should be coded when the co-participant for the family reports a participant as having been diagnosed with a particular disorder. In most cases, family report alone should not be used to assigne any of the FTLD spectrum subtypes, or of parkinsonian disorders other than Parkinson's disease.

2. **Medical records**

   Medical records should be from an examination that focused specifically on dementia; that was performed by a neurologist, geriatrician, or psychiatrist; and that includes a neurologic examination, an imaging study, and cogntitive testing (e.g., MMSE, Blessed, or more formal tests). A telephone interview may also be used to collect additional information.

3. **Examination**

   The participant must have been examined in person at your ADRC/institution or by genetic studies staff associated with your ADRC/institution to code as diagnosis by examination. Medical records may or may not have been used when assigning diagnosis.

4. **Autopsy**

   If the autopsy was performed at an outside institution, you must have the report to code as diagnosis by autopsy.

Coding Guidebook for **Form A4:** Participant Medications

INSTRUCTIONS: *This form is to be completed by the clinician or ADRC staff. The purpose of this form is to record all prescription medications taken by the participant within* **the two weeks before the current visit**. *If the participant is receiving any treatments known to significantly impact Alzheimer's disease (AD) or Alzheimer's disease related dementias (ADRD) biomarkers as part of their clinical care at the time of clinical assessment (e.g., they are receiving lecanemab infusions), the treatment should be included on both this form and the A4a ADRD–Specific Treatments form.*

For prescription medications not listed here, please follow the instructions at the end of this form. OTC (non-prescription) medications need not be reported; however, a short list of medications that could be either prescription or OTC follows the prescription list.

Is the participant currently taking any medications? ☐ 0 No **(END FORM HERE)** ☐ 1 Yes

NOTE: The purpose of this form is to record all prescription medications taken by the participant within the two weeks before the current visit. Non-prescription (OTC) medications need not be reported; however, a short list of common OTC medications follows the prescription list. This form lists the 100 drugs most commonly reported by subjects in the UDS for the years 2015– 2023. The drugs are ordered alphabetically by their generic names. If applicable, one or more commercial (brand) names are listed in parentheses.

MEDICATION NAME	RXNorm
☐ acetaminophen-HYDROcodone (Hycet, Vicodin)	214182
☐ albuterol (Proventil, ProAir HFA, RespiClick, Ventolin)	435
☐ alendronate (Binosto, Fosamax)	46041
☐ allopurinol (Aloprim, Duzallo, Zyloprim)	519
☐ alprazolam (Xanax)	596
☐ amlodipine (Norvasc)	17767
☐ apixaban (Eliquis)	1364430
☐ atenolol (Tenormin)	1202
☐ atorvastatin (Lipitor)	83367
☐ benazepril (Lotensin)	18867
☐ bupropion (Aplenzin, Budeprion, Wellbutrin, Zyban)	42347
☐ calcium acetate (Calphron, Eliphos, PhosLo Phoslyra)	214342
☐ carbidopa-levodopa (Duopa, Rytary, Sinemet)	103990
☐ carvedilol (Coreg)	20352
☐ celecoxib (Celebrex)	140587
☐ cetirizine (Aller-Tec, Zyrtec)	20610
☐ citalopram (Celexa)	2556
☐ clonazepam (Klonopin)	2598
☐ clopidogrel (Plavix)	32968
☐ cyanocobalamin (Nascobal, Vitamin B12)	11248
☐ diclofenac (Flector, Cambia, Zipsor)	3355
☐ diltiazem (Cardizem, Cardia XT, DILT-XR, Tiazac)	3443
☐ donepezil (Adlarity, Aricept)	135447
☐ duloxetine (Cymbalta, Irenka)	72625
☐ enalapril (Vasotec)	3827

MEDICATION NAME	RXNorm
☐ ergocalciferol (Calcidol, Calciferol, Disdol, Vitamin D2)	4018
☐ escitalopram (Lexapro)	321988
☐ esomeprazole (Nexium)	283742
☐ estradiol (Estrace, Estrogel, Delestrogen, Yuvafem)	4083
☐ ezetimibe (Zetia)	341248
☐ ferrous sulfate (Feosol, Iron Supplement, Slow FE)	24947
☐ fexofenadine (Allegra, Wal-Flex)	87636
☐ finasteride (Propecia, Proscar)	25025
☐ fluoxetine (Prozac, Sarafem)	4493
☐ fluticasone (Flovent)	41126
☐ fluticasone nasal (Aller-Flo, Flonase)	1165656
☐ fluticasone-salmeterol (Advair, AirDuo)	284635
☐ furosemide (Lasix)	4603
☐ gabapentin (Gralise, Horizant, Neurontin)	25480
☐ galantamine (Razadyne, Reminyl)	4637
☐ glipizide (Glucotrol)	4821
☐ hydrochlorothiazide (Esidrix, Hydrodiuril, Microzide)	5487
☐ hydrochlorothiazide-triamterene (Dyazide, Maxzide)	258337
☐ latanoprost (Xalatan)	43611
☐ levothyroxine (Levoxyl, Synthroid, Tirosint)	10582
☐ lisinopril (Prinivil, Qbrelis, Zestril)	29046
☐ lorazepam (Ativan)	6470
☐ losartan (Cozaar)	52175
☐ lovastatin (Altocor, Altoprev, Mevacor)	6472

MEDICATION NAME	RXNorm
meloxicam (Mobic, Vivlodex)	41493
memantine (Namenda)	6719
metformin (Glucophage, Glumetza, Riomet)	6809
metoprolol (Lopressor, Toprol-XL)	6918
mirtazapine (Remeron)	15996
montelukast (Singulair)	88249
naproxen (Aleve, Anaprox, Naprosyn)	7258
niacin (Niacinol, Niacor, Niaspan, Nicotinic Acid)	7393
nifedipine (Adalat, Afeditab CR, Procardia)	7417
nitroglycerin (Nitro-Bid, Nitro-Dur, Nitro-Time, Nitrostat, Rectiv)	4917
omega-3 polyunsaturated fatty acids (Omacor, Lovaza, Vascazen)	4301
omeprazole (Prilosec, Zegerid)	7646
oxybutynin (Ditropan, Oxytrol, Urotrol)	32675
pantoprazole (Protonix)	40790
paroxetine (Paxil, Paxil CR, Pexeva)	32937
potassium chloride (K-Dur 10, K-Tab, Klor-con)	8591

MEDICATION NAME	RXNorm
pravastatin (Pravachol)	42463
quetiapine (Seroquel)	51272
ranitidine (Wal-Zan, Zantac)	9143
rivastigmine (Exelon)	183379
rosuvastatin (Crestor, Ezallor)	301542
sertraline (Zoloft)	36437
sildenafil (Viagra, Revatio)	136411
simvastatin (FloLipid, Zocor)	36567
tamsulosin (Flomax)	77492
terazosin (Hytrin)	37798
tramadol (ConZip, Ryzolt, Ultram)	10689
trazodone (Desyrel, Oleptro)	10737
valsartan (Diovan)	69749
venlafaxine (Effexor)	39786
warfarin (Coumadin, Jantoven)	11289
zolpidem (Ambien, Edluar, Intermezzo, Zolpimist)	39993

Commonly reported medications that may be purchased over the counter
(but that may also be prescription) :

MEDICATION NAME	RXNorm
acetaminophen (Actamin, Feverall, Ofirmev, Panadol, Tempra, Tylenol)	161
ascorbic acid (Acerola C, C Complex, Vitamin C)	1151
aspirin (Ecotrin)	1191
biotin (Appearex, coenzyme R, Nail-ex, Vitamin H)	1588
calcium acetate (Calphorn, Domeboro)	214342
calcium carbonate (Caltrate, Rolaids, Tums)	1897
calcium carbonate/cholecalciferol (Cal-Quick, Caltrate-Plus D)	608343
calcium carbonate/ergocalciferol (O Cal-D)	1008264
cholecalciferol (Decara, Replesta, Vitamin D3)	2418
chondroitin-glucosamine (Cidaflex, Osteo Bi-Flex)	1008567

MEDICATION NAME	RXNorm
docusate (Colace, Dioctyl SS, Ducsate Calcium, Dulcoease)	82003
folic acid (Folic Acid, Folvite)	4511
glucosamine (Glucosamine Hydrochloride, Optiflex-G, Synovacin)	4845
ibuprofen (Advil, Motrin, Nuprin)	5640
loratadine (Alavert, Allerclear, Claritin, Tavist)	28889
melatonin (Melatonin, Melatonin Time Release)	6711
polyethylene glycol 3350 (Clearlax, Miralax)	221147
turmeric (Curcumin, Turmeric Root)	1114883
ubidecarenone (Co Q-10)	21406
vitamin E (Alpha E, Aquasol-E, Aquavite-E, Centrum Singles)	11256

For each medication, find and select the appropriate check box. If a reported drug is not on the list, enter the medication name on one of the lines listed as "Specify" at the end of the form. For all medications specified at the end of the Form, associated RXnorm codes must also be recorded. The RXnorm codes may be determined by using the RXNav tool located at ***https://lhncbc.nlm.nih.gov/RxNav/.*** In the rare case in which an RXCUI is not available in the RXNorm database, enter 0 for the RXCUI.

If a medication is not listed above:

Specify the drug or brand name and determine its RXNorm code by using the RXNav: https://lhncbc.nlm.nih.gov/RxNav/

☐ **SPECIFY:** _____ _____

☐ **SPECIFY:** _____ _____

☐ **SPECIFY:** _____ _____

☐ **SPECIFY:** _____ _____

☐ **SPECIFY:** _____ _____

Coding Guidebook for **Form A4a:** ADRD–Specific Treatments

***INSTRUCTIONS**: This form should be used to record treatments expected to significantly impact Alzheimer disease and related dementias (ADRD) biomarkers, whether a disease-modifying treatment that is FDA-approved for ADRD and received as part of clinical care or an investigational treatment received as part of a clinical trial. For treatments received as part of clinical care, only those that are FDA-approved for disease-modification of ADRD should be included on this form. If the participant is receiving one of these treatments as part of their clinical care at the time of clinical assessment (e.g., they are receiving lecanemab infusions), the treatment should be included on both this form and the A4 Medication form. Participation in any ADRD drug trial over an individual's lifetime should be included. If available, the ClinicalTrials.gov identifier should be entered into the "specific treatment and/or trial" cell. Information on the type of treatment can be found via ClinicalTrials.gov and is summarized in* "Alzheimer's disease drug development pipeline." [1] *This form should be completed by the clinician based on participant interview and/or co-participant report. Check only <u>one</u> box per question, unless otherwise stated.*

IVP **FVP**

Record all current and previous FDA-approved treatment(s) for disease-modification of ADRD (e.g., anti-amyloid antibodies) and/or trial(s) for investigational ADRD treatments. Review and update all information at each visit. For example, if a participant was in a trial and was blinded as to their treatment status on visit date 1, enter **Unknown** clinical trial group. If, at visit 2, the participant has entered an Open Label Extension and learned that they were in the placebo group, enter **Placebo** for the group on the first row, and **Active treatment** for the group on the second row, with appropriate start and end dates.

1. **1.** Has the participant ever been prescribed a treatment or been enrolled in a clinical trial of a treatment expected to modify ADRD biomarkers?

☐ 0 No **(END FORM HERE)**
☐ 1 Yes
☐ 9 Unknown **(END FORM HERE)**

N/A **1a.** Since the last UDS visit, is new information available concerning any of the participant's prescribed treatments or clinical trial(s) of a treatment expected to modify ADRD biomarkers?

☐ 0 No **(END FORM HERE)**
☐ 1 Yes
☐ 9 Unknown **(END FORM HERE)**

2. **2.** Please provide information about the clinical treatment(s) and/or trial(s)
(If participant is exposed to more than two treatments and/or trials, use extended table on Page 2):

Primary Drug Target *(check all that apply)*	**Specific treatment and/ or trial**	**Start date** *(99/9999 =Unknown)*	**End date** *(month/year) (99/9999=Unknown; 88/8888=Ongoing)*	**How was the treatment provided?**	**If clinical trial, in which group was the participant?**
☐ 1 Amyloid beta ☐ 1 Tau ☐ 1 Inflammation ☐ 1 Synaptic plasticity/ neuroprotection ☐ 1 Other target(s) _____	_____ *NCT–*_____			☐ 1 Clinical care ☐ 2 Clinical trial ☐ 3 Clinical care and clinical trial	☐ 1 Active treatment ☐ 2 Placebo ☐ 9 Unknown

Primary drug target: To find the <u>primary drug target, see the "mechanism of action"</u> in Table 2 from "Alzheimer's disease drug development pipeline: 2024" by Cummings.

Specific treatment and/or trial: See link above, use "Clinical trial NCT# from Table 2 or the clinicaltrials.gov website. If NCT is unknown, leave blank.

Start date: The first date that the drug was ever given (approximate month and year). If unknown, enter 99/9999.

End date: The last date that the drug was given; if currently on the treatment, enter 88/8888. If unknown, enter 99/9999.

How the treatment was provided? Clinical care is a treatment prescribed by a clinician for the patient's benefit; a clinical trial is registered and for research purposes.

If clinical trial, in which group was the participant? If the participant does not know whether they received the active treatment or placebo as part of a clinical trial, select **9=Unknown**.

[1] Cummings et al., "Alzheimer's disease drug development pipeline: 2024," Alzheimer's and Dementia. 2024 April 24; 10(2):e12465.

IVP	FVP			
3.	3.	Has the participant ever experienced amyloid related imaging abnormalities–edema (ARIA-E), amyloid related imaging abnormalities–hemorrhage (ARIA-H), or other major adverse events associated with treatments expected to modify ADRD biomarkers?		☐ 0 No **(END FORM HERE)** ☐ 1 Yes ☐ 9 Unknown **(END FORM HERE)**
N/A	3a.	Since the last UDS visit, is new information available concerning the participant's experience of amyloid related imaging abnormalities–edema (ARIA-E), amyloid related imaging abnormalities–hemorrhage (ARIA-H), or other major adverse events associated with treatments expected to modify ADRD biomarkers?		☐ 0 No **(END FORM HERE)** ☐ 1 Yes ☐ 9 Unknown **(END FORM HERE)**

Please include any ARIA-E or ARIA-H, regardless of symptoms or severity.

3a.	3b.			
		What major adverse events associated with treatments expected to modify ADRD biomarkers did they experience? *(check all that apply)*	**1.** ☐ 1 Amyloid related imaging abnormalities–edema (ARIA-E) **2.** ☐ 1 Amyloid related imaging abnormalities–hemorrhage (ARIA-H)	**3.** ☐ 1 Other issues _____ _____

Examples of major adverse events include ARIA-E, ARIA-H, cardiac rhythm abnormalities, liver dysfunction, hypotension, blood clots, kidney failure, severe skin rash, vision or ocular problems, and falls. These issues should be directly related to the treatments.

2. 2. Please provide information about the clinical treatment(s) and/or trial(s)
(continued from Page 1):

Primary Drug Target *(check all that apply)*	**Specific treatment and/ or trial**	**Start date** *(99/9999 =Unknown)*	**End date** *(month/year) (99/9999=Unknown; 88/8888=Ongoing)*	**How was the treatment provided?**	**If clinical trial, in which group was the participant?**
☐ 1 Amyloid beta ☐ 1 Tau ☐ 1 Inflammation ☐ 1 Synaptic plasticity/ neuroprotection ☐ 1 Other target(s) _____	_____ *NCT–*_____			☐ 1 Clinical care ☐ 2 Clinical trial ☐ 3 Clinical care and clinical trial	☐ 1 Active treatment ☐ 2 Placebo ☐ 9 Unknown
☐ 1 Amyloid beta ☐ 1 Tau ☐ 1 Inflammation ☐ 1 Synaptic plasticity/ neuroprotection ☐ 1 Other target(s) _____	_____ *NCT–*_____			☐ 1 Clinical care ☐ 2 Clinical trial ☐ 3 Clinical care and clinical trial	☐ 1 Active treatment ☐ 2 Placebo ☐ 9 Unknown
☐ 1 Amyloid beta ☐ 1 Tau ☐ 1 Inflammation ☐ 1 Synaptic plasticity/ neuroprotection ☐ 1 Other target(s) _____	_____ *NCT–*_____			☐ 1 Clinical care ☐ 2 Clinical trial ☐ 3 Clinical care and clinical trial	☐ 1 Active treatment ☐ 2 Placebo ☐ 9 Unknown

IVP FVP

☐ 1 Amyloid beta ☐ 1 Tau ☐ 1 Inflammation ☐ 1 Synaptic plasticity/ neuroprotection ☐ 1 Other target(s) _____	_____ *NCT–*_____			☐ 1 Clinical care ☐ 2 Clinical trial ☐ 3 Clinical care and clinical trial	☐ 1 Active treatment ☐ 2 Placebo ☐ 9 Unknown
☐ 1 Amyloid beta ☐ 1 Tau ☐ 1 Inflammation ☐ 1 Synaptic plasticity/ neuroprotection ☐ 1 Other target(s) _____	_____ *NCT–*_____			☐ 1 Clinical care ☐ 2 Clinical trial ☐ 3 Clinical care and clinical trial	☐ 1 Active treatment ☐ 2 Placebo ☐ 9 Unknown
☐ 1 Amyloid beta ☐ 1 Tau ☐ 1 Inflammation ☐ 1 Synaptic plasticity/ neuroprotection ☐ 1 Other target(s) _____	_____ *NCT–*_____			☐ 1 Clinical care ☐ 2 Clinical trial ☐ 3 Clinical care and clinical trial	☐ 1 Active treatment ☐ 2 Placebo ☐ 9 Unknown
☐ 1 Amyloid beta ☐ 1 Tau ☐ 1 Inflammation ☐ 1 Synaptic plasticity/ neuroprotection ☐ 1 Other target(s) _____	_____ *NCT–*_____			☐ 1 Clinical care ☐ 2 Clinical trial ☐ 3 Clinical care and clinical trial	☐ 1 Active treatment ☐ 2 Placebo ☐ 9 Unknown

Coding Guidebook for **Form A5-D2:** Participant Health History / Clinician-assessed Medical Conditions

***INSTRUCTIONS**: This form is to be completed by the clinician or ADRC staff based on the medical history interview with the participant and co–participant, as well as review of any medical records that are available. Any conditions identified during the visit should be included on the form. Check only <u>one</u> box per question, unless otherwise stated.*

IVP | FVP — Section 1 – Cigarette smoking, alcohol, and substance use

Cigarette smoking

Questions 1a to 1e should be coded based on cigarette smoking only, not cigar, pipe, vape (tobacco), or chewing tobacco.

1a. / 1a. Has the participant smoked <u>more than</u> 100 cigarettes in their life —
(IF NO OR UNKNOWN,SKIP TO QUESTION 1f)
☐ 0 No ☐ 1 Yes ☐ 9 UNK

1b. / 1b. Total years smoked **(777=years provided at previous UDS visit, 999 = Unknown)** ___ ___ ___

If the exact number of years smoked is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown**.

1c. / 1c. Average number of packs smoked per day:
☐ 1 1 cigarette to less than ½ pack
☐ 2 ½ pack to less than 1 pack
☐ 3 1 pack to less than 1½ packs
☐ 4 1½ packs to less than 2 packs
☐ 5 2 packs or more
☐ 9 Unknown

1d. / 1d. Has the participant smoked within <u>the last 30 days</u>?
☐ 0 No ☐ 1 Yes ☐ 9 UNK

1e. / 1e. If the participant quit smoking, specify the age at which they last smoked *(i.e., quit)*
(777 = age provided at previous UDS visit, 888 = N/A, 999 = unknown) ___ ___ ___

If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown**. If they still smoke, enter **888=N/A**.

Alcohol use

1f. / 1f. In the past 12 months, how often has the participant had a drink containing alcohol?
(IF NEVER OR UNKNOWN, SKIP TO QUESTION 1i)
☐ 0 Never
☐ 1 Monthly or less
☐ 2 2-4 times a month
☐ 3 2-3 times a week
☐ 4 4 or more times a week
☐ 9 Unknown

This may be a drink containing any amount of alcohol, including less than the amount in the standard drink defined in Question 1g.

1g. / 1g. On a day when the participant drinks alcoholic beverages, how many standard drinks does the participant typically consume? *(**Standard drink:** 12oz of regular beer, 5oz of wine, 1.5oz of distilled spirits)*
☐ 1 1 or 2
☐ 2 3 to 4
☐ 3 5 to 6
☐ 4 7 to 9
☐ 5 10 or more
☐ 9 Unknown

1h. / 1h. In the past 12 months, how often did the participant have six or more drinks containing alcohol in one day?
☐ 0 Never
☐ 1 Less than once a month
☐ 2 Monthly
☐ 3 Weekly
☐ 4 Daily or almost daily
☐ 9 Unknown

Question 1h refers to "six or more standard drinks containing alcohol in one day."

Substance use

1i. / 1i. Has the participant used substances including prescription or recreational drugs that caused significant impairment in one or more of the following areas: work, driving, legal, social, or others.

Question 1i is meant to capture substance use that caused significant impairment (not to simply capture any substance use that did not cause significant impairment). Include alcohol use that caused significant impairment.

1i1. / 1i1. Within the past 12 months ☐ 0 No ☐ 1 Yes ☐ 9 UNK

1i2. / 1i2. Prior to 12 months ago ☐ 0 No ☐ 1 Yes ☐ 9 UNK

IVP	FVP	Section 1 – Cigarette smoking, alcohol, and substance use	*continued...*

1j.	1j.	In the past 12 months, how often has the participant consumed cannabis *(edibles, smoked, or vaporized)?*	☐0 Never ☐1 Monthly or less ☐2 2-4 times a week	☐3 2-3 times a week ☐4 4 or more times a week ☐9 Unknown

Question 1j should be answered based on any cannabis consumption independent of whether it caused significant impairment. Any cannabis derivatives (e.g., CBD, THC) should be included.

In the following sections *(pages 2-7)* record the presence or absence of a **history of these conditions**, as determined by the clinician's best judgment following the medical history interview with the participant and co-participant, as well as review of any medical records that are available.

A CONDITION SHOULD BE CONSIDERED ...

Absent:	Recent/Active:	Remote/Inactive:	Unknown (UNK)
It has never been present.	It happened within the last year or still requires active management.	It existed or occurred in the past *(more than one year ago)* but was resolved or there is no treatment currently under way.	There is insufficient information available to assess this condition.

Section 2 – Cardiovascular disease

			ABSENT	RECENT/ACTIVE	REMOTE/ INACTIVE	UNKNOWN
2a.	2a.	Heart attack *(heart artery blockage)* — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 2b)**	☐0	☐1	☐2	☐9

Myocardial infarction including STEMI (ST elevation myocardial infarction) and NSTEMI (non-ST elevation myocardial infarction). If myocardial infarction led to cardiac arrest, code both 2a and 2b. If myocardial infarction (troponin leak) was solely the consequence of cardiac arrest, code only 2b.

2a1.	2a1.	More than one heart attack?	☐0 No	☐1 Yes	☐9 UNK
2a2.	2a2.	Age at most recent heart attack **(777 = age provided at previous UDS visit, 999 = Unknown)**	___ ___ ___		

If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 2a2.

2b.	2b.	Cardiac arrest (heart stopped) — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 2c)**	☐0	☐1	☐2	☐9

This refers to clinical cardiac arrest not asymptomatic pauses, bradycardia, or heart block.

2b1.	2b1.	Age at most recent cardiac arrest **(777 = age provided at previous UDS visit, 999 = Unknown)**	___ ___ ___

If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 2b1.

2c.	2c.	Atrial fibrillation	☐0	☐1	☐2	☐9

Paroxysmal or chronic atrial fibrillation, including rate or rhythm-controlled.

2d.	2d.	Coronary artery angioplasty / endarterectomy / stenting	☐0	☐1	☐2	☐9

This does not include diagnostic coronary angiography without intervention.

2e.	2e.	Coronary artery bypass procedure — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 2f)**	☐0	☐1	☐2	☐9

2e1.	2e1.	Age at most recent surgery **(777 = age provided at previous UDS visit, 999 = Unknown)**	___ ___ ___

If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 2e1.

IVP	FVP	Section 2 – Cardiovascular disease *continued...*				
2f.	2f.	Pacemaker and/or defibrillator implantation — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 2g)**	☐0	☐1	☐2	☐9
2f1.	2f1.	Age at first implantation **(777 = age provided at previous UDS visit, 999 = Unknown)**	___ ___ ___			
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 2f1.				
2g.	2g.	Congestive heart failure (including pulmonary edema)	☐0	☐1	☐2	☐9
		American College of Cardiology (ACC) and American Heart Association (AHA) stage B, C, and D. Code left-sided, right-sided, and high-output heart failure.				
2h.	2h.	Heart valve replacement or repair — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 2i)**	☐0	☐1	☐2	☐9
2h1.	2h1.	Age at most recent procedure **(777 = age provided at previous UDS visit, 999 = Unknown)**	___ ___ ___			
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 2h1.				
2i.	2i.	Other cardiovascular disease **(SPECIFY):** _____	☐0	☐1	☐2	☐9
		Ask whether the participant has any cardiovascular disease other than those listed in Questions 2a-2h. If no, select **0=Absent**. If yes, record the condition in the space provided and select the appropriate box to specify whether **1=Recent/active** or **2=Remote/inactive.**				

Section 3 – Cerebrovascular disease

			ABSENT	RECENT/ACTIVE	REMOTE/ INACTIVE	UNKNOWN
3a.	3a.	Stroke by history, not exam (*imaging is not required*) — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 3b)**	☐0	☐1	☐2	☐9
		This question is focused on reported history of stroke. Include stroke reported during the interview with the participant and/or co-participant and/or medical record review. Imaging evidence of a stroke or evidence from a physical exam are not required as this question is focused on reported history. Include ischemic and hemorrhagic stroke.				
3a1.	3a1.	More than one stroke?		☐0 No	☐1 Yes	☐9 UNK
3a2.	3a2.	Age at most recent stroke **(777 = age provided at previous UDS visit, 999 = Unknown)**			___ ___ ___	
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 3a2.				

			NEVER IMPROVED	PARTIALLY IMPROVED	IMPROVED / BACK TO NORMAL	UNKNOWN
3a3.	3a3.	What is the status of stroke symptoms?	☐0	☐1	☐2	☐9
3a4.	3a4.	Carotid artery surgery or stenting? **(IF NO OR UNKNOWN, SKIP TO QUESTION 3b)**		☐0 No	☐1 Yes	☐9 UNK
3a5.	3a5.	Age at most recent carotid artery surgery or stenting **(777 = age provided at previous UDS visit, 999 = Unknown)**			___ ___ ___	
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 3a5.				

IVP	FVP		ABSENT	RECENT/ACTIVE	REMOTE/ INACTIVE	UNKNOWN
3b.	3b.	Transient ischemic attack (TIA) — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 4a)**	☐0	☐1	☐2	☐9
		Do not code transient global amnesia here. Code convincing (by history and/or medical record review) TIAs with typical TIA symptoms (such as aphasia, unilateral weakness or numbness, incoordination, amarousis fugax) and duration (less than 24 hours). Be aware that it is common for participants or co-participants to self-diagnose TIAs based on vague symptoms that are solely cognitive or non-focal neurologically, which the clinician may not necessarily code here as TIAs.				
3b1.	3b1.	Age at most recent TIA **(777 = age provided at previous UDS visit, 999 = Unknown)** ___ ___ ___				
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 3b1.				

Section 4 – Neurologic conditions

			ABSENT	RECENT/ACTIVE	REMOTE/ INACTIVE	UNKNOWN
4a.	4a.	Parkinson's disease (PD) — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 4b)**	☐0	☐1		☐9
		Parkinson's disease, sporadic or genetic. Do not include with parkinsonism who do not meet the criteria for Parkinson's disease. See 4b.				
4a1.	4a1.	Age at estimated PD symptom onset **(777 = age provided at previous UDS visit, 999 = Unknown)** ___ ___ ___				
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 4a1.				
4b.	4b.	Other parkinsonism disorder *(e.g., DLB)* — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 4c)**	☐0	☐1		☐9
		Include Dementia with Lewy Bodies, vascular parkinsonism, drug-induced parkinsonism, other secondary parkinsonism, progressive supranuclear palsy, multiple system atrophy.				
4b1.	4b1.	Age at parkinsonism disorder diagnosis **(777 = age provided at previous UDS visit, 999 = Unknown)** ___ ___ ___				
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 4b1.				
4c.	4c.	Epilepsy and/or history of seizures (excluding childhood febrile seizures) — **(IF REMOTE/INACTIVE, SKIP TO QUESTION 4c2, IF ABSENT OR UNKNOWN, SKIP TO QUESTION 4d)**	☐0	☐1	☐2	☐9
4c1.	4c1.	Age at first seizure (excluding childhood febrile seizures) **(777 = age provided at previous UDS visit, 999 = Unknown)** ___ ___ ___				
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 4c1.				
4c2.	4c2.	How many seizures has the participant had in the past 12 months? ☐0 None ☐1 1 or 2 ☐2 3 or more ☐9 Unknown				
4d.	4d.	Chronic headaches	☐0	☐1	☐2	☐9
		International Headache Society definition of chronic headaches: 15 or more headache episodes per month for at least 3 months.				
4e.	4e.	Multiple sclerosis	☐0	☐1	☐2	☐9
4f.	4f.	Normal–pressure hydrocephalus	☐0	☐1	☐2	☐9
		Participants should meet clinical criteria for NPH as well as radiologic evidence for NPH.				

IVP	FVP	Section 4 – Neurologic conditions *continued...*
4g.	4g.	Repetitive head impacts (e.g. from contact sports, intimate partner violence, or military duty), regardless of whether it caused symptoms. ☐ 0 No ☐ 1 Yes ☐ 9 UNK **(IF NO OR UNKNOWN, SKIP TO QUESTION 4h)**
		If the participant played a contact sport or served in the military but did not have known or suspected repetitive head impacts, code "no." Include military blast exposure.
4g1.	4g1.	Indicate the source(s) of exposure for repeated hits to the head: *(Check all that apply)* **4g1a.** ☐ 1 American football **4g1b.** ☐ 1 Soccer **4g1c.** ☐ 1 Ice hockey **4g1d.** ☐ 1 Boxing or mixed martial arts **4g1e.** ☐ 1 Other contact sport **4g1f.** ☐ 1 Intimate partner violence **4g1g.** ☐ 1 Military service **4g1h.** ☐ 1 Physical assault **4g1i.** ☐ 1 Other **(SPECIFY):** _____
4g2.	4g2.	Indicate the total length of time in years that the participant was exposed to repeated hits to the head *(e.g. playing American football for 7 years)* **(777 = years provided at previous UDS visit, 999 = Unknown)** ___ ___ ___
		If the exact length of time is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 4g2.
4h.	4h.	Head injury *(e.g. in a vehicle accident, being hit by an object, in a fall, while playing sports or biking, in an assault, or during military service)* that resulted in a period of feeling "dazed or confused," being unable to recall details of the injury, or loss of consciousness *(if multiple head injuries, consider most severe episode)*. ☐ 0 No ☐ 1 Yes ☐ 9 UNK **(IF NO OR UNKNOWN, SKIP TO QUESTION 5a)**
4h1.	4h1.	After a head injury, what was the longest period of time that the participant was unconscious? ☐ 0 Less than 5 minutes ☐ 1 5 minutes to less than 30 minutes ☐ 2 30 minutes to less than 24 hours ☐ 3 1 day to less than 7 days ☐ 4 7 days or more ☐ 8 Not applicable, no loss of consciousness ☐ 9 Unknown duration
4h2.	4h2.	After a head injury, what was the longest period that the participant was *"dazed or confused"* or unable to recall details of the injury? ☐ 0 Less than 5 minutes ☐ 1 5 minutes to less than 30 minutes ☐ 2 30 minutes to less than 24 hours ☐ 3 1 day to less than 7 days ☐ 4 7 days or more ☐ 8 Not applicable, never dazed and confused ☐ 9 Unknown duration
4h3.	4h3.	Total number of head injuries in which the participant felt "dazed or confused", unable to recall details of the injury or experienced loss of consciousness? ☐ 0 None ☐ 1 1-2 ☐ 2 3-5 ☐ 3 6-12 ☐ 4 13 or more ☐ 9 Unknown
4h4.	4h4.	Age of <u>first</u> head injury that resulted in a period of feeling *"dazed or confused,"* being unable to recall details of the injury, or loss of consciousness: **(777 = age provided at previous UDS visit, 999 = Unknown)** ___ ___ ___
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 4h4.
4h5.	4h5.	Age of <u>most recent</u> head injury that resulted in a period of feeling *"dazed or confused,"* being unable to recall details of the injury, or loss of consciousness: **(777 = age provided at previous UDS visit, 999 = Unknown)** ___ ___ ___
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 4h5. If only one head injury, enter the same age for 4h4 and 4h5.

IVP FVP Section 5 – Medical conditions

If any of the conditions still require active management and/or medications, please select "**Recent / Active**."

			ABSENT	RECENT/ACTIVE	REMOTE/ INACTIVE	UNKNOWN
5a.	5a.	Diabetes — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 5b)**	☐ 0	☐ 1	☐ 2	☐ 9
5a1.	5a1.	Which type?	☐ 1 Type 1 ☐ 2 Type 2 ☐ 3 Other *(diabetes insipidus, latent autoimmune diabetes/type 1.5, gestational diabetes, prediabetes)* ☐ 9 Unknown			
		Code prediabetes as **3=Other**.				
5a2.	5a2.	Treated with *(Check all that apply)*	**5a2a.** ☐ 1 Insulin **5a2b.** ☐ 1 Oral medications **5a2c.** ☐ 1 GLP-1 receptor agonist **5a2d.** ☐ 1 Other non-insulin, non-GLP-1 receptor agonist injection **5a2e.** ☐ 1 Diet **5a2f.** ☐ 1 Unknown			
		GLP-1 receptor agonist (injection or oral) such as semaglutide (Ozempic).				
5a3.	5a3.	Age at diabetes diagnosis **(777 = age provided at previous UDS visit, 999 = Unknown)**	___ ___ ___			
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 5a3.				
5b.	5b.	Hypertension *(or taking medication for hypertension)* — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 5c)**	☐ 0	☐ 1	☐ 2	☐ 9
5b1.	5b1.	Age at hypertension diagnosis **(777 = age provided at previous UDS visit, 999 = Unknown)**	___ ___ ___			
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 5b1.				
5c.	5c.	Hypercholesterolemia *(or taking medication for high cholesterol)* — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 5d)**	☐ 0	☐ 1	☐ 2	☐ 9
5c1.	5c1.	Age at hypercholesterolemia diagnosis **(777 = age provided at previous UDS visit, 999 = Unknown)**	___ ___ ___			
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 5c1.				
5d.	5d.	B12 deficiency	☐ 0	☐ 1	☐ 2	☐ 9
5e.	5e.	Thyroid disease	☐ 0	☐ 1	☐ 2	☐ 9
		Code conditions that cause abnormalities in thyroid hormones. This would include hyperthyroidism such as Graves' disease or hypothyroidism such as Hashimoto's thyroiditis.				
5f.	5f.	Arthritis — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 5g)**	☐ 0	☐ 1	☐ 2	☐ 9
5f1.	5f1.	Type of arthritis *(Check all that apply)*	**5f1a.** ☐ 1 Rheumatoid **5f1b.** ☐ 1 Osteoarthritis **5f1c.** ☐ 1 Other **(SPECIFY):** _____ **5f1d.** ☐ 1 Unknown			
		Examples of other arthritis: gout, psoriatic, traumatic.				
5f2.	5f2.	Regions affected *(Check all that apply)*	**5f2a.** ☐ 1 Upper extremity **5f2b.** ☐ 1 Lower extremity **5f2c.** ☐ 1 Spine **5f2d.** ☐ 1 Unknown			
		Indicate all regions that are affected by arthritis.				

			ABSENT	RECENT/ACTIVE	REMOTE/ INACTIVE	UNKNOWN
5g.	5g.	Incontinence — urinary *(occurring at least weekly)*	☐ 0	☐ 1	☐ 2	☐ 9
5h.	5h.	Incontinence — bowel *(occurring at least weekly)*	☐ 0	☐ 1	☐ 2	☐ 9
5i.	5i.	Sleep apnea — **(IF ABSENT, REMOTE/INACTIVE, OR UNKNOWN, SKIP TO QUESTION 5j)**	☐ 0	☐ 1	☐ 2	☐ 9
5i1.	5i1.	Typical use of breathing machine *(e.g. CPAP)* at night over the past 12 months	☐ 0 None ☐ 1 < 4 hours per night ☐ 2 > 4 hours per night ☐ 9 Unknown			
5i2.	5i2.	Typical use of an oral device or implanted breathing pacemaker for sleep apnea at night over the past 12 months	☐ 0 None ☐ 1 < 4 hours per night ☐ 2 > 4 hours per night ☐ 9 Unknown			
5j.	5j.	REM sleep behavior disorder (RBD)	☐ 0	☐ 1	☐ 2	☐ 9
		Convincing clinical diagnosis is sufficient to code, does not require polysomnogram evidence.				
5k.	5k.	Hyposomnia/Insomnia *(occurring at least weekly or requiring medication)*	☐ 0	☐ 1	☐ 2	☐ 9
5l.	5l.	Other sleep disorder **(SPECIFY):** _____	☐ 0	☐ 1	☐ 2	☐ 9
		Ask whether the participant has any sleep disorder other than those listed in Questions 5i–5k. If no, select **0=Absent**. If yes, record the condition in the space provided and select the appropriate box to specify whether **1=Recent/active** or **2=Remote/inactive.**				
5m.	5m.	Cancer, primary or metastatic — *(Exclude non-melanoma skin cancer. If multiple cancer diagnoses, report most recent diagnosis.* **IF ABSENT OR UNKNOWN, SKIP TO QUESTION 5n)**	☐ 0	☐ 1	☐ 2	☐ 9
		If there is history of more than one diagnosis of cancer (different origins), and one diagnosis is within the past year, and one diagnosis is more than one year ago, code only **1=Recent/Active**.				
5m1.	5m1.	Type of cancer	**5m1a.** ☐ 1 Primary/non-metastatic **5m1b.** ☐ 1 Metastatic **(CHECK ALL THAT APPLY)** **5m1b1.** ☐ 1 Metastatic to brain **5m1b2.** ☐ 1 Metastatic to sites other than brain **5m1c.** ☐ 1 Unknown			
		If the clinician has sufficient evidence of the participant having recent/active cancer is the last 12 months, select Primary/non-metastatic and/or Metastatic and specify the primary site(s) where the cancer started in Question 5m2. If results are pending to determine whether the cancer is metastatic, select Primary/non-metastatic and revise to Metastatic at a later date if it is found to be metastatic around the time of this UDS visit. If a participant has more than one diagnosis of cancer, code all diagnoses here and in the following questions.				
5m2.	5m2.	Primary site of cancer: *(Check all that apply)*	**5m2a.** ☐ 1 Blood **5m2b.** ☐ 1 Breast **5m2c.** ☐ 1 Colon **5m2d.** ☐ 1 Lung **5m2e.** ☐ 1 Prostate **5m2f.** ☐ 1 Other **(SPECIFY):** _____			
5m3.	5m3.	Type of cancer treatment *(Check all that apply)*	**5m3a.** ☐ 1 Radiation **5m3b.** ☐ 1 Surgical Resection **5m3c.** ☐ 1 Immunotherapy **5m3d.** ☐ 1 Bone marrow transplant **5m3e.** ☐ 1 Chemotherapy **5m3f.** ☐ 1 Hormone therapy **5m3g.** ☐ 1 Other **(SPECIFY):** _____			

IVP	FVP	Section 5 – Medical conditions *continued...*				
5m4.	5m4.	Age at most recent cancer diagnosis **(777 = age provided at previous UDS visit, 999 = Unknown)** ___ ___ ___				
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 5m4.				
			ABSENT	**RECENT/ACTIVE**	**REMOTE/ INACTIVE**	**UNKNOWN**
5n.	5n.	COVID-19 infection — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 5o)**	☐0	☐1	☐2	☐9
5n1.	5n1.	Requiring hospitalization?		☐0 No	☐1 Yes	☐9 UNK
5o.	5o.	Asthma/COPD/pulmonary disease	☐0	☐1	☐2	☐9
5p.	5p.	Chronic kidney disease — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 5q)**	☐0	☐1	☐2	☐9
		National Kidney Foundation Stage 1-5.				
5p1.	5p1.	Age at diagnosis **(777 = age provided at previous UDS visit, 999 = Unknown)** ___ ___ ___				
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 5p1.				
5q.	5q.	Liver disease — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 5r)**	☐0	☐1	☐2	☐9
5q1.	5q1.	Age at diagnosis **(777 = age provided at previous UDS visit, 999 = Unknown)** ___ ___ ___				
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 5q1.				
5r.	5r.	Peripheral vascular disease — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 5s)**	☐0	☐1	☐2	☐9
5r1.	5r1.	Age at diagnosis **(777 = age provided at previous UDS visit, 999 = Unknown)** ___ ___ ___				
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 5r1.				
5s.	5s.	Human Immunodeficiency Virus (HIV) — **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 5t)**	☐0	☐1	☐2	☐9
5s1.	5s1.	Age at diagnosis **(777 = age provided at previous UDS visit, 999 = Unknown)** ___ ___ ___				
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 5s1.				
5t.	5t.	Other medical conditions or procedures **(SPECIFY):** _____	☐0	☐1	☐2	☐9
		Ask whether the participant has any medical condition or procedure other than those listed in Questions 5m–5s. If no, select **0=Absent**. If yes, record the condition in the space provided and select the appropriate box to specify whether **1=Recent/active** or **2=Remote/inactive.** It is left to the discretion of the investigator to report other potentially important medical conditions or procedures.				

IVP FVP Section 6 – Psychiatric conditions

*In order to diagnose a disorder, **DSM-5-TR criteria require** that symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

			ABSENT	RECENT/ACTIVE	REMOTE/ INACTIVE	UNKNOWN
6a.	6a.	Depressive disorder				
6a1.	6a1.	Major depressive disorder (DSM-5-TR criteria*)	☐ 0	☐ 1	☐ 2	☐ 9
6a2.	6a2.	Other specified depressive disorder (DSM-5-TR criteria*)	☐ 0	☐ 1	☐ 2	☐ 9

Examples of other specified depressive disorders include: persistent depressive disorder (previously known as dysthymia), premenstrual dysphoric disorder (PMDD), substance/medication-induced depressive disorder, and depressive disorder due to another medical condition.

6a3.	6a3.	**If Recent/Active depressive disorder (Q6a1 or Q6a2),** choose if treated or untreated.	☐ 0 Untreated ☐ 1 Treated with medication and/or counseling

May also code treatement with electroconvulsive therapy or transcranial magnetic stimulation as **1=Treated**. Do **not** code self-treatment with vitamins, herbs, supplements, recreational drugs, or alcohol as **1=Treated**.

			ABSENT	RECENT/ACTIVE	REMOTE/ INACTIVE	UNKNOWN
6b.	6b.	Bipolar disorder (DSM-5-TR criteria*)	☐ 0	☐ 1	☐ 2	☐ 9
6c.	6c.	Schizophrenia or other psychosis disorder (DSM-5-TR criteria*)	☐ 0	☐ 1	☐ 2	☐ 9
6d.	6d.	Anxiety disorder (DSM-5-TR criteria*) **(IF ABSENT OR UNKNOWN, SKIP TO QUESTION 6e)**	☐ 0	☐ 1	☐ 2	☐ 9

Anxiety disorder should only be selected if DSM-5-TR criteria are met. See criteria for specific anxiety disorders below.

6d1.	6d1.	Generalized Anxiety Disorder	☐ 0	☐ 1	☐ 2	☐ 9
6d2.	6d2.	Panic Disorder	☐ 0	☐ 1	☐ 2	☐ 9
6d3.	6d3.	Obsessive–compulsive disorder (OCD)	☐ 0	☐ 1	☐ 2	☐ 9
6d4.	6d4.	Other **(SPECIFY):** _____	☐ 0	☐ 1	☐ 2	☐ 9

Ask whether the participant has any anxiety disorder other than those listed in Questions 6d1–6d3. If no, select **0=Absent**. If yes, record the condition in the space provided and select the appropriate box to specify whether **1=Recent/active** or **2=Remote/ inactive.**

6e.	6e.	Post-traumatic stress disorder (PTSD) (DSM-5-TR criteria*)	☐ 0	☐ 1	☐ 2	☐ 9
6f.	6f.	Developmental neuropsychiatric disorders *(e.g., autism spectrum disorder [ASD], attention-deficit hyperactivity disorder [ADHD], dyslexia)*	☐ 0	☐ 1	☐ 2	☐ 9

Down syndrome is appropriate to code here if associated with a developmental neuropsychiatric disorder.

6g.	6g.	Other psychiatric disorders **(SPECIFY):** _____	☐ 0	☐ 1	☐ 2	☐ 9

Ask whether the participant has any psychiatric disorder other than those listed in Questions 6a–6f. If no, select **0=Absent**. If yes, record the condition in the space provided and select the appropriate box to specify whether **1=Recent/active** or **2=Remote/ inactive.**

Section 7 – Menstrual and reproductive health

If questions about menstrual and reproductive health are relevant to this participant, continue to question 7a. Otherwise, **END FORM HERE**.

7a.	N.A.	How old was the participant when they had their first menstrual period? **(888 = Never had a menstrual period, 999 = Unknown) — (IF NEVER HAD A MENSTRUAL PERIOD, SKIP TO 7d)**	___ ___ ___

If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 7a.

IVP	FVP	Section 7 – Menstrual and reproductive health *continued...*
7b.	7a.	How old was the participant when they had their last menstrual period? **(777 = age provided at previous UDS visit, 888 = Still menstruating, 999 = Unknown) —** **(IF STILL MENSTRUATING, SKIP TO QUESTION 7d)** ___ ___ ___
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 7b.
7c.	7b.	If the participant has stopped having menstrual periods, please indicate the reason. *(Check all that apply)* **1.** ☐ 1 Natural menopause **2.** ☐ 1 Hysterectomy (surgical removal of uterus) **3.** ☐ 1 Surgical removal of both ovaries **4.** ☐ 1 Chemotherapy for cancer or another condition **5.** ☐ 1 Radiation treatment or other damage/injury to reproductive organs **6.** ☐ 1 Hormonal supplements (e.g. the Pill, injections, Mirena, HRT) **7.** ☐ 1 Anti-estrogen medication such as Tamoxifen, anostrozole (Arimidex), exemestane (Aromasin), or letrozole (Femara) **8.** ☐ 1 Unsure **9.** ☐ 1 Other **(SPECIFY):** _____
7d.	7c.	Has the participant taken female hormone replacement pills or patches (e.g. estrogen)? **(IF NO OR UNKNOWN, SKIP TO QUESTION 7e)** ☐ 0 No ☐ 1 Yes ☐ 9 UNK
		Do not include topical or intravaginal hormone gel or cream.
7d1.	7c1.	How many years in total? **(777 = years provided at previous UDS visit, 999 = Unknown)** ___ ___ ___
		If the exact number of years is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 7d1.
7d2.	7c2.	Age at first use **(777 = age provided at previous UDS visit, 999 = Unknown)** ___ ___ ___
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 7d2.
7d3.	7c3.	Age at last use **(777 = age provided at last UDS visit, 888= Still presently using, 999 = Unknown)** ___ ___ ___
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 7d3.
7e.	7d.	Has the participant ever taken birth control pills? **(IF NO OR UNKNOWN, END FORM HERE)** ☐ 0 No ☐ 1 Yes ☐ 9 UNK
7e1.	7d1.	How many years in total? **(777 = years provided at previous UDS visit, 999 = Unknown)** ___ ___ ___
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 7e1.
7e2.	7d2.	Age at first use **(777 = age provided at previous UDS visit, 999 = Unknown)** ___ ___ ___
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 7e2.
7e3.	7d3.	Age at last use **(777 = age provided at previous UDS visit, 888= Still presently using, 999 = Unknown)** ___ ___ ___
		If the exact age is unknown, ask the participant and/or co-participant to estimate. If they cannot estimate, enter **999=Unknown** for Question 7e3.

Coding Guidebook for **Form B1:** EVALUATION FORM – Vital Signs and Anthropometrics

INSTRUCTIONS: *This form is to be completed by the clinician or appropriately trained research personnel.*

IVP FVP Section 1 – Participant vital signs and anthropometrics

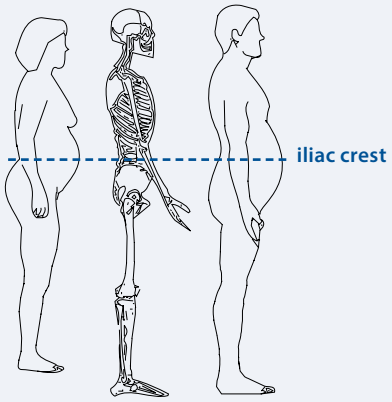
1. **1.** Participant height *(inches)* __ __ . __ *(88.8 = not assessed)*

If height cannot be measured (e.g., if subject is confined to a wheelchair or unable to stand), enter **88.8=Not assessed**.

2. **2.** Participant weight *(lbs.)* __ __ __ *(888 = not assessed)*

If weight cannot be measured (e.g., if subject is confined to a wheelchair or unable to stand), enter **888=Not assessed**.

Instructions for measuring waist and hip circumference in adults



Waist circumference should be measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest, using a stretch resistant tape. **Hip circumference** should be measured around the widest portion of the buttocks, with the tape parallel to the floor.

For both measurements: Participant should stand with feet close together, arms at the side and body weight evenly distributed, and should wear little clothing. The participant should be relaxed, and the measurements should be taken at the end of a normal expiration. Each measurement should be taken twice and entered here. If the difference between the two measurements exceeds 0.5 inches, the two measurements should be repeated.

Source: *Waist circumference and waist–hip ratio: report of a WHO expert consultation, Geneva, 8–11 December 2008.*

Source: *NHLBI Obesity Education Initiative,* nhlbi.nih.gov

3. **3.** Enter two waist circumference measurements *(inches):*

- Measurement 1 __ __ __ *(888 = not assessed)*
- Measurement 2 __ __ __ *(888 = not assessed)*

4. **4.** Enter two hip circumference measurements *(inches):*

- Measurement 1 __ __ __ *(888 = not assessed)*
- Measurement 2 __ __ __ *(888 = not assessed)*

5. **5.** Enter two readings spaced at least one minute apart for each arm.
See detailed instructions below.

5a. **5a.** Participant blood pressure - **Left arm**:

- Reading 1 __ __ __ / __ __ __ *(888/888= not assessed)*
- Reading 2 __ __ __ / __ __ __ *(888/888= not assessed)*

5b.	**5b.**		Participant blood pressure - **Right arm**:		
			• Reading 1	__ __ __ / __ __ __	*(888/888= not assessed)*
			• Reading 2	__ __ __ / __ __ __	*(888/888= not assessed)*
6.	**6.**	Participant resting heart rate *(pulse)*		__ __ __	*(888 = not assessed)*

If pulse cannot be obtained, enter **888=Not assessed**.

Steps for proper blood pressure measurement

STEP 1 - Properly prepare the participant:

- Have the participant relax, sitting in a chair *(feet on floor, back supported)* for >5 minutes
- The participant should avoid caffeine, exercise, and smoking for at least 30 minutes before measurement.
- Ensure that participant has emptied his/her bladder.
- Neither the participant nor the observer should talk during the rest period or during the measurement.
- Remove all clothing covering the location of cuff placement.
- Measurements made while the participant is sitting or lying on an examining table do not fulfill these criteria.

STEP 2 - Use proper technique for BP measurements

- Use a BP measurement device that has been validated and ensure that the device is calibrated periodically.
- Support the participant's arm *(e.g., have it resting on a desk)*.
- Position the middle of the cuff on the participant's upper arm at the level of the right atrium *(midpoint of the sternum)*.
- Use the correct cuff size, such that the bladder encircles 80% of the arm, and note if a larger- or smaller-than-normal cuff size is used.
- Either the stethoscope diaphragm or bell may be used for auscultatory readings.

STEP 3 - Take proper measurements

- Take two BP readings in both arms.
- Separate the second set of measurements from the first by one minute.
- For auscultatory determinations, use a palpated estimate of radial pulse obliteration pressure to estimate SBP. Inflate the cuff 20-30 mm Hg above this level for an auscultatory determination of the BP level.
- For auscultatory readings, deflate the cuff pressure 2 mm Hg per second, and listen for Korotkoff sounds.

STEP 4 - Properly document accurate BP readings

- Record SBP and DBP. If using the auscultatory technique, record SBP and DBP as onset of the first Korotkoff sound and disappearance of all Korotkoff sounds, respectively, using the nearest even number.
- Record the two readings of SBP and DBP in the left arm, and the two readings of SBP and DBP in the right arm.

STEP 5 - Give BP readings and interpretation to the participants

- It is recommended to provide participants with the SBP/DBP readings both orally, and in writing.

Source: Checklist for accurate measurement of BP adapted from AHA Guidelines, Whelton PK et al., *Hypertension*. 2018; 71: e13-e11.

Coding Guidebook for **Form B3:** Unified Parkinson's Disease Rating Scale (UPDRS[1]) —Motor Exam

INSTRUCTIONS: *This form is to be completed by the clinician or other trained health professional. The motor exam should be administered to all participants. Clinician should record results as observed regardless of whether there are non-parkinsonian contributions or explanations for the findings. This form is intended to 1) determine the degree of parkinsonism on any visit, and 2) track the degree of parkinsonism over time. The UPDRS is not intended to establish the presence or absence of parkinsonism. For additional clarification and scoring instructions, see* **UDS Coding Guidebook** *for* **Form B3**. *Check only one box per question.*

For video-recorded examples of administration, see Perlmutter JS. Assessment of Parkinson disease manifestations. Curr Protoc Neurosci. 2009 Oct; Chapter 10: Unit10.1. doi: 10.1002/0471142301.ns1001s49.

This form is to be completed only when an in-person encounter has occurred, and a comprehensive neurologic examination has been performed. Do not complete this form if the encounter was conducted via phone or video.

IVP	FVP		
		☐	*(Optional)* **If the clinician completes the UPDRS examination and determines all items are normal, check this box.** If this box is checked, all items will default to 0 in the database.

1.	**1.**	**Speech**	☐ 0 Normal ☐ 1 Slight loss of expression, diction and/or volume ☐ 2 Monotone, slurred but understandable; moderately impaired. ☐ 3 Marked impairment, difficult to understand. ☐ 4 Unintelligible ☐ 8 Untestable **(SPECIFY):** _____
2.	**2.**	**Facial expression**	☐ 0 Normal ☐ 1 Minimal hypomimia, could be normal "poker face" ☐ 2 Slight but definitely abnormal diminution of facial expression ☐ 3 Moderate hypomimia; lips parted some of the time ☐ 4 Masked or fixed facies with severe or complete loss of facial expression; lips parted ¼ inches or more ☐ 8 Untestable **(SPECIFY):** _____
		3. Tremor at rest	
3a.	**3a.**	**Face, lips, chin**	☐ 0 Absent ☐ 1 Slight and infrequently present ☐ 2 Mild in amplitude and persistent; or moderate in amplitude, but only intermittently present ☐ 3 Moderate in amplitude and present most of the time ☐ 4 Marked in amplitude and present most of the time ☐ 8 Untestable **(SPECIFY):** _____
3b.	**3b.**	**Right hand**	☐ 0 Absent ☐ 1 Slight and infrequently present ☐ 2 Mild in amplitude and persistent; or moderate in amplitude, but only intermittently present ☐ 3 Moderate in amplitude and present most of the time ☐ 4 Marked in amplitude and present most of the time ☐ 8 Untestable **(SPECIFY):** _____
3c.	**3c.**	**Left hand**	☐ 0 Absent ☐ 1 Slight and infrequently present ☐ 2 Mild in amplitude and persistent; or moderate in amplitude, but only intermittently present ☐ 3 Moderate in amplitude and present most of the time ☐ 4 Marked in amplitude and present most of the time ☐ 8 Untestable **(SPECIFY):** _____
3d.	**3d.**	**Right foot**	☐ 0 Absent ☐ 1 Slight and infrequently present ☐ 2 Mild in amplitude and persistent; or moderate in amplitude, but only intermittently present ☐ 3 Moderate in amplitude and present most of the time ☐ 4 Marked in amplitude and present most of the time ☐ 8 Untestable **(SPECIFY):** _____

[1]Fahn S, Elton RL, UPDRS Development Committee. The Unified Parkinson's Disease Rating Scale. In Fahn S, Marsden CD, Calne DB, Goldstein M, eds. Recent developments in Parkinson's disease, Vol. 2. Florham Park, NJ: Macmillan Healthcare Information, 1987:153–163, 293–304. Reproduced by permission of the author.

IVP	FVP	3. Tremor at rest	
3e.	3e.	Left foot	☐ 0 Absent ☐ 1 Slight and infrequently present ☐ 2 Mild in amplitude and persistent; or moderate in amplitude, but only intermittently present ☐ 3 Moderate in amplitude and present most of the time ☐ 4 Marked in amplitude and present most of the time ☐ 8 Untestable **(SPECIFY):** _____

		4. Action or postural tremor of hands	
4a.	4a.	Right hand	☐ 0 Absent ☐ 1 Slight; present with action ☐ 2 Moderate in amplitude, present with action ☐ 3 Moderate in amplitude with posture holding as well as action ☐ 4 Marked in amplitude; interferes with feeding ☐ 8 Untestable **(SPECIFY):** _____
4b.	4b.	Left hand	☐ 0 Absent ☐ 1 Slight; present with action ☐ 2 Moderate in amplitude, present with action ☐ 3 Moderate in amplitude with posture holding as well as action ☐ 4 Marked in amplitude; interferes with feeding ☐ 8 Untestable **(SPECIFY):** _____

		5. Rigidity (*judged on passive movement of major joints with participant relaxed in sitting position; cogwheeling to be ignored*)	
5a.	5a.	Neck	☐ 0 Absent ☐ 1 Slight or detectable only when activated by mirror or other movements ☐ 2 Mild to moderate ☐ 3 Marked, but full range of motion easily achieved ☐ 4 Severe; range of motion achieved with difficulty ☐ 8 Untestable **(SPECIFY):** _____
5b.	5b.	Right upper extremity	☐ 0 Absent ☐ 1 Slight or detectable only when activated by mirror or other movements ☐ 2 Mild to moderate ☐ 3 Marked, but full range of motion easily achieved ☐ 4 Severe; range of motion achieved with difficulty ☐ 8 Untestable **(SPECIFY):** _____
5c.	5c.	Left upper extremity	☐ 0 Absent ☐ 1 Slight or detectable only when activated by mirror or other movements ☐ 2 Mild to moderate ☐ 3 Marked, but full range of motion easily achieved ☐ 4 Severe; range of motion achieved with difficulty ☐ 8 Untestable **(SPECIFY):** _____
5d.	5d.	Right lower extremity	☐ 0 Absent ☐ 1 Slight or detectable only when activated by mirror or other movements ☐ 2 Mild to moderate ☐ 3 Marked, but full range of motion easily achieved ☐ 4 Severe; range of motion achieved with difficulty ☐ 8 Untestable **(SPECIFY):** _____
5e.	5e.	Left lower extremity	☐ 0 Absent ☐ 1 Slight or detectable only when activated by mirror or other movements ☐ 2 Mild to moderate ☐ 3 Marked, but full range of motion easily achieved ☐ 4 Severe; range of motion achieved with difficulty ☐ 8 Untestable **(SPECIFY):** _____

IVP	FVP	6. Finger taps *(participant taps thumb with index finger in rapid succession)*	
6a.	6a.	Right hand	☐ 0 Normal ☐ 1 Mild slowing and/or reduction in amplitude ☐ 2 Moderately impaired; definite and early fatiguing; may have occasional arrests in movement ☐ 3 Severely impaired; frequent hesitation in initiating movements or arrests in ongoing movement ☐ 4 Can barely perform the task. ☐ 8 Untestable **(SPECIFY):** _____
6b.	6b.	Left hand	☐ 0 Normal ☐ 1 Mild slowing and/or reduction in amplitude ☐ 2 Moderately impaired; definite and early fatiguing; may have occasional arrests in movement ☐ 3 Severely impaired; frequent hesitation in initiating movements or arrests in ongoing movement ☐ 4 Can barely perform the task. ☐ 8 Untestable **(SPECIFY):** _____
		7. Hand movements *(participant opens and closes hands in rapid succession)*	
7a.	7a.	Right hand	☐ 0 Normal ☐ 1 Mild slowing and/or reduction in amplitude ☐ 2 Moderately impaired; definite and early fatiguing; may have occasional arrests in movement ☐ 3 Severely impaired; frequent hesitation in initiating movements or arrests in ongoing movement ☐ 4 Can barely perform the task. ☐ 8 Untestable **(SPECIFY):** _____
7b.	7b.	Left hand	☐ 0 Normal ☐ 1 Mild slowing and/or reduction in amplitude ☐ 2 Moderately impaired; definite and early fatiguing; may have occasional arrests in movement ☐ 3 Severely impaired; frequent hesitation in initiating movements or arrests in ongoing movement ☐ 4 Can barely perform the task. ☐ 8 Untestable **(SPECIFY):** _____
		8. Rapid alternating movements of hands *(pronation-supination movements of hands, vertically and horizontally, with as large an amplitude as possible, both hands simultaneously)*	
8a.	8a.	Right hand	☐ 0 Normal ☐ 1 Mild slowing and/or reduction in amplitude ☐ 2 Moderately impaired; definite and early fatiguing; may have occasional arrests in movement ☐ 3 Severely impaired; frequent hesitation in initiating movements or arrests in ongoing movement ☐ 4 Can barely perform the task. ☐ 8 Untestable **(SPECIFY):** _____
8b.	8b.	Left hand	☐ 0 Normal ☐ 1 Mild slowing and/or reduction in amplitude ☐ 2 Moderately impaired; definite and early fatiguing; may have occasional arrests in movement ☐ 3 Severely impaired; frequent hesitation in initiating movements or arrests in ongoing movement ☐ 4 Can barely perform the task. ☐ 8 Untestable **(SPECIFY):** _____

IVP	FVP	9. Leg agility *(participant taps heel on the ground in rapid succession, picking up entire leg; amplitude should be at least 3 inches)*	
9a.	9a.	**Right leg**	☐ 0 Normal ☐ 1 Mild slowing and/or reduction in amplitude ☐ 2 Moderately impaired; definite and early fatiguing; may have occasional arrests in movement ☐ 3 Severely impaired; frequent hesitation in initiating movements or arrests in ongoing movement ☐ 4 Can barely perform the task. ☐ 8 Untestable **(SPECIFY):** _____
9b.	9b.	**Left leg**	☐ 0 Normal ☐ 1 Mild slowing and/or reduction in amplitude ☐ 2 Moderately impaired; definite and early fatiguing; may have occasional arrests in movement ☐ 3 Severely impaired; frequent hesitation in initiating movements or arrests in ongoing movement ☐ 4 Can barely perform the task. ☐ 8 Untestable **(SPECIFY):** _____
10.	10.	**Arising from chair** *(participant attempts to rise from a straight-backed chair, with arms folded across chest)*	☐ 0 Normal ☐ 1 Slow; or may need more than one attempt ☐ 2 Pushes self up from arms of seat. ☐ 3 Tends to fall back and may have to try more than one time, but can get up without help ☐ 4 Unable to arise without help ☐ 8 Untestable **(SPECIFY):** _____
11.	11.	**Posture**	☐ 0 Normal ☐ 1 Not quite erect, slightly stooped posture; could be normal for older person ☐ 2 Moderately stooped posture, definitely abnormal; can be slightly leaning to one side ☐ 3 Severely stooped posture with kyphosis; can be moderately leaning to one side ☐ 4 Marked flexion with extreme abnormality of posture ☐ 8 Untestable **(SPECIFY):** _____
12.	12.	**Gait**	☐ 0 Normal ☐ 1 Walks slowly; may shuffle with short steps, but no festination (hastening steps) or propulsion ☐ 2 Walks with difficulty, but requires little or no assistance; may have some festination, short steps, or propulsion ☐ 3 Severe disturbance of gait requiring assistance ☐ 4 Cannot walk at all, even with assistance ☐ 8 Untestable **(SPECIFY):** _____
13.	13.	**Posture stability** *(response to sudden, strong posterior displacement produced by pull on shoulders while participant erect with eyes open and feet slightly apart; participant is prepared)*	☐ 0 Normal erect ☐ 1 Retropulsion, but recovers unaided ☐ 2 Absence of postural response; would fall if not caught by examiner ☐ 3 Very unstable, tends to lose balance spontaneously ☐ 4 Unable to stand without assistance ☐ 8 Untestable **(SPECIFY):** _____
14.	14.	**Body bradykinesia and hypokinesia** *(combining slowness, hesitancy, decreased arm swing, small amplitude, and poverty of movement in general)*	☐ 0 None ☐ 1 Minimal slowness, giving movement a deliberate character; could be normal for some persons; possibly reduced amplitude ☐ 2 Mild degree of slowness and poverty of movement which is definitely abnormal; alternatively, some reduced amplitude ☐ 3 Moderate slowness, poverty or small amplitude of movement ☐ 4 Marked slowness, poverty or small amplitude of movement ☐ 8 Untestable **(SPECIFY):** _____
15.	15.	**Total UPDRS Score** *(If one or more items are checked "8=Untestable", enter 888)*	___ ___ ___ *(0-108, 888)*

If any of Q1-Q14 are checked **8=Untestable**, enter 888; else sum up responses for Q1-Q14. The total will be calculated automatically if using electronic data capture.

Coding Guidebook for **Form B4:** CDR® Dementia Staging Instrument PLUS NACC FTLD Behavior & Language Domains (CDR® Plus NACC FTLD)

INSTRUCTIONS: *This form is to be completed by the clinician or other trained health professional, based on co-participant report and behavioral and neurological exam of the participant. In the extremely rare instances when no co-participant is available, the clinician or other trained health professional must complete this form using all other available information and his/her best clinical judgment. Score only as decline from previous level due to cognitive loss, not impairment due to other factors, such as physical disability.*

The Washington University ADRC provides a CDR training website for ADRC personnel. This CDR training is required and may be accessed online at https://knightadrc.wustl.edu/cdr-training-application/

Use all information and make the best judgment. Score each category as independently as possible. Select only one box for each category, rating impairment as decline from the person's usual level due to cognitive loss alone, not impairment due to other factors such as physical disability. Occasionally, the evidence is ambiguous and the clinician's best judgment is that a category could be rated in either one of two adjacent boxes, such as **1=Mild** or **2=Moderate** impairment. In that situation, the standard procedure is to select the box of greater impairment.

Aphasia is taken into account by assessing both language and non-language function in each cognitive category. If aphasia is present to a greater degree than the general dementia, the participant is rated according to the general dementia. Supply evidence of non-language cognitive function.

A box score of 0 for Memory **(M=0)** applies to participants who, in the clinician's judgment, have no memory impairment or have inconsistent slight forgetfulness. The adjective "slight" indicates that there is not even a suggestion that everyday function has been affected by a memory change. In contrast, a box score of 0.5 in Memory indicates a consistent memory change and also suggests that the change may very subtly affect everyday performance (e.g., having to return to the grocery store after forgetting an item on the list).

Before scoring the CDR boxes, the clinician is to synthesize and evaluate all information: the report of the co-participant, the report (and performance) of the participant, and the clinician's own observations. It may be that an inobservant co-participant reports no memory problems, whereas the participant self-reports memory problems; if the clinician's judgment is that the individual is correct, then a box score of 0.5 for Memory can be given **(M=0.5)**. The converse also is true: a 0.5 box score can be given when the co-participant reports a problem but the participant does not. It is also possible for the clinician to rate Memory as 0.5 **(M=0.5)** if they believe a problem exists — even though neither the co-participant nor the participant reports a problem.

CDR Sum of Boxes
Calculate the sum of values for all answers and enter the total score in the space provided.

Global CDR
The global CDR is derived from the scores in each of the six categories ("box score") as follows:

- Memory (M) is the primary category, and all others are secondary.
- CDR = M if at least three secondary categories are given the same score as memory. Whenever three or more secondary categories are given a score greater or less than the memory score, CDR = score of majority of secondary categories on whichever side of M has the greater number of secondary categories. However, when three secondary categories are scored on one side of M and two secondary categories are scored on the other side of M, then CDR = M.
- When M = 0.5, CDR = 1 if at least three of the other categories are scored 1 or greater. If M = 0.5, then CDR cannot be 0; it can only be 0.5 or 1.
- If M = 0, then CDR = 0 unless there is impairment (0.5 or greater) in two more secondary categories, in which case CDR = 0.5.

Although applicable to most Alzheimer's disease situations, these rules do not cover all possible scoring combinations. Unusual circumstances that occasionally occur in AD, and may be expected in non-Alzheimer's dementia as well, are scored as follows:

1. With ties in the secondary categories on one side of M, choose the tied scores closest to M for CDR (e.g., if M and another secondary category = 3, two secondary categories = 2, and two secondary categories = 1, then CDR = 2).
2. When only one or two secondary categories are given the same score as M, CDR = M as long as no more than two secondary categories are on either side of M.
3. When M = 1 or greater, CDR cannot be 0; in this circumstance, CDR = 0.5 when the majority of secondary categories are 0.

The CDR scoring algorithm can be accessed online at https://knightadrc.wustl.edu/professionals-clinicians/cdr-dementia-staging-instrument/cdr-scoring-algorithm/.

IVP	FVP	Section 1 – CDR® Dementia Staging Instrument[1]					
		Impairment					
		Please enter scores (below):	None = 0	Questionable = 0.5	Mild = 1	Moderate = 2	Severe = 3
1.	1.	**Memory**	No memory loss, or slight inconsistent forgetfulness	Consistent slight forgetfulness; partial recollection of events; "benign" forgetfulness	Moderate memory loss, more marked for recent events; defect interferes with everyday activities	Severe memory loss; only highly learned material retained; new material rapidly lost	Severe memory loss; only fragments remain
2.	2.	**Orientation**	Fully oriented	Fully oriented except for slight difficulty with time relationships	Moderate difficulty with time relationships; oriented for place at examination; may have geographic disorientation elsewhere	Severe difficulty with time relationships; usually disoriented to time, often to place	Oriented to person only
3.	3.	**Judgment & Problem Solving**	Solves everyday problems, handles business and financial affairs well; judgment good in relation to past performance	Slight impairment in solving problems, similarities, and differences	Moderate difficulty in handling problems, similarities, and differences; social judgment usually maintained	Severely impaired in handling problems, similarities, and differences; social judgment usually impaired	Unable to make judgments or solve problems
4.	4.	**Community Affairs**	Independent function at usual level in job, shopping, volunteer and social groups	Slight impairment in these activities	Unable to function independently at these activities, although may still be engaged in some; appears normal to casual inspection	No pretense of independent function outside the home; appears well enough to be taken to functions outside the family home	No pretense of independent function outside the home; appears too ill to be taken to functions outside the family home
5.	5.	**Home & Hobbies**	Life at home, hobbies, and intellectual interests well maintained	Life at home, hobbies, and intellectual interests slightly impaired	Mild but definite impairment of function at home; more difficult chores abandoned; more complicated hobbies and interests abandoned	Only simple chores preserved; very restricted interests, poorly maintained	No significant function in the home
6.	6.	**Personal Care**	Fully capable of self-care (= 0)		Needs prompting	Requires assistance in dressing, hygiene, keeping of personal effects	Requires much help with personal care; frequent incontinence
7./8.	7./8.	**CDR Sum of Boxes**			**Global CDR**		

[1]Morris JC. The Clinical Dementia Rating (CDR): Current version and scoring rules. Neurology 43(11):2412-4, 1993. Copyright© Lippincott, Williams & Wilkins. Reproduced by permission.

In addition to the factors investigated within the CDR, two additional constructs — "Behavior, Comportment, and Personality" and "Language" — have been appended as the **NACC FTLD Behavior & Language Domains**, which will aid in the identification of participants with frontotemporal dementia and/or primary progressive aphasia, respectively. Because of their specialized nature, instructions for the scoring of each item are outlined below.

Behavior, Comportment, and Personality

This item should be completed by a clinician or other trained health professional who is skilled in the assessment of FTLD, based on informant report and a review of the participant's cognitive, functional, and behavioral status. This domain is intended to assess changes in personality, aberrant behaviors, and changes in interpersonal relationships. The kinds of specific issues that might fall under these rubrics include: loss of insight, disinhibition, apathy, social withdrawal and disengagement, emotional lability, easy distractibility, reduced empathy for the feelings of others, impulsivity, and changes in eating habits and table manners. A key element of each of these is the degree to which these behaviors impact interpersonal relationships.

Language

This item should be completed by a clinician or other trained health professional who is well versed in aphasia and aphasic disorders, based on information derived from the informant and also from clinical assessment of the patient's language functions in the course of the clinical interview and the mental status examination. This domain is intended to assess changes in language. The components of language that are primarily of interest include: spontaneous speech, auditory comprehension, object naming, reading and writing. Using these in combination, the goal is to assess the participant's ability to create and understand various forms of information. The rate at which these are generated or comprehended is also of interest.

IVP FVP Section 2 - NACC FTLD Behavior & Language Domains

Impairment

		Please enter scores *(below):*	None = 0	Questionable = 0.5	Mild = 1	Moderate = 2	Severe = 3
9.	9.	**Behavior, Comportment, & Personality**[2]	Socially appropriate behavior	Questionable changes in comportment, empathy, appropriateness of actions	Mild but definite changes in behavior	Moderate behavioral changes, affecting interpersonal relationships and interactions in a significant manner	Severe behavioral changes, making interpersonal interactions all unidirectional
10.	10.	**Language**[3]	No language difficulty, or occasional mild tip-of-the-tongue	Consistent mild word-finding difficulties; simplification of word choice; circumlocution; decreased phrase length; and/or mild comprehension difficulties	Moderate word-finding difficulty in speech; cannot name objects in environment; reduced phrase length and/or agrammatical speech and/or reduced comprehension in conversation and reading	Moderate to severe impairments in either speech or comprehension; has difficulty communicating thoughts; writing may be slightly more effective	Severe comprehension deficits; no intelligible speech

[2]Excerpted from the *Frontotemporal Dementia Multicenter Instrument & MR Study* (Mayo Clinic, UCSF, UCLA, UW).
[3]Excerpted from the *PPA-CDR: A modification of the CDR for assessing dementia severity in patients with primary progressive aphasia* (Johnson N, Weintraub S, Mesulam MM), 2002.

Coding Guidebook for **Form B5:** BEHAVIORAL ASSESSMENT —

Neuropsychiatric Inventory Questionnaire (NPI-Q[1])

INSTRUCTIONS*: This form is to be completed by the clinician or other trained health professional based on co-participant interview, as described by the training video. (This is not to be completed by the participant as a paper-and-pencil self-report.) Check only <u>one</u> box for each category of response.*

ADRC personnel must be certified as an NPI-Q interviewer through the online training system developed by the University of California Los Angeles and NACC. The NPI-Q Interviewer Certification system may be accessed through the NACC website at https://naccdata.org/data-collection/training/npiq-certification. The procedures established in the training system must be followed to complete this form.

The Neuropsychiatric Inventory – Questionnaire (NPI-Q) was developed and cross-validated with the standard NPI to provide a brief assessment of neuropsychiatric symptomatology in routine clinical practice settings (Kaufer et al., J Neuropsychiatry Clin Neurosci 2000, 12:233-239). The NPI-Q is adapted from the NPI (Cummings et al., Neurology 1994; 44:2308-2314), a validated informant-based interview that assesses neuropsychiatric symptoms over the previous month. The original NPI included 10 neuropsychiatric domains; two others, Nighttime Behavioral Disturbances and Appetite/Eating Changes, have subsequently been added.

Each of the 12 NPI-Q domains contains a screening question that reflects cardinal symptoms of that domain. Initial responses to each domain's screening question are "Yes" (present), "No" (absent), or "Unknown". If the response to the domain question is "No" or "Unknown", the interviewer goes to the next domain. If "Yes", the interviewer then rates the Severity of the symptoms present within the last month on a 3-point scale.

It is recommended that responses to the NPI-Q be reviewed for completeness by the interviewer and to clarify uncertainties after each administration.

The NPI and NPI-Q are both copyright-protected by Jeffrey L. Cummings, MD. The NPI-Q was developed by Daniel Kaufer, MD an is used with permission. **Use of the NPI or NPI-Q in investigational studies sponsored in whole or part by for-profit entities is prohibited without express written consent.**

For inquiries regarding the NPI-Q, contact:

Jeffrey L. Cummings, MD (cumminj@ccf.org)
Cleveland Clinic Lou Ruvo Center for Brain Health
Mail Code Las Vegas, 888 W Bonneville
Las Vegas, NV 89106

The NPI-Q can be found at www.NPItest.net

Please answer the following questions based on <u>changes</u> that have occurred since the participant first began to experience memory (i.e., cognitive) problems. **Select 1=Yes <u>only</u> if the symptom(s) has been present <u>in the last month</u>. Otherwise, select 0=No.** *(NOTE: for the UDS, please administer the NPI-Q to all participants.)*

For each item marked **1=Yes**, rate the SEVERITY of the symptom (how it affects the participant):

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)

The wording of the original NPI-Q focused on changes that have occurred since the participant first began to experience *memory* problems. However, in order to assess neuropsychiatric symptoms associated with etiologies other than Alzheimer's disease, the NPI-Q instructions have been edited to capture changes that have occurred since the participant first began to experience *cognitive* problems.

For participants who are cognitively normal or whose cognition has not yet been evaluated — Please report any behaviors or symptoms that were present within the last month, ignoring behaviors and symptoms that are usual for the participant and have been customary throughout his/her life.

If the co-participant does not answer a question, select **9=Unknown**.

IVP	FVP										
1.	1.	**NPI CO-PARTICIPANT:** ☐1 Spouse ☐2 Child ☐3 Other (SPECIFY): _____									
						SEVERITY					
				Yes	No	Unk		Mild	Mod	Sev	Unk
2.	2.	**Delusions** – Does the patient have false beliefs, such as thinking that others are stealing from him/her or planning to harm him/her in some way?	2a.	☐1	☐0	☐9	2b.	☐1	☐2	☐3	☐9
3.	3.	**Hallucinations** – Does the patient have hallucinations such as false visions or voices? Does he or she seem to hear or see things that are not present?	3a.	☐1	☐0	☐9	3b.	☐1	☐2	☐3	☐9
4.	4.	**Agitation/Aggression** – Is the patient resistive to help from others at times, or hard to handle?	4a.	☐1	☐0	☐9	4b.	☐1	☐2	☐3	☐9
5.	5.	**Depression/Dysphoria** – Does the patient seem sad or say that he/she is depressed?	5a.	☐1	☐0	☐9	5b.	☐1	☐2	☐3	☐9
6.	6.	**Anxiety** – Does the patient become upset when separated from you? Does he/she have any other signs of nervousness such as shortness of breath, sighing, being unable to relax, or feeling excessively tense?	6a.	☐1	☐0	☐9	6b.	☐1	☐2	☐3	☐9
7.	7.	**Elation/Euphoria** – Does the patient appear to feel too good or act excessively happy?	7a.	☐1	☐0	☐9	7b.	☐1	☐2	☐3	☐9
8.	8.	**Apathy/Indifference** – Does the patient seem less interested in his/her usual activities or in the activities and plans of others?	8a.	☐1	☐0	☐9	8b.	☐1	☐2	☐3	☐9
9.	9.	**Disinhibition** – Does the patient seem to act impulsively, for example, talking to strangers as if he/she knows them, or saying things that may hurt people's feelings?	9a.	☐1	☐0	☐9	9b.	☐1	☐2	☐3	☐9
10.	10.	**Irritability/Lability** – Is the patient impatient and cranky? Does he/she have difficulty coping with delays or waiting for planned activities?	10a.	☐1	☐0	☐9	10b.	☐1	☐2	☐3	☐9
11.	11.	**Motor disturbance** – Does the patient engage in repetitive activities such as pacing around the house, handling buttons, wrapping string, or doing other things repeatedly?	11a.	☐1	☐0	☐9	11b.	☐1	☐2	☐3	☐9
12.	12.	**Nighttime behaviors** – Does the patient awaken you during the night, rise too early in the morning, or take excessive naps during the day?	12a.	☐1	☐0	☐9	12b.	☐1	☐2	☐3	☐9
13.	13.	**Appetite/Eating** – Has the patient lost or gained weight, or had a change in the type of food he/she likes?	13a.	☐1	☐0	☐9	13b.	☐1	☐2	☐3	☐9

Geriatric Depression Scale (GDS)[1]

INSTRUCTIONS: This form is to be completed by the clinician or other trained health professional, based on participant response. For additional clarification and examples, see UDS Coding Guidebook for Initial Visit Packet, Form B6. Check only one answer per question.

This form is intended for completion by clinician or other trained health professional as a direct participant interview. The form is not to be administered to the co-participant. If your Center prefers to administer the entire 30-item GDS, please first administer this 15-item form and score appropriately; then administer the remaining 15 items on a separate non-UDS form.

The Geriatric Depression Scale was developed by Stanford University as a basic screening measure for depression in older adults. Further information is available online at http://www.stanford.edu/~yesavage/GDS.html.

☐ Check this box and enter "88" below for the Total GDS Score **if and only if the participant:** 1.) does not attempt the GDS, or 2.) answers fewer than 12 questions.

Instruct the participant: "In the next part of this interview, I will ask you questions about your feelings. Some of the questions I will ask you may not apply, and some may make you feel uncomfortable. For each question, please answer "yes" or "no," depending on how you have been feeling **in the past week, including today**."

Select **9=Did not answer** if the subject is unable or unwilling to answer a question.

IVP	FVP		Yes	No	Did not answer
1.	1.	Are you basically satisfied with your life?	☐ 0	☐ 1	☐ 9
2.	2.	Have you dropped many of your activities and interests?	☐ 1	☐ 0	☐ 9
3.	3.	Do you feel that your life is empty?	☐ 1	☐ 0	☐ 9
4.	4.	Do you often get bored?	☐ 1	☐ 0	☐ 9
5.	5.	Are you in good spirits most of the time?	☐ 0	☐ 1	☐ 9
6.	6.	Are you afraid that something bad is going to happen to you?	☐ 1	☐ 0	☐ 9
7.	7.	Do you feel happy most of the time?	☐ 0	☐ 1	☐ 9
8.	8.	Do you often feel helpless?	☐ 1	☐ 0	☐ 9
9.	9.	Do you prefer to stay at home, rather than going out and doing new things?	☐ 1	☐ 0	☐ 9
10.	10.	Do you feel you have more problems with memory than most?	☐ 1	☐ 0	☐ 9
11.	11.	Do you think it is wonderful to be alive now?	☐ 0	☐ 1	☐ 9
12.	12.	Do you feel pretty worthless the way you are now?	☐ 1	☐ 0	☐ 9
13.	13.	Do you feel full of energy?	☐ 0	☐ 1	☐ 9
14.	14.	Do you feel that your situation is hopeless?	☐ 1	☐ 0	☐ 9
15.	15.	Do you think that most people are better off than you are?	☐ 1	☐ 0	☐ 9
16.	16.	Sum all checked answers for a Total GDS Score *(max score = 15; did not complete = 88)*			

Calculate the sum of values for all checked "Yes" or "No" answers and enter the total score in the space provided. The calculation may include a maximum of three unanswered items, and the final sum must be prorated for the number of unanswered items (see instructions below for prorating scores). If more than three items are unanswered, however, the test must be considered incomplete and the Total GDS Score entered as **88=Did not complete**.

PRORATING SCORES (what to do if the participant does not answer up to three items): If up to three of the 15 items are unanswered (i.e., responses are **9=Did not answer**), add the total score on the completed items plus an estimated score for the unanswered items to get a total score. The estimated score for unanswered items is calculated as:

(Total score of completed items / # of completed items) * (# of unanswered items)

You may get a fractional answer that requires rounding. For example, if the subject got a score of 5 for 12 completed items, then the estimated total score is 5 + [(5/12) * 3] = 6.25. Since the decimal portion of this value is <0.50, the total GDS score is 6.

[1]Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version. Clinical Gerontology: A Guide to Assessment and Intervention 165–173, NY: The Haworth Press, 1986. Reproduced by permission of the publisher.

TELEPHONE VISIT:

ASSESSMENT OF EMOTIONAL FUNCTIONING

While likely an infrequent occurrence, some participants may produce elevated scores on the Geriatric Depression Scale, suggesting the presence of significant emotional distress or suicidal ideation. If not already in place, it is strongly recommended that centers adopt guidelines for handling these situations remotely, including identifying the present location and address of any participant who demonstrates emotional distress. The following set of questions represents one example of how to manage elevated depression scores on the GDS when assessed by phone.

These guidelines are for certified interviewers when they suspect or detect significant emotional distress or suicidal ideation. "Significant emotional distress" is suggested by a score greater than 8 on the Geriatric Depression Scale or by any responses during the encounter that suggest significant emotional distress, such as statements regarding suicide, hopelessness, or lasting depressed mood.

Please note that the following questions are intended only as an example. Centers may substitute their own script.

If GDS > 8, or if you suspect the participant is significantly distressed, then say:

1. "Your response to some of the questions suggests to me that you might be experiencing some significant emotional distress at this time. Is that true?" ☐ No ☐ Yes

If "No," then say: **"Thanks. If you do, we recommend you speak with someone you feel comfortable talking to – a family member, your physician, a counselor, or your clergy person."** Continue with administration.

2. If "Yes," then say: **"I see. I need to ask you a couple more questions."**

2a. **"In the past month have you thought you would be better off dead or wished you were dead?"** ☐ No ☐ Yes

2b. **"In the past month have you wanted to harm yourself?"** ☐ No ☐ Yes

2c. **"In the past month have you thought about suicide?"** ☐ No ☐ Yes

2d. **"In the past month have you had a suicide plan?"** ☐ No ☐ Yes

2e. **"In the past month have you attempted suicide?"** ☐ No ☐ Yes

If responses to 2b through 2e are "No," then say: **"Thank you. We recommend you speak with a family member, your physician, or another professional like a psychologist, clergy person, or counselor to get help with your distress."** Continue with administration

If any response to 2b-2e is "Yes," then say: **"We strongly recommend that you speak with a family member, your physician, or another professional like a psychologist, clergyman, or counselor to get help with your distress. I will let one of our study clinicians and one of the lead investigators at our ADRC know about your distress level so they can follow up with you and perhaps assist you in finding help."**

Call the on-duty study clinican immediately and inform them of the participant's status and review the call with them. Study clinician will contact the participant by phone and follow up as per Center protocol.

Save a copy of all emails and other documents related to this event.

SUICIDAL IDEATION		
ADRC CCC PI notified date:	Follow up with participant:	
	Follow-up date:	☐ No follow up required
ADRC staff initials:	Outcome/follow-up comments:	

Complete the form above and attach it to the test administration booklet for data entry in the ADRC website for the study. Update with any follow-up information as it is received. Attach all correspondence to this document and file in participant's file.

Coding Guidebook for **Form B7:** FUNCTIONAL ASSESSMENT —

NACC Functional Assessment Scale (FAS[1])

***INSTRUCTIONS**: This form is to be completed by the clinician or other trained health professional, based on information provided by the co-participant. Indicate the level of performance for each activity by checking the <u>one</u> appropriate response.*

This form is intended for completion by clinician or other trained health professional per co-participant interview. The intent of the FAS is to assess change in an individual's specific functional activities, relative to previously attained abilities, that are caused by cognitive dysfunction. Select the most accurate response, based on the co-participant's assessment.

IVP	FVP	In the past four weeks, did the subject have difficulty or need help with:	Not applicable *(e.g., never did)*	Normal	Has difficulty, but does by self	Requires assistance	Dependent	Unknown
1.	1.	Writing checks, paying bills, or balancing a checkbook	☐ 8	☐ 0	☐ 1	☐ 2	☐ 3	☐ 9
2.	2.	Assembling tax records, business affairs, or other papers	☐ 8	☐ 0	☐ 1	☐ 2	☐ 3	☐ 9
3.	3.	Shopping alone for clothes, household necessities, or groceries	☐ 8	☐ 0	☐ 1	☐ 2	☐ 3	☐ 9
4.	4.	Playing a game of skill such as bridge or chess, working on a hobby	☐ 8	☐ 0	☐ 1	☐ 2	☐ 3	☐ 9
5.	5.	Heating water, making a cup of coffee, turning off the stove	☐ 8	☐ 0	☐ 1	☐ 2	☐ 3	☐ 9
6.	6.	Preparing a balanced meal	☐ 8	☐ 0	☐ 1	☐ 2	☐ 3	☐ 9
7.	7.	Keeping track of current events	☐ 8	☐ 0	☐ 1	☐ 2	☐ 3	☐ 9
8.	8.	Paying attention to and understanding a TV program, book, or magazine	☐ 8	☐ 0	☐ 1	☐ 2	☐ 3	☐ 9
9.	9.	Remembering appointments, family occasions, holidays, medications	☐ 8	☐ 0	☐ 1	☐ 2	☐ 3	☐ 9
10.	10.	Traveling out of the neighborhood, driving, or arranging to take public transportation	☐ 8	☐ 0	☐ 1	☐ 2	☐ 3	☐ 9

If the co-participant indicates that the participant no longer performs a particular task, it is reasonable to probe further and ask if they think the participant *could* still do the task. This will help tease out the relevant cognitive impairment.

If the co-participant believes the participant did the activity but cannot speak to the participant's potential changes in that activity, then they should select **9=Unknown**.

[1]Adapted from table 4 of Pfeffer RI, Kurosaki TT, Harrah CH, et al. Measurement of functional activities of older adults in the community. J Gerontol 37:323–9, 1982. Copyright© 1982. The Gerontological Society of America. Reproduced by permission of the publisher.

Coding Guidebook for **Form B8:** EVALUATION FORM — Neurological Examination Findings

INSTRUCTIONS: *This form should be completed by a clinician with experience in performing a comprehensive neurologic examination, assessing the presence/absence of neurological signs, and rating the degree of any abnormalities. Additionally, the clinician should have experience in completing each of the assessment measures associated with the gateway questions if any key neurologic findings are present. Check only one box per question.*

Use the information obtained at the neurological exam to indicate the neurological findings, using your best clinical judgment to ascribe those symptoms to a particular clinical syndrome.

IVP / FVP Section 1 – Examiner & examination questions

1. / 1. Which of the following was completed on this participant?
- ☐ 0 No neurologic examination **(END FORM HERE)**
- ☐ 1 Comprehensive neurologic examination as suggested in the UDS Coding Guidebook
- ☐ 2 Focused or partial neurologic examination performed in-person
- ☐ 3 Focused or partial neurologic examination performed via video

Note that a neurologic exam can only take place in person or via video. If a visit is only done via telephone, select **0 = No neurologic exam**.

2. / 2. Were there abnormal neurological exam findings?
- ☐ 0 No abnormal findings **(END FORM HERE;** *If this box is checked, all items will default to 0 = Absent in the database***)**
- ☐ 1 Yes

Section 2 – Specific clinical findings

Section 2A – Parkinsonian signs

3. / 3.
- ☐ 0 No abnormal signs in this section are present **(SKIP TO SECTION 2B;** *If this box is checked, Q3a through Q3n will default to 0 = Absent in the database***)**
- ☐ 1 Yes (***IF YES –*** *complete questions 3a–3n and consider completing additional measures as described on page 3*)
- ☐ 8 Not assessed **(SKIP TO SECTION 2B;** *If this box is checked, Q3a through Q3n will default to 8 = Not Assessed in the database***)**

If any of the parkinsonian signs listed below are present, select **1=Yes**. Otherwise, select **0=No** and skip to Section 2B. If parkinsonian symptoms were not assessed, select **8=Not assessed** and skip to Section 2B.

		FINDING:	Absent	Focal or Unilateral	Bilateral & Largely Symmetric	Bilateral & Largely Asymmetric	Not Assessed
3a.	3a.	**Slowing of fine motor movements**	☐ 0	☐ 1	☐ 2	☐ 3	☐ 8

This refers to movements such as finger tapping, hand pronation-supination, or foot- or toe-tapping. Significant slowing, even if slight or mild, is sufficient to report.

3b.	3b.	**Limb tremor at rest**	☐ 0	☐ 1	☐ 2	☐ 3	☐ 8

A definite rest tremor, even if only intermittent, is sufficient to report.

3c.	3c.	**Limb tremor - postural**	☐ 0	☐ 1	☐ 2	☐ 3	☐ 8
3d.	3d.	**Limb tremor - kinetic**	☐ 0	☐ 1	☐ 2	☐ 3	☐ 8
3e.	3e.	**Limb rigidity - arm**	☐ 0	☐ 1	☐ 2	☐ 3	☐ 8

Rigidity should be judged on passive movement of major joints with participant relaxed in sitting position; cogwheeling and paratonia (gegenhalten) to be ignored. Any degree of rigidity is sufficient to report.

Remote/telephone visit: Since this exam finding cannot be assessed adequately remotely, check "not assessed" if the encounter was conducted via a remote video visit.

3f.	3f.	**Limb rigidity - leg**	☐ 0	☐ 1	☐ 2	☐ 3	☐ 8

Remote/telephone visit: Since this exam finding cannot be assessed adequately remotely, check "not assessed" if the encounter was conducted via a remote video visit.

IVP	FVP	Section 2 – Specific clinical findings *continued...*					
		Section 2A – Parkinsonian signs					
		FINDING:			Absent	Present	Not Assessed
3g.	3g.	**Limb dystonia - arm**	☐0	☐1	☐2	☐3	☐8
3h.	3h.	**Limb dystonia - leg**	☐0	☐1	☐2	☐3	☐8
3i.	3i.	**Chorea**	☐0	☐1	☐2	☐3	☐8
3j.	3j.	**Decrement in amplitude of fine motor movements**			☐0	☐1	☐8
		Instruct the participant to perform rapid alternating movements of the fingers (finger tapping repeatedly), hands (flexing and extending the fingers repeatedly), legs (stomping on the floor repeatedly) and feet (tapping of the toe portion of the foot repeatedly) at least 10 times. If the amplitude and/or speed on the 6th to 10th movements is/are less than on the 1st to 4th movements, then check that a decrement is present.					
3k.	3k.	**Axial rigidity**			☐0	☐1	☐8
		For example, increased tone, greater in the neck and trunk than in the limbs.					
3l.	3l.	**Postural instability**			☐0	☐1	☐8
		Postural instability involves inadequate response to sudden, strong posterior displacement produced by pull on shoulders while participant is erect with eyes open and feet slightly apart; participant is prepared. Taking more than two steps or requiring the examiner to catch the participant are examples of postural instability. Any degree of postural instability is sufficient to select **1=Present**. **Remote/telephone visit:** Since this exam finding cannot be assessed adequately remotely, check "not assessed" if the encounter was conducted via a remote video visit.					
3m.	3m.	**Facial masking**			☐0	☐1	☐8
3n.	3n.	**Stooped posture**			☐0	☐1	☐8
		Section 2B – Cortical/pyramidal/other signs					
4.	4.	☐0 No abnormal signs in this section are present **(SKIP TO SECTION 2C;** *If this box is checked, Q4a through Q4q will default to 0=Absent in the database)* ☐1 Yes (***IF YES –*** *complete questions 4a–4q and consider completing additional measures as described on page 3*) ☐8 Not assessed **(SKIP TO SECTION 2C;** *If this box is checked, Q4a through Q4q will default to 8 = Not Assessed in the database***)**					
		If any of the cortical, pyramidal, and other signs listed below are present, select **1=Yes**. Otherwise, select **0=No** and skip to Section 2C. If cortical, pyramidal, and other signs were not assessed, select **8=Not assessed** and skip to Section 2C.					
		FINDING:	Absent	Focal or Unilateral	Bilateral & Largely Symmetric	Bilateral & Largely Asymmetric	Not Assessed
4a.	4a.	**Limb apraxia**	☐0	☐1	☐2	☐3	☐8
4b.	4b.	**Face or limb findings in UMN distribution***	☐0	☐1	☐2	☐3	☐8
		Remote/telephone visit: Since this exam finding cannot be assessed adequately remotely, check "not assessed" if the encounter was conducted via a remote video visit.					
4c.	4c.	**Face or limb findings in an LMN distribution***	☐0	☐1	☐2	☐3	☐8
		Remote/telephone visit: Since this exam finding cannot be assessed adequately remotely, check "not assessed" if the encounter was conducted via a remote video visit.					
4d.	4d.	**Visual field cut**	☐0	☐1	☐2	☐3	☐8
		Remote/telephone visit: Since this exam finding cannot be assessed adequately remotely, check "not assessed" if the encounter was conducted via a remote video visit.					

IVP	FVP	Section 2 – Specific clinical findings *continued...*					
		FINDING:			Absent	Present	Not Assessed
4e.	4e.	**Limb ataxia**	☐0	☐1	☐2	☐3	☐8
4f.	4f.	**Myoclonus**	☐0	☐1	☐2	☐3	☐8
		Myoclonus: a sudden shocklike twitching of muscles or parts of muscles without any rhythm or pattern. Myoclonus, if present, usually begins distally in one upper limb and may spread proximally. The frequency and amplitude of myoclonic jerks typically increase with tactile stimulation (i.e., stimulus-sensitive myoclonus) and action (i.e., action myoclonus). Typically, a peripheral stimulus that induces myoclonic jerks is not associated with an enhanced somatosensory-evoked potential, and the latency from stimulus to jerk is brief — just sufficient to have reached the cortex and returned to the periphery (i.e., approximately 40 milliseconds in the upper limb). These features are distinct from most other forms of cortical reflex myoclonus (which is associated with enhanced somatosensory-evoked potential and a longer stimulus-to-jerk latency).					
4g.	4g.	**Unilateral Somatosensory loss** *(localized to the brain; disregard sensory changes localized to the spinal cord or peripheral nerves)*			☐0	☐1	☐8
		Remote/telephone visit: Since this exam finding cannot be assessed adequately remotely, check "not assessed" if the encounter was conducted via a remote video visit.					
4h.	4h.	**Aphasia** *(disregard complaints of mild dysnomia if not viewed as reflecting a clinically significant change)*			☐0	☐1	☐8
4i.	4i.	**Alien limb phenomenon**			☐0	☐1	☐8
		Involuntary motor activity of a limb in conjunction, often accompanied by a feeling of estrangement from that limb.					
4j.	4j.	**Hemispatial neglect**			☐0	☐1	☐8
		Remote/telephone visit: Since this exam finding cannot be assessed adequately remotely, check "not assessed" if the encounter was conducted via a remote video visit.					
4k.	4k.	**Prosopagnosia**			☐0	☐1	☐8
4l.	4l.	**Simultanagnosia**			☐0	☐1	☐8
4m.	4m.	**Optic ataxia**			☐0	☐1	☐8
		Remote/telephone visit: Since this exam finding cannot be assessed adequately remotely, check "not assessed" if the encounter was conducted via a remote video visit.					
4n.	4n.	**Apraxia of gaze**			☐0	☐1	☐8
4o.	4o.	**Vertical +/- horizontal gaze palsy****			☐0	☐1	☐8
		Remote/telephone visit: Since this exam finding cannot be assessed adequately remotely, check "not assessed" if the encounter was conducted via a remote video visit.					
4p.	4p.	**Dysarthria***			☐0	☐1	☐8
4q.	4q.	**Apraxia of speech**			☐0	☐1	☐8
		For example, difficulty with articulation or prosody/rhythm.					

**UMN findings could include weakness in a pyradmidal pattern, hyper-reflexia, Babinski or Hoffman sign present, or spasticity; LMN findings could include weakness due to neuromuscular dysfunction, muscle wasting/atrophy, or fasciculations. These findings could be consistent with a cerebrovascular insult or with a degenerative disorder such as ALS, PLS, SMA, PSP, CBS, etc.*
***Do not mark Present if only reduction of upgaze is present.*

IVP	FVP	Section 2 – Specific clinical findings	*continued...*

Section 2C – Gait

5.	5.	☐ 0 No abnormal signs in this section are present **(END FORM HERE)** ☐ 1 Yes (***IF YES*** *- complete question 5a and consider completing additional measures as described on page 3)* ☐ 8 Not assessed **(END FORM HERE)**

If any of the gait signs listed below are present, select **1=Yes**. Otherwise, select **0=No** and end form here. If gait signs were not assessed, select **8=Not assessed** and end form here.

5a.	5a.	**Finding***:* ☐ 1 Hemiparetic gait (spastic) ☐ 2 Foot drop gait (lower motor neuron) ☐ 3 Ataxic gait ☐ 4 Apractic magnetic gait ☐ 5 Hypokinetic/parkinsonian gait ☐ 6 Antalgic gait	☐ 7 Other **(SPECIFY):** _____ _____ _____

Section 2D – Additional measures

There are ***<u>several additional clinical measures</u>*** to consider for completion depending on the findings and the suspicion of the clinical syndrome; *these include, but are not limited to, the following:*

a) If there are any features of a movement disorder *(e.g., bradykinesia, tremor, rigidity, postural instability, etc.):*
Consider completing Form B3 UPDRS, or the MDS-UPDRS

b) If there are any features of ALS *(e.g., upper motor neuron dysfunction and/or lower motor neuron dysfunction):*
Consider completing the ALSFRS-R

c) If there are any features of PSP- Richardson's syndrome *(e.g., parkinsonism, postural instability, supranuclear gaze palsy, etc.):*
Consider completing the PSPRS

d) If there are any features of corticobasal syndrome *(e.g., limb rigidity, limb apraxia, myoclonus, dystonia, corticol sensory loss, alien limb phenomenon, etc.):*
Consider completing the PSPRS and/or the CBFS

e) If there are any features of complex visual processing dysfunction (*e.g. hemineglect, visual agnosia, simultanagnosia, optic ataxia, ocular apraxia, apraxia of eyelid opening, etc.):*
Consider completing a standardized measure assessing PCA

f) If there are any features of aphasia or apraxia of speech *(e.g., NIH Stroke Scale, Progressive Aphasia Severity Scale, Western Aphasia Battery, etc.)*:
Consider completing a standardized measure assessing speech and language

g) If there are clinical and/or imaging findings suggesting a vascular contribution to the clinical presentation:
Consider completing NIH Stroke Scale, Hachinski Ischemic Scale, etc.

Section 2E – Glossary of abbreviations

ALS	= *Amyotrophic Lateral Sclerosis*
ALSFRS-R	= *Amyotrophic Lateral Sclerosis Functional Rating Scale–Revised*
CBS	= *Corticobasal Syndrome*
CBFS	= *Cortical Basal ganglia Functional Scale*
LMN	= *Lower Motor Neuron*
MDS-UPDRS	= *Movement Disorders Society - Unified Parkinson's Disease Rating Scale*
PCA	= *Posterior Cortical Atrophy*
PLS	= *Primary Lateral Sclerosis*
PSP	= *Progressive Supranuclear Palsy*
PSPRS	= *Progressive Supranuclear Palsy Rating Scale*
SMA	= *Spinal Muscular Atrophy*
UMN	= *Upper Motor Neuron*
UPDRS	= *Unified Parkinson's Disease Rating Scale*

Coding Guidebook for **Form B9:** Clinician Judgment of Symptoms

INSTRUCTIONS: *This form is to be completed by the clinician. Questions below are not intended for direct administration to participant or co-participant. For all questions the clinician must use their best judgment about whether symptoms are present and make their estimate when symptoms began based on information from participant and co-participant . Check only one box per question.*

The purpose of this Form is to provide a clinical description of the symptoms the participant is currently experiencing and the approximate age of onset of symptoms. The form is meant to describe changes in the participant's cognitive, behavioral, or motor function compared with their usual or customary function in these areas. Typically, changes that would have occurred within the last five to ten years would be recorded on this form, but changes that occurred even earlier could be included, if the clinician judges that they represent a change from a stable level of usual or customary function. Any changes that meet these criteria are part of the current syndrome for the purposes of this form. Cognitive, behavioral, or motor changes that are present, but had their onset many years ago, for instance in childhood or early adulthood, would not be denoted on this form if they are similar in type and severity to what they have always been for this participant. The Form should be completed by a clinician, and conclusions should be based on information obtained from the participant, co-participant, medical records, and/or observation. Results from the neuropsychological test battery (except for the MoCA) and imaging should not be used to determine answers for this Form but may be used to make the clinical or etiologic diagnosis on Forms D1a and D1b.

IVP FVP Section 1 – Changes across domains

Throughout Form B9, "*prior to onset of current syndrome*" refers to the overall cognitive/behavioral/motor syndrome.

Reported by participant

IVP	FVP			
1.	1.	Does the participant report a decline in any cognitive domain *(relative to stable baseline prior to onset of current syndrome)?*	☐ 0 No ☐ 1 Yes	☐ 8 Could not be assessed / participant is too impaired

Decline in cognition refers to changes in the participant's usual or customary memory and non-memory cognitive functions. Select **1=Yes** if the participant reports a current (i.e., recent) decline in memory or non-memory cognitive function. This question refers to cognition only and not behavior, motor, or other non-memory symptoms. If, based upon the clinician's judgment, the participant is too impaired to provide an answer to this question, then select **8 = Could not be assessed/participant is too impaired.**

2.	2.	Does the participant report a change in any motor domain *(relative to stable baseline prior to onset of current syndrome)?*	☐ 0 No ☐ 1 Yes	☐ 8 Could not be assessed / participant is too impaired
3.	3.	Does the participant report the development of any significant neuropsychiatric/ behavioral symptoms *(relative to stable baseline prior to onset of current syndrome)?*	☐ 0 No ☐ 1 Yes	☐ 8 Could not be assessed / participant is too impaired

Given the episodic nature of neuropsychiatric/behavioral symptoms, "stable baseline" refers to the participant's predominant behavioral state prior to the onset of the current syndrome (which could be cognitive, neuropsychiatric / behavioral or both).

Reported by co–participant

4.	4.	Does the co-participant report a decline in any cognitive domain *(relative to stable baseline prior to onset of current syndrome)?*	☐ 0 No ☐ 1 Yes	☐ 8 There is no co-participant

Decline refers to cognitive change(s) in the participant's usual or customary memory and non-memory cognitive functions. Select **1 = Yes** if the co-participant reports a current (i.e., recent) decline in the participant's cognitive function(s). This question refers to cognition only and not behavior, motor, or other non-memory symptoms. Every effort should be made to have a co-participant present at UDS visits; however, if there is no co-participant, select **8 = There is no co-participant**.

5.	5.	Does the co-participant report a change in any motor domain *(relative to stable baseline prior to onset of current syndrome)?*	☐ 0 No ☐ 1 Yes	☐ 8 There is no co-participant
6.	6.	Does the co-participant report the development of any significant neuropsychiatric/ behavioral symptoms *(relative to stable baseline prior to onset of current syndrome)?*	☐ 0 No ☐ 1 Yes	☐ 8 There is no co-participant

Given the episodic nature of neuropsychiatric/behavioral symptoms, "stable baseline" refers to the participant's predominant behavioral state prior to the onset of the current syndrome (which could be cognitive, neuropsychiatric / behavioral or both).

IVP | FVP — Section 1 – Changes across domains *continued...*

Reported by clinician

IVP	FVP		
7.	7.	Does the participant have any neuropsychiatric/behavioral symptoms, decline in any cognitive domains, or changes in any motor domains?	☐0 No **(END FORM HERE)** ☐1 Yes

Cognitive decline refers to changes in the participant's usual or customary memory or non-memory cognitive abilities reported or observed at the current visit. Neuropsychiatric/behavioral symptoms refers to meaningful changes from the predominant behavioral state prior to the onset of the current syndrome.

If the clinician is certain that there has been no meaningful (i.e., clinically significant) neuropsychiatric/behavioral change and no decline in the participant's memory or non-memory cognitive abilities, select **0 = No** and END THE FORM HERE.

If the clinician is certain that there has been a meaningful decline or change, select **1 = Yes** and complete questions 8 - 10.

In the following sections record the phenotype of clinically meaningful symptoms or absence of a **history of these symptoms**, as determined by the clinician's best judgment following the medical history interview with the participant and co-participant.

Section 2 – Cognitive impairment

Consider if the participant currently is meaningfully impaired, **relative to stable baseline prior to onset of current syndrome**:

8.	8.	Based on the clinician's judgment, is the participant currently experiencing meaningful impairment in cognition?	☐0 No **(SKIP TO QUESTION 11)** ☐1 Yes

9.	9.	Indicate whether the participant is meaningfully impaired in the following cognitive domains or has fluctuating cognition:			
		Cognitive	**No**	**Yes**	**Unknown**
9a.	9a.	**Memory** — Does the participant forget conversations or dates, repeat questions or statements, or misplace things more than usual?	☐0	☐1	☐9
9b.	9b.	**Orientation** — Does the participant have trouble knowing the day, month, and year, forget names of people they know well, get lost in familiar locations, or not recognize familiar locations?	☐0	☐1	☐9
9c.	9c.	**Executive function *(judgment, planning, and problem–solving)*** — Does the participant have trouble planning complex activities like trips, financial transactions, parties, or group meetings?	☐0	☐1	☐9
9d.	9d.	**Language** — Does the participant have hesitant speech, have trouble finding words, use inappropriate words without self-correction, or have trouble with speech comprehension?	☐0	☐1	☐9
9e.	9e.	**Visuospatial function** — Does the participant have difficulty interpreting visual stimuli or finding their way around in familiar environments?	☐0	☐1	☐9
9f.	9f.	**Attention/concentration** — Does the participant have a short attention span or limited ability to concentrate? Are they easily distracted?	☐0	☐1	☐9
9g.	9g.	**Fluctuating cognition** — Does the participant exhibit pronounced variation in attention and alertness, noticeably over hours or days—for example, long lapses or periods of staring into space, or times when their ideas have a disorganized flow?	☐0	☐1	☐9
9h.	9h.	**Other (SPECIFY):** _____	☐0	☐1	

For Questions 9a–9g, select **9 = Unknown** only if the answer cannot be determined based upon information gathered from the participant, co-participant, medical records, and/or observation. If the participant exhibits a meaningful decline in any ability (or abilities) other than those listed, select **1 = Yes** for Question 9h and briefly describe under "Other (specify)".

9i.	9i.	If any of the cognitive symptoms in 9a–9h are present, at what age did they begin? (*The clinician must use their best judgment to estimate an age of onset. If multiple symptoms with different ages of onset are identified, denote the age of the earliest symptom.)* **(777 = age provided at previous UDS visit)**	___ ___ ___

Cognitive decline refers to changes in the participant's usual or customary memory or non-memory cognitive abilities reported or observed at the current visit. Age of onset of cognitive decline should correspond to the predominant symptom that was first recognized as a change in the participant's cognitive abilities.

If the exact age is unknown, the clinician should estimate to the nearest decade. For example, if the co-participant says that cognitive decline started in the participant's 50s or 60s, estimate age 55 or 60.

IVP	FVP	Section 2 – Cognitive impairment				*continued...*

				No	Yes	Unknown
10.	10.	**Mode of onset of cognitive impairment:** Indicate the mode of onset for the **most prominent** cognitive problem that is causing the participant's complaints and/or affecting the participant's function.	☐ 1 Gradual ☐ 2 Subacute ☐ 3 Abrupt	☐ 4 Other **(SPECIFY):** _____ ☐ 99 Unknown		

This question refers to the pattern of onset of the cognitive change (i.e., when change in cognition was first noticed). The clinician should choose the option that most closely resembles the pattern of onset of the participant's cognitive symptom(s).

If the mode of onset was other than those listed, select **4 = Other (specify)** and briefly describe in the space provided.

Select **99 = Unknown** only if no information is available to allow the clinician to ascertain the mode of onset.

Section 3 – Neuropsychiatric symptoms and behavioral changes

Consider if the participant manifests – ***in the last month*** – clinically meaningful neuropsychiatric symptoms or change in behavior **relative to stable baseline** (i.e., predominant behavioral state prior to the onset of the current syndrome). Clinically meaningful change refers to symptoms or changes that are evident most days in a given four-week period.

11.	11.	Based on the clinician's judgment, does the participant manifest clinically meaningful neuropsychiatric symptoms or meaningful change in behavior?	☐ 0 No **(SKIP TO QUESTION 14)** ☐ 1 Yes		

Neuropsychiatric symptoms or changes in behavior refers to significant symptoms or meaningful change or decline from the participant's usual or customary (predominant) behavioral state prior to the onset of the current syndrome.

If the clinician is certain that there have been no neuropsychiatric symptoms or meaningful (i.e., clinically significant) in the participant's behavior, select **0 = No** and skip to Question 14.

If the clinician is certain that there has been a meaningful decline, select **1 = Yes** and complete Questions 12–13.

12.	12.	Specify the phenotype of clinically meaningful neuropsychiatric symptoms or meaningful change in behavior that has manifested ***in the last month***.			

The responses below should reflect the clinician's best judgement taking into account information obtained from the participant, co-participant, medical records, and/or observation, including any neuropsychiatric or mood rating scales administered during this visit.

			Mood, motivation, and agitation	No	Yes	Unknown

QUESTIONS 12a – 12u: If the symptoms assessed in Questions 12a – 12u are reported or observed to reflect the participant's condition at this clinical evaluation based upon information gathered from the participant, co-participant, medical records, and/or observation, then select **1=Yes**; otherwise, select **0=No**. Select **9=Unknown** only if the answer cannot be determined based upon information gathered from the participant, co-participant, medical records, and/or observation.

12a.	12a.		**Apathy/withdrawal** — Has the participant lost interest in the world around them, lost interest in doing things, or lack motivation for starting new activities?	☐ 0	☐ 1	☐ 9
12b.	12b.		**Depressed mood** — Does the participant seem sad or depressed, or say that they feel sad or depressed?	☐ 0	☐ 1	☐ 9
12c.	12c.		**Anxiety** — Does the participant seem very nervous, worried, or frightened for no apparent reason? Do they seem very tense or fidgety? Do they seem afraid to be apart from caregivers or from others that they trust?	☐ 0	☐ 1	☐ 9
12d.	12d.		**Euphoria** — Does the participant seem too cheerful or too happy for no reason, manifest a persistent and abnormally good mood, or find humor where others do not?	☐ 0	☐ 1	☐ 9
12e.	12e.		**Irritability** — Does the participant get irritated and easily disturbed? Are their moods very interchangeable? Are they abnormally impatient?	☐ 0	☐ 1	☐ 9
12f.	12f.		**Agitation** — Is the participant easily distressed or angered, or hard to handle, or uncooperative, or resistive to care or to help from others?	☐ 0	☐ 1	☐ 9
12g.	12g.		If any of the mood–related behavioral changes in 12a–12f are present, at what age did they begin? (*The clinician must use their best judgment to estimate an age of onset. If multiple symptoms with different ages of onset are identified, denote the age of the earliest symtpom.)* **(777 = age provided at previous UDS visit)**	___ ___ ___		

IVP	FVP	Section 3 – Neuropsychiatric symptoms and behavioral changes *continued...*			
		Psychosis and impulse control	**No**	**Yes**	**Unknown**
12h.	12h.	**Visual hallucinations** - Does the participant exhibit visual perceptions without a stimulus?	☐0	☐1	☐9
12h1.	12h1.	**IF YES,** do their hallucinations include patterns that are not definite objects, such as pixelation of flat uniform surfaces?	☐0	☐1	☐9
12h2.	12h2.	**IF YES,** do their hallucinations include well-formed and detailed images of objects or people, either as independent images or as part of other objects?	☐0	☐1	☐9
12i.	12i.	**Auditory hallucinations** - Does the participant exhibit auditory perceptions without a stimulus?	☐0	☐1	☐9
12i1.	12i1.	**IF YES,** do the auditory hallucinations include simple sounds like knocks or other simple sounds?	☐0	☐1	☐9
12i2.	12i2.	**IF YES,** do the auditory hallucinations include complex sounds like voices speaking words, or music?	☐0	☐1	☐9
12j.	12j.	**Delusions** - Does the participant have fixed, idiosyncratic beliefs that are not true? For example, insisting that others are trying to harm them or steal from them? Have they said that family members or staff are not who they say they are, or that the house is not their home?	☐0	☐1	☐9
		Idiosyncratic refers to ideas that are held uniquely by the participant that do not reflect ideas shared by the participant's cultural, religious or social environment/group.			
12k.	12k.	**Aggression** — Does the participant shout angrily, slam doors, attempt to hit or hurt others, or exhibit other verbally or physically aggressive behaviors?	☐0	☐1	☐9
12l.	12l.	If any of the psychosis and impulse control –related behavioral changes in 12h–12k are present, at what age did they begin? (*The clinician must use their best judgment to estimate an age of onset. If multiple symptoms with different ages of onset are identified, denote the age of the earliest symtpom.)* **(777 = age provided at previous UDS visit)** ___ ___ ___			
		Personality	**No**	**Yes**	**Unknown**
12m.	12m.	**Disinhibition** — Does the participant act impulsively without thinking, say things that are not usually done or said in public, or do things that are embarrassing to caregivers or others, or do they talk personally to strangers or have disregard for personal hygiene?	☐0	☐1	☐9
12n.	12n.	**Personality change** — Does the participant exhibit bizarre behavior or behavior uncharacteristic of the participant, such as unusual collecting, suspiciousness *(without delusions),* unusual dress, or unusual eating behaviors?	☐0	☐1	☐9
12o.	12o.	**Loss of empathy** — Does the participant fail to take others' feelings into account?	☐0	☐1	☐9
12p.	12p.	**Obsessions and/or compulsions** — Does the participant repeatedly and excessively focus on particular ideas or activities, or have they developed new habits, like physical behaviors or stereotypical verbal phrases?	☐0	☐1	☐9
12q.	12q.	**Explosive anger** — Does the participant have a "short fuse"? Do they display explosive outbursts of anger or rage?	☐0	☐1	☐9
12r.	12r.	**Substance use** — Does the participant currently show evidence of excessive consumption of recreational, psychoactive, or typically abused substances *(substantial increase compared with prior habits, and beyond medical necessity if prescribed substance)*?	☐0	☐1	☐9
12r1.	12r1.	**IF YES,** record substance(s) involved: *(Check all that apply)* **12r1a.** ☐1 Alcohol **12r1b.** ☐1 Sedative/hypnotic **12r1c.** ☐1 Opiate **12r1d.** ☐1 Cocaine **12r1e.** ☐1 Cannabis **12r1f.** ☐1 Other **(SPECIFY):** _____			
12s.	12s.	If any of the personality–related behavioral changes in 12m–12r are present, at what age did they begin? (*The clinician must use their best judgment to estimate an age of onset. If multiple symptoms with different ages of onset are identified, denote the age of the earliest symtpom.)* **(777 = age provided at previous UDS visit)** ___ ___ ___			

IVP	FVP	Section 3 – Neuropsychiatric symptoms and behavioral changes *continued...*			
		REM sleep	**No**	**Yes**	**Unknown**
12t.	12t.	**REM sleep behavior disorder** — While sleeping, does the participant appear to repeatedly act out their dreams *(e.g., punch or flail their arms, shout, or scream)*?	☐0	☐1	☐9
12t1.	12t1.	**IF YES,** at what age did the dream enactment behavior begin? (*The clinician must use their best judgment to estimate an age of onset.*) **(777 = age provided at previous UDS visit)**	___ ___ ___		
12t2.	12t2.	Was REM sleep behavior disorder confirmed by polysomnography?	☐0	☐1	☐9
		Other	**No**	**Yes**	**Unknown**
12u.	12u.	**Other behavioral changes (SPECIFY):** _____	☐0	☐1	

If the participant exhibits a meaningful decline in any behavior other than those listed, select **1 = Yes** for Question 12u and briefly describe under "Other".

13.	13.	**Overall mode of onset for behavioral changes:** Indicate the mode of onset for the **most prominent** behavioral problem that is causing the participant's complaints and/or affecting the participant's function.	☐1 Gradual ☐2 Subacute ☐3 Abrupt	☐4 Other **(SPECIFY):** _____ ☐99 Unknown

The clinician should choose the option that most closely resembles the mode of onset of behavioral symptoms for the participant.

If the mode of onset was other than those listed, select **4 = Other** and briefly describe in the space provided.

Select **99 = Unknown** only if no information is available to allow the clinician to ascertain the mode of onset.

Section 4 – Motor changes

Consider if the participant currently has meaningful change in motor function **that represents a change relative to a stable baseline prior to the current syndrome and is potentially due to a disorder affecting the central nervous system:**

14.	14.	Based on the clinician's judgment, is the participant currently experiencing any meaningful changes in motor function?	☐0 No **(SKIP TO QUESTION 19)** ☐1 Yes

Decline or changes in motor/movement refers to meaningful decline from the participant's usual or customary level (for example, as evidenced by gait disorder, falls, tremor, and slowness) reported or observed at the current visit.

If the clinician is certain that there have been no meaningful changes or decline in motor or movement, select **0 = No** and skip to Question 19.

If the clinician is certain that there has been a meaningful decline, select **1 = Yes** and complete Questions 15 –18.

15.	15.	Indicate whether the participant has meaningful change in motor function:			
		Motor	**No**	**Yes**	**Unknown**

QUESTIONS 15a – 15h: If the symptoms assessed in Questions 15a – 15h are reported or observed to reflect the participant's condition at this clinical evaluation based upon information gathered from the participant, co-participant, medical records, and/or observation, then select **1 = Yes**; otherwise, select **0 = No**. Select **9 = Unknown** only if the answer cannot be determined based upon information gathered from the participant, co-participant, medical records, and/or observation.

15a.	15a.	**Gait disorder** — Has the participant's walking changed, not specifically due to arthritis, injury, or peripheral neuropathy? Are they unsteady, or do they shuffle when walking, have little or no arm-swing, or drag a foot?	☐0	☐1	☐9
15b.	15b.	**Falls** — Has the participant had an increase in frequency of falls compared with their stable baseline prior to the current syndrome?	☐0	☐1	☐9
15c.	15c.	**Slowness** — Has the participant noticeably slowed down in walking, moving, or writing by hand, other than due to an injury or illness?	☐0	☐1	☐9
15d.	15d.	**Tremors** — Has the participant had rhythmic shaking, especially in the hands, arms, legs, head, mouth, or tongue?	☐0	☐1	☐9
15e.	15e.	**Limb weakness** — Has the participant noticed a change *(abrupt or gradual)* in limb function such that an arm and/or leg is weak compared to their prior baseline?	☐0	☐1	☐9

IVP	FVP	Section 4 – Motor changes				*continued...*
15f.	15f.	**Change in facial expression** — Has the participant's facial expression changed or become more "wooden," or masked and unexpressive?	☐0	☐1	☐9	
15g.	15g.	**Change in speech** — Has the participant noted a change in speech (*abrupt or gradual)* such that speech is slurred, or the ability to articulate the tongue and lips to form words and sentences has declined compared to their baseline?	☐0	☐1	☐9	
15h.	15h.	If changes in motor function are present in 15a–15g, at what age did they begin? (*The clinician must use their best judgment to estimate an age of onset. If multiple symptoms with different ages of onset are identified, denote the age of the earliest symtpom.)* **(777 = age provided at previous UDS visit)**	___ ___ ___			

Age of onset of motor symptoms should correspond to the predominant symptom that was first recognized as a change in the participant's motor function (Question 15 above). If the exact age is unknown, the clinician should estimate to the nearest decade. For example, if the co-participant says that motor symptoms started in the participant's 50s or 60s, estimate age 55 or 60. Do not enter the age of diagnosis (if applicable).

16.	16.	**Mode of onset for motor changes:** Indicate the mode of onset for the **most prominent** motor problem that is causing the participant's complaints and/or affecting the participant's function.	☐1 Gradual ☐2 Subacute ☐3 Abrupt	☐4 Other **(SPECIFY):** _____ ☐99 Unknown

Select the option that most closely resembles the mode of onset of motor symptoms for the participant.
If the mode of onset was other than those listed, select **4 = Other (specify)** and briefly describe in the space provided.
Select **99 = Unknown** only if no information is available to allow the clinician to ascertain the mode of onset.

			No	Yes	Unknown
17.	17.	Were changes in motor function suggestive of parkinsonism?	☐0	☐1	☐9

Select **1 = Yes** if one or more of the following symptoms is present: gait disorder, falls, slowness, tremor, change in facial expression, etc.

18.	18.	Were changes in motor function suggestive of amyotrophic lateral sclerosis (ALS) *(e.g., changes in muscle strength, or muscle twitches in one or more limbs, or slurred speech)*?	☐0	☐1	☐9	

Select **1 = Yes** if one or more of the following symptoms is present: weakness and/or muscle twitches in one or more limbs, slurred speech, etc.

Section 5 – Overall course of decline and predominant domain

19.	19.	Overall course of decline of cognitive/behavioral/motor syndrome:	☐1 Gradually progressive ☐2 Stepwise ☐3 Static ☐4 Fluctuating ☐5 Improved ☐8 Not applicable ☐9 Unknown

Select the appropriate number to indicate the overall decline in cognitive/behavioral/motor functions during the course of the illness. Fluctuating course does not refer to the short-term fluctuations that are part of DLB. Select **9 = Unknown** only if no information is available to allow the clinician to describe the overall course of the syndrome.

20.	20.	Indicate the **predominant** domain that was first recognized as changed in the participant:	☐1 Cognition ☐2 Behavior ☐3 Motor function ☐8 Not applicable ☐9 Unknown

Select the appropriate number to indicate which domain appears to be the first to have changed in the participant. Choose only one domain as predominantly changing first, based on the clinician's best judgment. Select **9 = Unknown** only if no information is available to allow the clinician to describe the predominantly changed domain.

GUIDANCE FOR COMPLETING D1a AND D1b

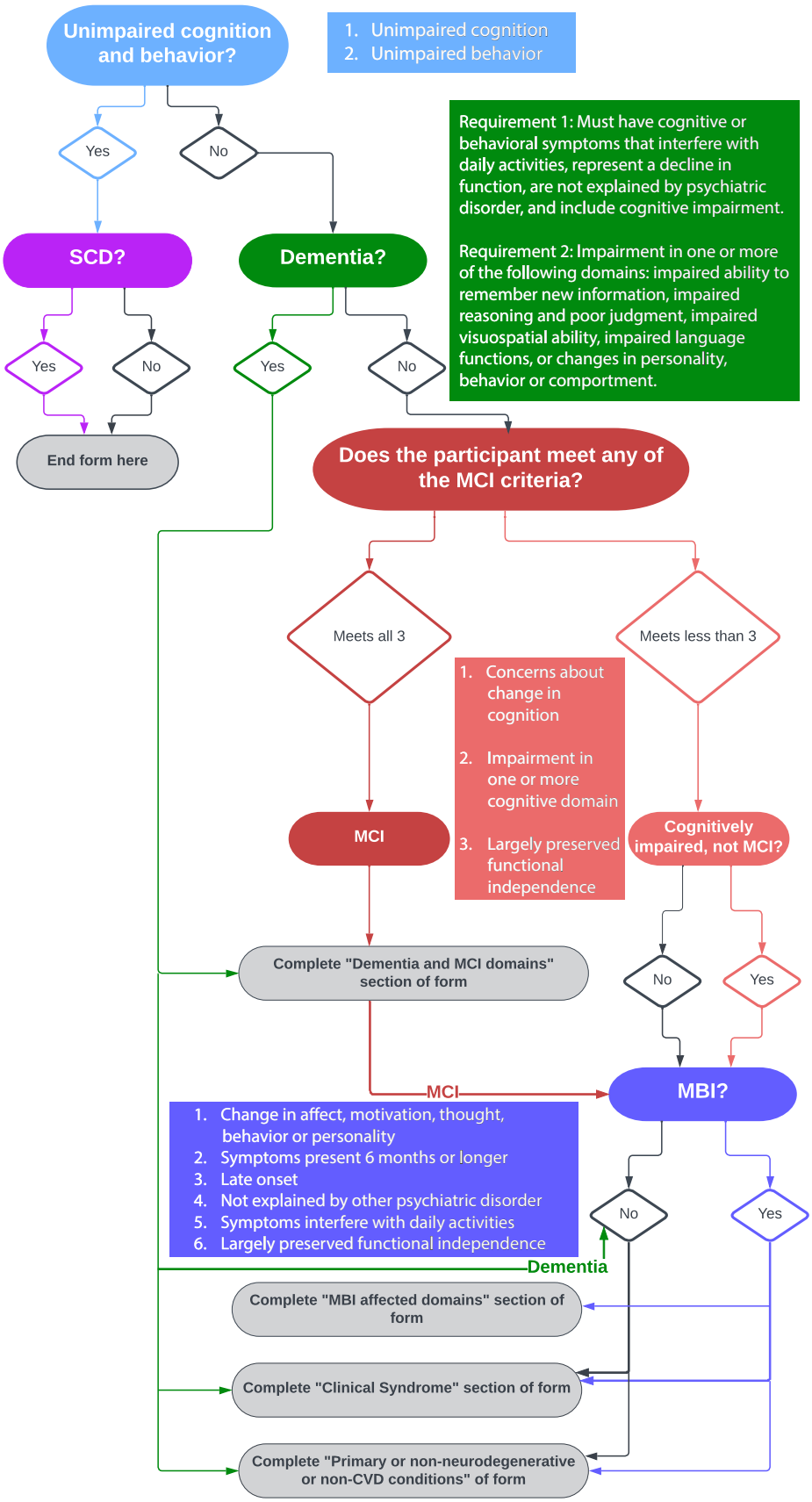
These two forms can be done flexibly based on the Center's workflow and without restrictive requirements.

One suggested practice is to have clinicians provisionally complete D1a at the time clinical assessment. D1a would be reviewed at consensus (along with the now available neuropsychological data) and the clinical staging and syndrome can be updated as needed. This would be followed by completing D1b after considering any available biomarker or imaging data.

Alternatively, Centers can complete both D1a and D1b at consensus. In this scenario, a good practice would be to review clinical information and neuropsychological data first while completing D1a (blind to biomarkers) followed by completion of D1b after reviewing any available biomarker or imaging data.

Coding Guidebook for **Form D1a:** Clinical Syndrome

INSTRUCTIONS: *This form is to be completed by the clinician. Check only <u>one</u> box per question. The flowchart below provides an overview of Form D1a and the sections you fill out for each diagnosis.*



IVP	FVP	
1.	1.	Diagnosis method—*responses in this form are based on diagnosis by a:* ☐1 Single clinician ☐2 Formal consensus panel ☐3 Other *(e.g., Two or more clinicians or other informal group)*

Select **2=A formal consensus panel** (preferred method) if the diagnosis was made by a group of clinicians (e.g., neurologists, psychiatrists, neuropsychologists, geriatricians, advanced practice providers, etc.) who convene on a regular basis to discuss and decide upon the final diagnosis. It is preferable that each formal consensus panel have at least one neuropsychologist and one physician present. With new MBI criteria, psychiatry input is recommended. In the case of an ad hoc consensus group (e.g., two or more clinicians or other informal group), select **3=Other**.

Section 1 – Level of impairment – *Unimpaired cognition, SCD, MCI/MBI, or dementia*

2.	2.	**Does the participant have:** 1. Unimpaired cognition *(e.g., cognitive performance and functional status (i.e., CDR) judged to be unimpaired)?* *AND* 2. Unimpaired behavior *(i.e., the participant does not exhibit behavior sufficient to diagnose MBI - see MBI section starting at Q7) or dementia due to FTLD or LBD and/or FTLD behavior and language domains=0?* ☐0 No **(SKIP TO QUESTION 3)** ☐1 Yes **(CONTINUE TO QUESTION 2a)** *Note: For those with longstanding cognitive impairment that does not represent a decline from their usual functioning, consider checking* **Question 5b** *for a diagnosis of* **"Cognitively Impaired, Not MCI/dementia"**.

Select **1= Yes** if the participant has normal cognition and does not have behavioral symptoms or changes sufficient to diagnose MBI, MCI or dementia due to AD, FTD or DLB. "Unimpaired" is defined as: (1) Unimpaired cognition (for example, cognitive performance and functional status (i.e., CDR) judged to be unimpaired); and (2) Unimpaired behavior (i.e., the participant does not exhibit behavioral symptoms or changes sufficient to diagnose MBI, MCI, or dementia due to any cause such as AD, FTLD or LBD). Clinical judgment should be used in situations where testing and clinical history or observation are conflicting to determine a stage.

Subjective Cognitive Decline

2a.	2a.	Does the participant report 1) significant concerns about changes in cognition **AND** 2) no neuropsychological evidence of decline **AND** 3) no functional decline?	☐0 No **(END FORM HERE)** ☐1 Yes

Use your best clinical judgment based on your impression of the participant's complaints and your review of the participant's response to concerns about changes in cognition (refer to UDSv4 form A1, Section 2, Questions 18-20). If your Center administers the optional ECog or CCI or other measures, these may also be considered in responding to Question 2a. Considering all available information (3 SCD UDSv4 self report items, interview and exam, and optional ECog or CCI, if obtained), does the participant appear to perceive their cognitive functioning as having declined, especially over the past few years. Concerns would be regarded as "significant" if the participant a) sought medical attention for this issue, b) expresses concern, worry or anxiety related to perceived cognitive decline, or c) a knowledgeable informant and/or clinician also perceives changes in cognitive function. Clinicians less familiar with this area may find it helpful to review "The characterisation of subjective cognitive decline" by Jessen et al. (Lancet Neurology 2020; https://doi.org/10.1016/S1474-4422(19)30368-0).

2b.	2b.	As a clinician, are you confident that the subjective cognitive decline is clinically meaningful?	☐0 No **(END FORM HERE)** ☐1 Yes **(END FORM HERE)**

Provide a level of confidence based on the available information and your clinical judgement that clinically meaningful subjective cognitive decline is present.

Dementia criteria

Requirement #1:
Participant has cognitive or behavioral (neuropsychiatric) symptoms that meet <u>all of the following criteria</u>:

- Interfere with ability to function as before at work or at usual activities
- Represent a decline from previous levels of functioning
- Are not explained by delirium or major psychiatric disorder
- Include cognitive impairment detected and diagnosed through a combination of: 1) history-taking; 2) objective assessment *(bedside or neuropsychological testing)*

Requirement #2:
Participant must have impairment in <u>one* or more</u> of the following domains:

- Impaired ability to acquire and remember new information
- Impaired reasoning and handling of complex tasks, poor judgment
- Impaired visuospatial abilities
- Impaired language functions
- Changes in personality, behavior, or comportment

** In the event of single-domain impairment (e.g., language in PPA, behavior in bvFTD, visuospatial in posterior cortical atrophy, etc.), the participant must not fulfill criteria for MCI.*

IVP	FVP	Section 1 – Level of impairment – *Unimpaired cognition, SCD, MCI/MBI, or dementia*	*continued...*
3.	3.	Does the participant meet criteria for dementia? ☐0 No **(CONTINUE TO QUESTION 4)** ☐1 Yes **(SKIP TO QUESTION 6a)**	

Review the criteria listed above Question 3 to determine whether the participant meets the criteria for all-cause dementia. These criteria are adapted from the McKhann all-cause dementia criteria (2011) to allow a single domain to be affected for a diagnosis of dementia.

MCI core clinical criteria

Check all criteria that apply in Q4.

4.	4.	☐1 Clinical concern about decline in cognition compared to participant's prior level of lifelong or usual cognitive function *(e.g., based on input from participant, co-participant, and/or the clinician's judgment, CDR SB 0.5+, etc.)* ☐1 Impairment in one or more cognitive domains, compared to participant's estimated prior level of lifelong or usual cognitive function, or supported by objective longitudinal neuropsychological evidence of decline ☐1 Largely preserved functional independence OR functional dependence that is not related to cognitive decline *(e.g., based on clinical judgment)*

Please check all criteria that apply. If all three criteria are checked, choose **1=Yes (MCI)** for Q4b. If fewer than 3 criteria are met, choose **0=No** for Q4b and consider checking Question 5b for a diagnosis of "Cognitively Impaired, Not MCI/dementia" or a diagnosis of MBI on Question 7.

Refer to the criteria described in: *Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, Fox NC, Gamst A, Holtzman DM, Jagust WJ, Petersen RC, Snyder PJ, Carrillo MC, Thies B, Phelps CH. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement. 2011 May;7(3):270-9. doi: 10.1016/j.jalz.2011.03.008. Epub 2011 Apr 21. PMID: 21514249; PMCID: PMC3312027.*

If all three criteria are checked, choose **1=Yes** *for Q4b. If less than 3 criteria are met, choose* **0=No** *for Q4b. If only some of the criteria from Q4 are checked, continue to Q5.*

4b.	4b.	Does the participant meet all three of the above criteria for MCI (amnestic or non-amnestic)?	☐0 No **(CONTINUE TO QUESTION 5)** ☐1 Yes **(SKIP TO QUESTION 6a)**

Cognitively impaired, not MCI/dementia

The purpose of the "Cognitively impaired, not MCI/dementia" category is to capture those individuals with evidence of cognitive impairment or decline who do not meet formal MCI criteria.

Check all applicable criteria for cognitively impaired, not MCI/dementia in Q5, *using any relevant data.*

5.	5.	☐1 Evidence of functional impairment *(e.g., CDR SB>0 and/or FAS>0)*, but available cognitive testing is judged to be normal ☐1 Cognitive testing is abnormal but no clinical concern or functional decline (e.g., CDR SB=0 and FAS=0) ☐1 Longstanding cognitive difficulties, not representing a decline from their usual function *(e.g., early developmental differences remote TBI, other medical condition with clear effects on cognition)* ☐1 Other **(SPECIFY):** _____

Please check all criteria that apply. If the participant has any conditions contributing to impairment (*e.g., substance abuse or medications*), these should be identified in Section 3.

If the cognitive impairment is of recent onset (*i.e., not longstanding impairment*), indicate the cognitive symptom(s) in Form B9 - Clinician Judgment of Symptoms.

5b.	5b.	Does the participant meet any criteria for cognitively impaired, not MCI/dementia?	☐0 No **(SKIP TO QUESTION 7)** ☐1 Yes **(SKIP TO QUESTION 7)**

Affected Domains - Dementia and MCI

Choose domains that are impaired at the current visit based on clinical judgment informed by clinical history and neuropsychological testing. Select one or more as **Impaired**; all others will default to **unimpaired** in the NACC database.

Note on ***behavior changes***: For patients with *dementia* who have behavior changes, record the presence of behavioral changes here (not in the following MBI section) by marking Q6f as **Impaired** and Q7 as **0 = No**. For behavioral changes in the context of an MCI (or as an isolated) symptom, consider a diagnosis of MBI in the next section.

			Impaired
6a.	6a.	Memory	☐ 1
6b.	6b.	Language	☐ 1
6c.	6c.	Attention	☐ 1
6d.	6d.	Executive	☐ 1
6e.	6e.	Visuospatial	☐ 1
6f.	6f.	Behavioral *(for participants with dementia only; see MBI for MCI participants)*	☐ 1
6g.	6g.	Apraxia	☐ 1

Mild Behavioral Impairment (MBI) core clinical criteria

Neuropsychiatric and other behavioral symptoms are common in ADRC participants as recorded in several ratings such as GDS and NPI-Q. Multiple studies have shown that their presence accelerates onset of MCI and or dementia. Mild Behavioral Impairment (MBI) is a novel syndrome that can be the prodrome of many types/etiologies of dementia. The purpose of this section is to further classify the phenotype and possible causes of neuropsychiatric and other behavioral symptoms recorded in other sections of the UDS4. The first step here is to assess whether or not such symptoms meet diagnostic criteria for MBI and to characterize the MBI phenotype (e.g., affective, motivational, etc.). Later in the form the form rater(s) are asked to assess the contribution of specific DSM-5-TR psychiatric disorders to the emergence of these symptoms. ***For these discussions, if possible, it is recommended that a (geriatric) psychiatrist be involved in these case discussions and reference to DSM-5-TR be available.*** All Centers should have access through their online library access to the DSM-5TR so as to review the relevant DSM-5-TR criteria.

Begin with review of neuropsychiatric and other behavioral symptoms rated on the GDS, NPI-Q, form B9 (or any other relevant symptom ratings that your Center uses such as the Mild Behavioral Impairment checklist (MBI-C)). **If no such symptoms are recorded a diagnosis of MBI cannot be made and you can check "No" to question 7 and skip to question 8.**

If neuropsychiatric and other behavioral symptoms are recorded on one or more of these ratings these should be the basis for considering a diagnosis of MBI. Specifically, based on these ratings, assess whether the participant, co-participant, or clinician **identify 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. If the answer is **NO, a diagnosis of MBI cannot be made and you can check "No" to question 7 and skip to question 8.**

If **YES** to the above, to make a diagnosis of MBI ***ALL*** of the following must be true about these symptoms (using best clinical judgment):

- They have been present at least intermittently for the last six months or longer.
- They have onset later in life (i.e., age > ~50, unless early onset neurodegenerative syndrome is suspected).
- They CANNOT be explained by delirium, other psychiatric disorder by DSM –5TR criteria (including persistently symptomatic longstanding disorder ***OR*** recurrent long-standing disorder).
- They interfere with at least one of these: work, interpersonal relationships, social activities.
- There is largely preserved independence in other functional abilities (no change from prior manner/level of functioning or uses minimal aids or assistance).

For additional training information, please refer to the following clinical training webinars on the NACC website:

- Mild Behavioral Impairment Webinar
- Operationalizing "Impaired, not MCI" in UDSv4
- D1a Form Training

- 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, unless early onset neurodegenerative syndrome is suspected)
- Not explained by delirium, other psychiatric disorder by DSM criteria (including recent onset, longstanding or recurrence of longstanding disorder).
- 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.	7.	Does the participant meet criteria for MBI? *(If participant meets criteria for dementia an MBI diagnosis is excluded.)*	☐ 0 No **(SKIP TO QUESTION 8)** ☐ 1 Yes **(CONTINUE TO QUESTION 7a)**

Review the criteria listed above Question 7 to determine whether the participant meets the criteria for MBI. If a participant meets the criteria for dementia in Question 3, select **0 = No** for Q7.

IVP FVP Section 1 – Level of impairment – *Unimpaired cognition, SCD, MCI/MBI, or dementia* *continued...*

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
7a.	7a.	Motivation *(e.g., apathy symptoms on Form B9)*	☐ 0	☐ 1
7b.	7b.	Affective regulation *(e.g., anxiety, irritability, depression, and/or euphoria symptoms on Form B9)*	☐ 0	☐ 1
7c.	7c.	Impulse control *(e.g., obsessions/compulsions, personality change, and/or substance abuse symptoms on Form B9)*	☐ 0	☐ 1
7d.	7d.	Social appropriateness *(e.g., disinhibition, personality change, and/or loss of empathy symptoms on Form B9)*	☐ 0	☐ 1
7e.	7e.	Thought content/perception *(e.g., delusions and/or hallucinations on Form B9)*	☐ 0	☐ 1

Section 2 – Clinical syndrome

The purpose of Section 2 is to assign a predominant clinical syndrome to participants with dementia and, when appropriate MCI or MBI, using all available clinical, exam, and neuropsychiatric data. This should be done using clinical information and cognitive/neuropsychological testing, **ideally *without* reference to biomarker data** (which is incorporated into the Etiological Diagnoses section in Form D1b). This is not always possible and thus Q9 allows centers to record when biomarker data is known and may have influenced the clinical diagnosis.

A single syndrome should be assigned and clinical judgment used to determine the most prominent symptoms. If middle or late stages, use the initial presenting issues to determine a predominant syndrome (*i.e., amnestic vs dysexecutive, which usually co-occur*).

8.	8.	Is there a predominant clinical syndrome? *Note that the participant may not meet any clinical criteria or may not have a predominant syndrome (for instance, this is common for MCI and "impaired, not MCI"). In this case, select "No."*	☐ 0 No **(SKIP TO QUESTION 10)** ☐ 1 Yes

Select the predominant syndrome as present; all others will defualt to Absent in the NACC database.

			Present
8a.	8a.	Amnestic predominant syndrome	☐ 1

A clinical syndrome defined by the presence of persistent, predominant, and progressive decline for over 6 months in episodic anterograde memory function. Objective deficits on delayed memory recall testing are a central feature. Other cognitive domains may also be involved but did not precede the primary episodic anterograde memory deficit.

Exclusion criteria include a history of sudden onset or active primary psychiatric conditions that could better explain episodic memory testing.

Dubois B, Feldman HH, Jacova C, Dekosky ST, Barberger-Gateau P, Cummings J, Delacourte A, Galasko D, Gauthier S, Jicha G, Meguro K, O'brien J, Pasquier F, Robert P, Rossor M, Salloway S, Stern Y, Visser PJ, Scheltens P. Research criteria for the diagnosis of Alzheimer's disease: revising the NINCDS-ADRDA criteria. Lancet Neurol. 2007 Aug;6(8):734-46. doi: 10.1016/S1474-4422(07)70178-3. PMID: 17616482.

8b.	8b.	Dysexecutive predominant syndrome	☐ 1

A clinical syndrome defined by the presence of persistent, predominant and progressive decline for over 6 months in any core executive cognitive function (i.e. working memory, cognitive flexibility and/or inhibition) in the absence of predominant behavioural features (e.g. would not meet criteria for the clinical syndrome of behavioural variant frontotemporal dementia).

Evidence of impaired executive functions are obtained by participant and/or co-participant reports in conjunction with formal evaluation of cognitive performance on mentally effortful tasks that require conscious active manipulation of abstract and/or simultaneous information streams.

Exclusion criteria include a history of sudden onset or other medical conditions severe enough to account for related symptoms (e.g. primary psychiatric, cerebrovascular, infectious, toxic, inflammatory or metabolic disorders).

Townley RA, Graff-Radford J, Mantyh WG, Botha H, Polsinelli AJ, Przybelski SA, Machulda MM, Makhlouf AT, Senjem ML, Murray ME, Reichard RR, Savica R, Boeve BF, Drubach DA, Josephs KA, Knopman DS, Lowe VJ, Jack CR Jr, Petersen RC, Jones DT. Progressive dysexecutive syndrome due to Alzheimer's disease: a description of 55 cases and comparison to other phenotypes. Brain Commun. 2020;2(1):fcaa068. doi: 10.1093/braincomms/fcaa068. Epub 2020 May 27. PMID: 32671341; PMCID: PMC7325839.

8c. **8c.** Primary visual presentation (such as posterior cortical atrophy (PCA) syndrome) ☐1

A clinical syndrome defined by a gradually progressive decline in visual processing and other posterior cognitive functions. Cognitive features must include at least three of the following as early or presenting features:

Space perception deficit	Alexia
Simultanagnosia	Left/right disorientation
Object perception deficit	Acalculia
Constructional dyspraxia	Limb apraxia (not limb-kinetic)
Environmental agnosia	Apperceptive prosopagnosia
Oculomotor apraxia	Agraphia
Dressing apraxia	Homonymous visual field defect
Optic ataxia	Finger agnosia

Supportive neuroimaging features:

- Predominant occipito-parietal or occipito-temporal pattern found in any of the following imaging modalities:
  - Atrophy on CT/MRI
  - Hypometabolism on FDG-PET
  - Hypoperfusion on SPECT

There is a relatively spared function in the following cognitive domains: anterograde memory, speech and language, executive, and behavior in the early stages.

Exclusion criteria include:

- A brain tumor or mass sufficient to explain symptoms
- Significant vascular disease including focal stroke sufficient to explain symptoms
- Evidence of afferent visual cause (e.g., optic nerve, chiasm, or tract damage)
- Evidence of other identifiable causes for cognitive impairment (e.g., renal failure)

Crutch SJ, Schott JM, Rabinovici GD, Murray M, Snowden JS, van der Flier WM, Dickerson BC, Vandenberghe R, Ahmed S, Bak TH, Boeve BF, Butler C, Cappa SF, Ceccaldi M, de Souza LC, Dubois B, Felician O, Galasko D, Graff-Radford J, Graff-Radford NR, Hof PR, Krolak-Salmon P, Lehmann M, Magnin E, Mendez MF, Nestor PJ, Onyike CU, Pelak VS, Pijnenburg Y, Primativo S, Rossor MN, Ryan NS, Scheltens P, Shakespeare TJ, Suárez González A, Tang-Wai DF, Yong KXX, Carrillo M, Fox NC; Alzheimer's Association ISTAART Atypical Alzheimer's Disease and Associated Syndromes Professional Interest Area. Consensus classification of posterior cortical atrophy. Alzheimers Dement. 2017 Aug;13(8):870-884. doi: 10.1016/j.jalz.2017.01.014. Epub 2017 Mar 2. PMID: 28259709; PMCID: PMC5788455.

8d. **8d.** Primary progressive aphasia (PPA) syndrome: ☐1

Select 1=Present if the participant meets the core clinical criteria for PPA.

ROOT DIAGNOSIS OF PRIMARY PROGRESSIVE APHASIA (PPA)[1]
Both core criteria must be present:

1. Most prominent clinical feature is a new and progressive difficulty with language (i.e., retrieving, using, repeating, sequencing, or understanding words).
2. The language disorder (aphasia) should be the most prominent deficit at symptom onset and for the initial phases of the disease.

[1]Mesulam, M.-M., 2003. Primary progressive aphasia: A language-based dementia. New England Journal of Medicine 348, 1535-1542.

Criteria for the semantic variant PPA
I. Clinical diagnosis of semantic variant PPA
Both of the following core features must be present:

1. Impaired confrontation naming
2. Impaired single-word comprehension

At least 3 of the following other diagnostic features must be present:

1. Impaired object knowledge, particularly for low-frequency or low-familiarity items
2. Surface dyslexia or dysgraphia
3. Spared repetition
4. Spared speech production (grammar and motor speech)

II. Imaging-supported semantic variant PPA diagnosis

Both of the following criteria must be present:

1. Clinical diagnosis of semantic variant PPA
2. Imaging must show one or more of the following results:
    a. Predominant anterior temporal lobe atrophy
    b. Predominant anterior temporal lobe hypoperfusion or hypometabolism on SPECT or PET

III. Semantic variant PPA with definite pathology

Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present:

1. Clinical diagnosis of semantic variant PPA
2. Histopathologic evidence of a specific neurodegenerative pathology (e.g., FTLD-tau, FTLD-TDP, AD, other)
3. Presence of a known pathogenic mutation

Abbreviations: AD = Alzheimer's disease; FTLD = frontotemporal lobar degeneration; PPA = primary progressive aphasia

Diagnostic criteria for logopenic variant PPA

I. Clinical diagnosis of logopenic variant PPA

Both of the following core features must be present:

1. Impaired single-word retrieval in spontaneous speech and naming
2. Impaired repetition of sentences and phrases

At least 3 of the following other features must be present:

1. Speech (phonologic) errors in spontaneous speech and naming
2. Spared single-word comprehension and object knowledge
3. Spared motor speech
4. Absence of frank agrammatism

II. Imaging-supported logopenic variant diagnosis

Both criteria must be present:

1. Clinical diagnosis of logopenic variant PPA
2. Imaging must show at least one of the following results:
    a. Predominant left posterior perisylvian or parietal atrophy on MRI
    b. Predominant left posterior perisylvian or parietal hypoperfusion or hypometabolism on SPECT or PET

III. Logopenic variant PPA with definite pathology

Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present

1. Clinical diagnosis of logopenic variant PPA
2. Histopathologic evidence of a specific neurodegenerative pathology (e.g. AD, FTLD-tau, FTLD-TDP, other)
3. Presence of a known pathogenic mutation

Diagnostic features for the nonfluent/agrammatic variant PPA

I. Clinical diagnosis of nonfluent/agrammatic variant PPA

At least one of the following core features must be present:

1. Agrammatism in language production
2. Effortful, halting speech with inconsistent speech sound errors and distortions (apraxia of speech)

At least 2 of 3 of the following other features must be present:

1. Impaired comprehension of syntactically complex sentences
2. Spared single-word comprehension
3. Spared object knowledge

II. Imaging-supported nonfluent/agrammatic variant diagnosis

Both of the following criteria must be present:

1. Clinical diagnosis of nonfluent/agrammatic variant PPA
2. Imaging must show one or more of the following results:
    a. Predominant left posterior fronto-insular atrophy on MRI or
    b. Predominant left posterior fronto-insular hypoperfusion or hypometabolism on SPECT or PET

III. Nonfluent/agrammatic variant PPA with definite pathology

Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present:

1. Clinical diagnosis of nonfluent/agrammatic variant PPA
2. Histopathologic evidence of a specific neurodegenerative pathology (e.g., FTLD-tau, FTLD-TDP, AD, other)
3. Presence of a known pathogenic mutation

Abbreviations: AD = Alzheimer's disease; FTLD = frontotemporal lobar degeneration; PPA = primary progressive aphasia

Diagnostic features for primary progressive apraxia of speech
A clinical syndrome defined by a gradually progressive impairment in planning and programming movements required for speech production. There is generally phonetic (sound level errors, distorted substitutions and additions), and/or prosodic impairment (slow rate or segmented speech).

Clinical criteria include:
- Insidious onset and progressive worsening of speech disturbance
- Apraxia of speech is the only or dominant speech disturbance at the time of testing
- Dysarthria can be present but must be less severe than the apraxia of speech
- Any evidence of aphasia is considered equivocal

Supportive clinical speech features:
- Slow overall speech rate
- Lengthened intersegment durations
- Increased sound distortions or distorted sound substitutions with increased length of syllables (i.e., -cat, catnip, catapult, catastrophe)
- Syllable segmentation within words > 1 syllable and/or across words in phrases/sentences
- Audible or visible articulatory groping; speech initiation difficult, false starts/restarts
- Lengthened vowel and/or consonant segments
- Sound prolongations (beyond lengthened segments)
- Deliberate, slowly sequenced, segmented and/or distorted speech sequential motion rates in comparison with speech alternating motion rates
- Inaccurate (off-target in place or manner) speech alternating motion rates (as in rapid repetition of puh, puh, puh)
- Reduced words per speech breath group relative to maximum vowel duration

Exclusion criteria include:
- Pattern of deficits are better accounted for by other nondegenerative nervous system or medical disorders
- Cognitive disturbance is better accounted for by a psychiatric diagnosis
- Unequivocal evidence of aphasia on detailed language/neuropsychiatric testing (i.e. – patient may meet root criteria for primary progressive aphasia)
- Dysarthria is deemed more severe than apraxia of speech
- Prominent initial deficits in the following cognitive domains: episodic memory, visuoperceptual, or behavioral
- Prominent initial symptoms that may meet criteria for other overlapping clinical syndromes: progressive supranuclear palsy, corticobasal syndrome, or motor neuron disease.

Botha H, Josephs KA. Primary Progressive Aphasias and Apraxia of Speech. Continuum (Minneap Minn). 2019 Feb;25(1):101-127. doi: 10.1212/CON.0000000000000699. PMID: 30707189; PMCID: PMC6548538.
Josephs KA, Duffy JR, Strand EA, Machulda MM, Senjem ML, Master AV, Lowe VJ, Jack CR Jr, Whitwell JL. Characterizing a neurodegenerative syndrome: primary progressive apraxia of speech. Brain. 2012 May;135(Pt 5):1522-36. doi: 10.1093/brain/aws032. Epub 2012 Mar 1. PMID: 22382356; PMCID: PMC3338923.

IVP	FVP	Section 2 – Clinical syndrome *continued...*
8d1.	8d1.	**If present,** select one: ☐ 1 Semantic PPA ☐ 2 Logopenic PPA ☐ 3 Nonfluent/agrammatic PPA ☐ 5 Primary progressive apraxia of speech ☐ 4 PPA other/not otherwise specified

Review the criteria above and select the PPA subtype. Select **4=PPA other/not otherwise specified** if the participant meets the core clinical criteria for PPA but cannot be further classified as logopenic, semantic, nonfluent/agrammatic, or primary progressive apraxia of speech.

8e.	8e.	Behavioral variant frontotemporal (bvFTD) syndrome	☐ 1

Select 1=Present if the participant meets the core clinical criteria for bvFTD below.
International consensus criteria for behavioural variant FTD (FTDC)
I. Neurodegenerative disease
The following symptom must be present to meet criteria for bvFTD.
A. Shows progressive deterioration of behaviour and/or cognition by observation or history (as provided by a knowledgeable informant).

II. Possible bvFTD

Three of the following behavioural/cognitive symptoms (A–F) must be present to meet criteria. Ascertainment requires that symptoms be persistent or recurrent, rather than single or rare events.

A. Early* behavioural disinhibition [one of the following symptoms (A1–A3) must be present]:
- A1. Socially inappropriate behaviour
- A2. Loss of manners or decorum
- A3. Impulsive, rash or careless actions

B. Early apathy or inertia [one of the following symptoms (B1–B2) must be present]:
- B1. Apathy
- B2. Inertia

C. Early loss of sympathy or empathy [one of the following symptoms (C1–C2) must be present]:
- C1. Diminished response to other people's needs and feelings
- C2. Diminished social interest, interrelatedness or personal warmth

D. Early perseverative, stereotyped or compulsive/ritualistic behaviour [one of the following symptoms (D1–D3) must be present]:
- D1. Simple repetitive movements
- D2. Complex, compulsive or ritualistic behaviours
- D3. Stereotypy of speech

E. Hyperorality and dietary changes [one of the following symptoms (E1–E3) must be present]:
- E1. Altered food preferences
- E2. Binge eating, increased consumption of alcohol or cigarettes
- E3. Oral exploration or consumption of inedible objects

F. Neuropsychological profile: executive/generation deficits with relative sparing of memory and visuospatial functions [all of the following symptoms (F1–F3) must be present]:
- F1. Deficits in executive tasks
- F2. Relative sparing of episodic memory
- F3. Relative sparing of visuospatial skills

III. Probable bvFTD

All of the following symptoms (A–C) must be present to meet criteria.

A. Meets criteria for possible bvFTD

B. Exhibits significant functional decline (by caregiver report or as evidenced by Clinical Dementia Rating Scale or Functional Activities Questionnaire scores)

C. Imaging results consistent with bvFTD [one of the following (C1–C2) must be present]:
- C1. Frontal and/or anterior temporal atrophy on MRI or CT
- C2. Frontal and/or anterior temporal hypoperfusion or hypometabolism on PET or SPECT

IV. Behavioural variant FTD with definite FTLD pathology

Criterion A and either criterion B or criterion C must be present to meet criteria.

A. Meets criteria for possible or probable bvFTD

B. Histopathological evidence of FTLD on biopsy or at post-mortem

C. Presence of a known pathogenic mutation

V. Exclusionary criteria for bvFTD

Criteria A and B must be answered negatively for any bvFTD diagnosis. Criterion C can be positive for possible bvFTD but must be negative for probable bvFTD.

A. Pattern of deficits is better accounted for by other non-degenerative nervous system or medical disorders

B. Behavioural disturbance is better accounted for by a psychiatric diagnosis

**As a general guideline, "early" refers to symptom presentation within the first 3 years.*
bvFTD = behavioral variant FTD

IVP	FVP	Section 2 – Clinical syndrome	*continued...*
8f.	8f.	Lewy body syndrome	☐1

Select **1=Present** if the participant meets criteria below for the clinical diagnosis of dementia with Lewy bodies (DLB).

Revised (2017[1]) criteria for the clinical diagnosis of dementia with Lewy Bodies (DLB):

1. Essential for a diagnosis of DLB is dementia, defined as a progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational functions, or with usual daily activities. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuoperceptual ability may be especially prominent and occur early.
2. Core clinical features (the first 3 typically occur early and may persist throughout the course):
   - Fluctuating cognition with pronounced variations in attention and alertness.
   - Recurrent visual hallucinations that are typically well-formed and detailed.
   - REM sleep behavior disorder, which may precede cognitive decline.
   - One or more spontaneous cardinal features of parkinsonism: these are bradykinesia (defined as slowness of movement and decrement in amplitude or speed), rest tremor, or rigidity.
3. Supportive clinical features:
   - Severe sensitivity to antipsychotic agents; postural instability.
   - Repeated falls.
   - Syncope or other transient episodes of unresponsiveness.
   - Severe autonomic dysfunction, e.g., constipation, orthostatic hypotension, urinary incontinence.
   - Hypersomnia.
   - Hyposmia.
   - Hallucinations in other modalities.
   - Systematized delusions.
   - Apathy.
   - Anxiety.
   - Depression.
4. Indicative biomarkers:
   - Reduced dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET.
   - Abnormal (low-uptake) 123iodine-MIBG myocardial scintigraphy.
   - Polysomnographic confirmation of REM sleep without atonia.
5. Supportive biomarkers:
   - Relative preservation of medial temporal lobe structures on CT/MRI scan.
   - Generalized low uptake on SPECT/PET perfusion/metabolism scan with reduced occipital activity 6 the cingulate island sign on FDG-PET imaging.
   - Prominent posterior slow-wave activity on EEG with periodic fluctuations in the pre-alpha/theta range.
6. Probable DLB can be diagnosed if:
   a) Two or more core clinical features of DLB are present, with or without the presence of indicative biomarkers,
   or
   b) Only one core clinical feature is present, but with one or more indicative biomarkers. Probable DLB should not be diagnosed on the basis of biomarkers alone.
7. Possible DLB can be diagnosed if:
   a) Only one core clinical feature of DLB is present, with no indicative biomarker evidence,
   or
   b) One or more indicative biomarkers is present but there are no core clinical features.
8. DLB is less likely:
   - In the presence of any other physical illness or brain disorder including cerebrovascular disease, sufficient to account in part or in total for the clinical picture, although these do not exclude a DLB diagnosis and may serve to indicate mixed or multiple pathologies contributing to the clinical presentation.
   - If parkinsonian features are the only core clinical feature and appear for the first time at a stage of severe dementia.

DLB should be diagnosed when dementia occurs before or concurrently with parkinsonism. The term Parkinson disease dementia (PDD) should be used to describe dementia that occurs in the context of well-established Parkinson disease. In a practice setting the term that is most appropriate to the clinical situation should be used, and generic terms such as Lewy body disease are often helpful. In research studies in which distinction needs to be made between DLB and PDD, the existing 1-year rule between the onset of dementia and parkinsonism continues to be recommended.
(For more information on the criteria above, visit the website of the Lewy Body Dementia Association at https://www.lbda.org/)

[1]*Recommendations for the clinical diagnosis of DLB by the Dementia with Lewy Bodies Consortium.*

McKeith IF, Boeve BF, Dickson DW, et al. Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium, Neurology 2017; 89: 88-100.

IVP	FVP	Section 2 – Clinical syndrome	*continued...*
8f1.	8f1.	**If present,** select one: ☐ 1 Dementia with Lewy bodies ☐ 2 Parkinson's disease ☐ 3 Parkinson's disease dementia syndrome	

Review the criteria above and select the Lewy body syndrome subtype.

Criteria for Parkinson's disease

A clinical syndrome defined by a gradually progressive motor parkinsonism due to clinically established or clinically probable Parkinson's disease. Diagnosing Parkinson's disease requires a 2-step process:

Step 1: The first essential criterion is parkinsonism, which is defined as:

- **Bradykinesia** (slowness of movement) +/- hypokinesia (decrement in amplitude or speed as movements are continued) in combination with at least 1 of the following:
  - **Rest tremor** (4-6 hz tremor in the fully resting limb, suppressed during movement initiation, but may re-emerge with prolonged posture)
  - **Rigidity** (lead-pipe resistance to passive movement)

Step 2: Diagnosing either clinically established Parkinson's disease or clinically probable Parkinson's disease.

Diagnosis of clinically established Parkinson's disease requires:

1. Absence of absolute exclusion criteria
2. At least two supportive criteria
3. No red flags

Diagnosis of clinically probable Parkinson's disease requires:

1. Absence of absolute exclusion criteria
2. Presence of red flags is counterbalanced by supportive criteria
   a. If one red flag is present there must be at least one supportive criterion; if two red flags, at least two supportive criteria are needed.
   b. If more than two red flags, clinically probable PD cannot be diagnosed

Supportive criteria:

1. Clear and dramatic beneficial response to dopaminergic therapy. To meet this criterion, during initial treatment, patients should have returned to normal or near-normal level of function.
2. Presence of levodopa-induced dyskinesia
3. Rest tremor of a limb, documented on clinical examination (in the past, or on current examination)
4. Positive results from at least one ancillary diagnostic test having a specificity greater than 80% for differential diagnosis of PD from other parkinsonian conditions. Currently available tests that meet this criterion include:
   a. Olfactory loss (in the anosmic or clearly hyposmic range, adjusted for age and sex)
   b. Metaiodobenzylguanidine (MIBG) scintigraphy clearly documenting cardiac sympathetic denervation

Red Flags

1. Rapid progression of gait impairment requiring regular use of wheelchair within 5 years of onset
2. A complete absence of progression of motor symptoms or signs over 5 or more years unless stability is related to treatment
3. Early bulbar dysfunction, defined as one of severe dysphonia, dysarthria (speech unintelligible most of the time), or severe dysphagia (requiring soft food, NG tube, or gastrostomy feeding) within the first 5 years of disease
4. Inspiratory respiratory dysfunction defined as either diurnal or nocturnal inspiratory stridor or frequent inspiratory sighs
5. Severe autonomic failure in the first 5 years of disease.
6. Recurrent (>1/y) falls because of impaired balance within 3 years of onset.
7. The presence of disproportionate anterocollis (dystonic in nature) or contractures of hand or feet within the first 10 years.
8. Absence of any of the common nonmotor features of disease despite 5 years disease duration. These include:
   - Sleep dysfunction: sleep-maintenance insomnia, excessive daytime somnolence, symptoms of rapid eye movement sleep behavior disorder
   - Autonomic dysfunction: constipation, daytime urinary urgency (ie, not simply nocturia), symptomatic orthostasis
   - Hyposmia
   - Psychiatric dysfunction: depression, anxiety, or hallucinations
9. Otherwise unexplained pyramidal tract signs, defined as pyramidal weakness or clear pathologic hyperreflexia (excluding mild reflex asymmetry in the more affected limb, and isolated extensor plantar response).
10. Bilateral symmetric parkinsonism throughout the disease course. The patient or caregiver reports bilateral symptom onset with no side predominance, and no side predominance is observed on objective examination.

Absolute Exclusion Criteria

For all absolute exclusion criteria and red flags, the criterion is assumed to not be met because of an alternate unrelated cause. For example, unilateral cerebellar abnormalities attributable to a cerebellar hemisphere stroke, or a wheelchair-bound state attributable to spinal cord injury would not necessarily be exclusion criteria.

The presence of any of these features rules out Parkinson's disease:

1. Unequivocal cerebellar abnormalities on examination, such as cerebellar gait, limb ataxia, or cerebellar oculomotor abnormalities (eg, sustained gaze-evoked nystagmus, macro square wave jerks, hypermetric saccades)
2. Downward vertical supranuclear gaze palsy, or selective slowing of downward vertical saccades
3. Diagnosis of probable behavioral variant frontotemporal dementia or primary progressive aphasia, defined according to consensus criteria within the first 5 y of disease
4. Parkinsonian features restricted to the lower limbs for more than 3 y
5. Treatment with a dopamine receptor blocker or a dopamine-depleting agent in a dose and time course consistent with drug-induced parkinsonism
6. Absence of observable response to high-dose levodopa despite at least moderate severity of disease
7. Unequivocal cortical sensory loss (ie, graphesthesia, stereognosis with intact primary sensory modalities), clear limb ideomotor apraxia, or progressive aphasia
8. Normal functional neuroimaging of the presynaptic dopaminergic system
9. Documentation of an alternative condition known to produce parkinsonism and plausibly connected to the patient's symptoms, or the expert evaluating physician, based on the full diagnostic assessment, believes that an alternative syndrome is more likely than PD.

Postuma RB, Berg D, Stern M, Poewe W, Olanow CW, Oertel W, Obeso J, Marek K, Litvan I, Lang AE, Halliday G, Goetz CG, Gasser T, Dubois B, Chan P, Bloem BR, Adler CH, Deuschl G. MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord. 2015 Oct;30(12):1591-601. doi: 10.1002/mds.26424. PMID: 26474316.

IVP	FVP	**Section 2 – Clinical syndrome** *continued...*	
8g.	**8g.**	Non-amnestic multidomain syndrome, not PCA, PPA, bvFTD, or DLB syndrome	☐1

This category of dementia syndrome refers to those with a pattern of test results on the neuropsychological battery in which the typical memory-predominant pattern of deficits is not present. This category would be used for subjects who fit none of the other defined syndromes in Questions 8c – 8f (i.e., PPA syndrome, primary visual presentation (such as posterior cortical atrophy (PCA) syndrome), the typical pattern of psychomotor slowing and visuospatial cognitive and behavioral deficits associated with DLB [reference Ferman T, Clin Neuropsychol 20:623, 2006], nor the executive deficits seen with bvFTD).

Clin Neuropsychol. 2006 Dec;20(4):623-36. Neuropsychological differentiation of dementia with Lewy bodies from normal aging and Alzheimer's disease. Ferman TJ1, Smith GE, Boeve BF, Graff-Radford NR, Lucas JA, Knopman DS, Petersen RC, Ivnik RJ, Wszolek Z, Uitti R, Dickson DW.

8h.	**8h.**	Primary supranuclear palsy (PSP) syndrome	☐1

Excerpted from Höglinger et al. (2017):

B1: Mandatory inclusion criteria

1. Sporadic occurrence*
2. Age 40 or older at onset** of first PSP-related symptom***
3. Gradual progression of PSP-related symptoms***

Core Features: We propose four core functional domains as characteristic clinical manifestations of PSP (ocular motor dysfunction **[O]**, postural instability **[P]**, akinesia **[A]**, and cognitive dysfunction **[C]**. In each domain, we propose three characteristic core clinical features, stratified by presumed levels of certainty (1 [highest], 2 [mid], and 3 [lowest]) that they contribute to the diagnosis of PSP.

LEVELS OF CERTAINTY	OCULAR MOTOR DYSFUNCTION	POSTURAL INSTABILITY	AKINESIA	COGNITIVE DYSFUNCTION
LEVEL 1	O1: Vertical supranuclear gaze palsy	P1: Repeated unprovoked falls within 3 years	A1: Progressive gait freezing within 3 years	C1: Speech/language disorder (i.e., nonfluent/ agrammatic variant of primary progressive aphasia or progressive apraxia of speech)
LEVEL 2	O2: Slow velocity of vertical saccades	P2: Tendency to fall on the pull-test within 3 years	A2: Parkinsonism, akinetic-rigid predominantly axial, and levodopa resistant	C2: Frontal cognitive/ behavioral presentation
LEVEL 3	O3: Frequent macro square wave jerks or "eyelid opening apraxia"	P3: More than two steps backward on the pull-test within 3 years	A3: Parkinsonism, with tremor and/or asymmetric and/or levodopa responsive	C3: Corticobasal syndrome

- Supportive Imaging findings
  - IF1 - Predominant midbrain atrophy on MRI or hypometabolism on FDG-PET
  - IF2 - Postsynaptic striatal dopaminergic degeneration

Guidance for Richardson's vs Non-Richardson's Syndromes

- Richardson's syndrome: (PSP-RS)
  - (P1 or P2) + (O1 or O2)
- Non-Richardson's phenotypes:
  - Probable PSP with progressive gait freezing (PSP-PGF)
    - (O1 or O2) + A1
  - Probable PSP with predominant parkinsonism (PSP-P)
    - (O1 or O2) + A2 or A3)
  - Probable PSP with predominant frontal presentation (PSP-F)
    - (O1 or O2) + C2
    -

Levels with lower numbers are considered to contribute higher certainty to a diagnosis of PSP that levels with higher numbers.

B2: Mandatory exclusion criteria

Clinical findings

1. Predominant, otherwise unexplained impairment of episodic memory, suggestive of AD
2. Predominant, otherwise unexplained autonomic failure, e.g., orthostatic hypotension (orthostatic reduction in blood pressure after 3 minutes standing 30mm Hg systolic or15mm Hg diastolic), suggestive of multiple system atrophy or Lewy body disease
3. Predominant, otherwise unexplained visual hallucinations or fluctuations in alertness, suggestive of dementia with Lewy bodies
4. Predominant, otherwise unexplained multisegmental upper and lower motor neuron signs, suggestive of motor neuron disease (pure upper motor neuron signs are not an exclusion criterion)
5. Sudden onset or step-wise or rapid progression of symptoms, in conjunction with corresponding imaging or laboratory findings, suggestive of vascular etiology, autoimmune encephalitis, metabolic encephalopathies, or prion disease
6. History of encephalitis
7. Prominent appendicular ataxia
8. Identifiable cause of postural instability, e.g., primary sensory deficit, vestibular dysfunction, severe spasticity, or lower motor neuron syndrome

Imaging findings

1. Severe leukoencephalopathy, evidenced by cerebral imaging
2. Relevant structural abnormality, e.g., normal pressure or obstructive hydrocephalus; basal ganglia, diencephalic,mesencephalic, pontine or medullary infarctions, hemorrhages, hypoxic-ischemic lesions, tumors, or malformation

Höglinger GU, Respondek G, Stamelou M, Kurz C, Josephs KA, Lang AE, Mollenhauer B, Müller U, Nilsson C, Whitwell JL, Arzberger T, Englund E, Gelpi E, Giese A, Irwin DJ, Meissner WG, Pantelyat A, Rajput A, van Swieten JC, Troakes C, Antonini A, Bhatia KP, Bordelon Y, Compta Y, Corvol JC, Colosimo C, Dickson DW, Dodel R, Ferguson L, Grossman M, Kassubek J, Krismer F, Levin J, Lorenzl S, Morris HR, Nestor P, Oertel WH, Poewe W, Rabinovici G, Rowe JB, Schellenberg GD, Seppi K, van Eimeren T, Wenning GK, Boxer AL, Golbe LI, Litvan I; Movement Disorder Society-endorsed PSP Study Group. Clinical diagnosis of progressive supranuclear palsy: The movement disorder society criteria. Mov Disord. 2017 Jun;32(6):853-864. doi: 10.1002/mds.26987. Epub 2017 May 3. PMID: 28467028; PMCID: PMC5516529.

IVP	FVP	Section 2 – Clinical syndrome *continued...*	
8h1.	8h1.	**If present,** select one: ☐ 1 Richardson's syndrome criteria ☐ 2 Non-Richardson's	
8i.	8i.	Traumatic encephalopathy syndrome	☐ 1

Excerpted from Katz et al. (2021):

Primary Diagnostic Criteria for TES:
I. Substantial Exposure to Repetitive Head Impacts[1]
History of substantial exposure to repetitive impacts to the head is required. These impacts may or may not have been associated with clinical symptoms or signs of concussion or TBI. Individuals should be screened for multiple possible sources of exposure over a lifetime. Examples or sources of substantial exposure to RHIs include the following:

- **Involvement in high-exposure contact or collision sports** such as (but not limited to) boxing, American (tackle) football, ice hockey, soccer, rugby, professional wrestling, mixed martial arts, and some other sports with high risk of exposure to RHIs (e.g., motocross and bull riding).
  - For American football, a minimum of 5 y of organized play is required. This minimum should include ≥ 2 y at the high school level or beyond. [The inclusion of level of play (i.e., high school) is based on clinical judgement, with limited evidence]. Nearly all of the participants in a published study establishing the 5 y threshold played at least high school level football[2]
  - Exposure risk thresholds for other contact or collision sports, or combinations or contact/collision sports, have not yet been established but should be a substantial number of years (e.g., ≥ 5 y) at a level of play involving routing RHIs.
- **Military service involving RHIs**, including (but not limited to) combat exposure to multiple blast and other explosions, noncombatant exposure to explosions (including breacher training – blasting and forced opening of locked doors), or multiple blows to the head over an extended period of time (e.g., pugil stick training – repeated blows with padded military training weapon.
  - Exposure risk thresholds for military service have not yet been established.
- **Other sources involving multiple head impacts** over an extended period of time, including (but not limited to) domestic violence (or intimate partner violence), head banging, and vocational activities such as breaching locked doors and other barriers by first responders.
  - Exposure risk thresholds for other sources have not yet been established.

II. Core Clinical Features[1]
Cognitive impairment or neurobehavioral dysregulation, or both, is required to meet TES criteria. A progressive course is also required to meet TES criteria.

- **Cognitive impairment (all 4 are required)**
  1. As reported by self or informant, or by clinician's report.
  2. Representing a significant decline from baseline functioning. The determination of baseline level of functioning may be challenging and require clinical judgment in cases where decline may have been during the period of RHI exposure.
  3. With deficits in episodic memory and/or executive functioning (additional domains may be impaired in addition to these).
  4. Substantiated by impaired performance on formal neuropsychological testing (if available), as defined by performance at a level of at least 1.5 SDs below appropriate norms, accounting for the individual's estimated premorbid functioning. If formal neuropsychological testing is not available, there should be substantial evidence of impairment below expected norms and/or a person's estimated baseline in episodic memory and/or executive functioning on a standardized mental status examination (e.g., Montreal Cognitive Assessment and Mini-Mental State Examination) by a clinician experienced in the evaluation of cognition.

- **Neurobehavioral dysregulation (all 3 are required)**
  1. As reported by self or informant, or by clinician's report.
  2. Representing a significant change from baseline functioning. The determination of baseline functioning may require clinical judgment in cases where change may have begun during the period of RHI exposure.
  3. With symptoms and/or observed behaviors representing poor regulation or control of emotions and/or behavior, including (but not limited to) explosiveness, impulsivity, rage, violent outbursts, having a short fuse (exceeding what might be described as periodic episodes or minor irritability), or emotional lability (often reported as mood swings), preferable substantiated by standardized measures that demonstrate clinical impairment in these domains. In most cases, standardized measures of neurobehvioral dysregulation will not be available, but there should be substantial evidence of change from a person's baseline. These symptoms and/or observed behaviors do not appear to represent a transient response to life events, e.g., divorce, death of a loved one, and financial problems.

- **Progressive course**
  There is evidence of progressive worsening of these clinical features over a period of at least 1 year in the absence of continued exposure to RHIs or TBI. The evidence should be supported by serial standardized testing (if available) or clear history supporting a change in functioning over time (e.g., clinician reports, job performance evaluations, or self- or informant report).

Abbreviations: RHI = repeated head impact; TBI = traumatic brain injury; TES = traumatic encephalopathy syndrome

[1] Katz DI, Bernick C, Dodick DW, Mez J, Mariani ML, Adler CH, Alosco ML, Balcer LJ, Banks SJ, Barr WB, Brody DL, Cantu RC, Dams-O'Connor K, Geda YE, Jordan BD, McAllister TW, Peskind ER, Petersen RC, Wethe JV, Zafonte RD, Foley ÉM, Babcock DJ, Koroshetz WJ, Tripodis Y, McKee AC, Shenton ME, Cummings JL, Reiman EM, Stern RA. National Institute of Neurological Disorders and Stroke Consensus Diagnostic Criteria for Traumatic Encephalopathy Syndrome. Neurology. 2021 May 4;96(18):848-863. doi: 10.1212/WNL.0000000000011850. Epub 2021 Mar 15. PMID: 33722990; PMCID: PMC8166432.

[2] Mez J, Daneshvar DH, Abdolmohammadi B, Chua AS, Alosco ML, Kiernan PT, Evers L, Marshall L, Martin BM, Palmisano JN, Nowinski CJ, Mahar I, Cherry JD, Alvarez VE, Dwyer B, Huber BR, Stein TD, Goldstein LE, Katz DI, Cantu RC, Au R, Kowall NW, Stern RA, McClean MD, Weuve J, Tripodis Y, McKee AC. Duration of American Football Play and Chronic Traumatic Encephalopathy. Ann Neurol. 2020 Jan;87(1):116-131. doi: 10.1002/ana.25611. Epub 2019 Nov 23. PMID: 31589352; PMCID: PMC6973077.

IVP FVP Section 2 – Clinical syndrome *continued...*

IVP	FVP		
8j.	8j.	Corticobasal syndrome (CBS)	☐1

Corticobasal Syndrome

A clinical syndrome defined by a gradually progressive decline in a constellation of neurologic functions including movement, cognition, and speech. CBS typically starts with asymmetric atypical parkinsonism and involves cortical sensory and cognitive features. The clinical syndrome can be due to pathological entities of Alzheimer's disease (CBS-AD), 4RTau corticobasal degeneration (CBS-CBD), and 4RTau-PSP (CBS-PSP).

For a diagnosis of CBS, a patient should satisfy:
- All mandatory criteria
- Two major criteria
- Two minor criteria

Mandatory criteria
- Insidious onset and gradual progression
- No sustained response to levodopa treatment

Major (bold) and *minor (italic)* criteria
- Motor features:
  - **Akinetic rigid syndrome**
    - *Focal or segmental myoclonus*
    - *Asymmetric dystonia*
- Cortical motor sensory features:
  - **Limb apraxia**
    - *Alien limb phenomenon*
    - *Cortical sensory loss or dyscalculia*
- Cognitive features:
  - **Speech and language impairment**
    - *Frontal executive dysfunction*
    - *Visuospatial deficits*

Mathew R, Bak TH, Hodges JR. Diagnostic criteria for corticobasal syndrome: a comparative study. J Neurol Neurosurg Psychiatry. 2012 Apr;83(4):405-10. doi: 10.1136/jnnp-2011-300875. Epub 2011 Oct 21. PMID: 22019546.

IVP	FVP		
8k.	8k.	Multiple system atrophy (MSA) syndrome	☐ 1

Excerpted from Wenning et al. (2022):

Diagnostic criteria for clinically probable multiple system atrophy

Essential features	A sporadic, progressive adult (>30 years) onset disease
	Clinically probable MSA
Core clinical features	At least two of: 1. Autonomic dysfunction defined as (at least one is required): • Unexplained voiding difficulties with post-void urinary residual volume • Unexplained urinary urge incontinence • Neurogenic OH (≥20/10 mmHg blood pressure drop) within 10 minutes of standing or head-up tilt test 2. Parkinsonism 3. Cerebellar syndrome (at least one of gait ataxia, limb ataxia, cerebellar dysarthria, or oculomotor features)
Supportive clinical (motor or non-motor) features	At least one[a]
MRI marker	Not required
Exclusion criteria	Absence

Supportive clinical features

Supportive motor features	**Supportive non-motor features**
• Rapid progression within 3 years of motor onset	• Stridor
• Moderate to severe postural instability within 3 years of motor onset	• Inspiratory sighs
• Craniocervical dystonia induced or exacerbated by L-dopa in the absence of limb dyskinesia	• Cold discolored hands and feet
• Severe speech impairment within3 years of motor onset	• Erectile dysfunction (below age of 60 years for clinically probable MSA)
• Severe dysphagia within 3 years of motor onset	• Pathologic laughter or crying
• Unexplained Babinski sign	
• Jerky myoclonic postural or kinetic tremor	
• Postural deformities	

[a] Excluding erectile dysfunction as an isolated feature.

Abbreviations: MSA = multiple system atrophy; MSA-P = MSA-parkinsonian type; MSA-C = MSA-cerebellar type; OH = orthostatic hypotension; MRI = magnetic resonance imaging.

Wenning GK, Stankovic I, Vignatelli L, Fanciulli A, Calandra-Buonaura G, Seppi K, Palma JA, Meissner WG, Krismer F, Berg D, Cortelli P, Freeman R, Halliday G, Höglinger G, Lang A, Ling H, Litvan I, Low P, Miki Y, Panicker J, Pellecchia MT, Quinn N, Sakakibara R, Stamelou M, Tolosa E, Tsuji S, Warner T, Poewe W, Kaufmann H. The Movement Disorder Society Criteria for the Diagnosis of Multiple System Atrophy. Mov Disord. 2022 Jun;37(6):1131-1148. doi: 10.1002/mds.29005. Epub 2022 Apr 21. PMID: 35445419; PMCID: PMC9321158.

8k1.	8k1.	**If present,** select one: ☐ 1 MSA-predominant cerebellar ataxia (MSA-C) ☐ 2 MSA-predominant Parkinsonism (MSA-P) ☐ 3 MSA-predominant dysautonomia

Review the criteria above and determie whether MSA-predominant cerebellar ataxia (MSA-C), MSA-predominant Parkinsonism (MSA-P), or MSA-predominant dysautonomia is present according to the **predominant** motor syndrome.

8l.	8l.	Other **(SPECIFY):** _____	☐ 1

IVP	FVP	Section 2 – Clinical syndrome *continued...*	
9.	9.	Indicate the source(s) of information used to assign the clinical syndrome: Select one or more as **Yes**; all others will default to **No** in the NACC database.	
		Indicate the types of information that was used to make the diagnosis of clinical syndrome. Collecting this information enables future researchers to understand the basis of the diagnosis, appreciate the context in which it was made, and account for varying practices across different research centers.	
			Yes
9a.	9a.	Clinical information (history, CDR)	☐1
9b.	9b.	Cognitive testing	☐1
9c.	9c.	Biomarkers (MRI, PET, CSF, plasma)	☐1

Section 3 – Primary or contributing non-neurodegenerative or non-CVD conditions

The purpose of Section 3 is to identify conditions or disorders that are present and potentially contributing to the clinical syndrome. This must be filled out for those 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 condition(s) as **Present**; if there are no primary or contributing non-neurodegenerative or non-CVD conditions, leave all conditions blank. All conditions left blank will default to **Absent** in the NACC database. *Only one diagnosis should be selected as **1 = Primary.***

*In order to diagnose a disorder, **DSM-5-TR criteria require** that symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. For more guidance see the **UDS Coding Guidebook, Form D1a**.

		Condition	Present		Primary	Contributing	Non-contributing
		QUESTIONS 10 – 18: These questions consider the etiologic contribution of specific psychiatric disorders to the participant's cognitive, neuropsychiatric/behavioral, or functional phenotype. Several psychiatric disorders (especially mood or anxiety disorders and chronic psychotic disorders) are accompanied by cognitive and/or functional changes. As well, given the high lifetime prevalence of psychiatric disorders in the USA it is important to record their presence in ADC participants even if they do not appear to be contributing to any cognitive, functional or neuropsychiatric/behavioral (e.g., when Major Depression is in remission). For the sake of diagnostic consistency across Centers, please consult the established taxonomy of the Diagnostic and Statistical Manual of Mental Disorders V-Text Revision (DSM-5-TR) regarding the diagnosis of the psychiatric conditions listed in Questions 10 – 18. If the psychiatric disorder is not present, leave all questions related to the particular psychiatric disorder blank/unchecked. If the psychiatric condition (regardless of whether it is active but successfully treated with medication or counseling) is present, select 1=Present, and indicate whether it is thought to be the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment.					
10.	10.	Major depressive disorder (DSM-5-TR criteria*)	☐1	10a.	☐1	☐2	☐3
11.	11.	Other specified depressive disorder (DSM-5-TR criteria*)	☐1	11a.	☐1	☐2	☐3
12.	12.	Bipolar disorder (DSM-5-TR criteria*)	☐1	12a.	☐1	☐2	☐3
13.	13.	Schizophrenia or other psychotic disorder (DSM-5-TR criteria*)	☐1	13a.	☐1	☐2	☐3
14.	14.	Anxiety disorder (DSM-5-TR criteria*)	☐1	14a.	☐1	☐2	☐3
		If **present**, **(SPECIFY)** *(check all that apply)*:					
14b.	14b.	☐1 Generalized anxiety disorder					
14c.	14c.	☐1 Panic disorder					
14d.	14d.	☐1 Obsessive-compulsive disorder (OCD)					
14e.	14e.	☐1 Other **(SPECIFY)** : _____					

IVP	FVP	Section 3 – Primary or contributing non-degenerative or non-CVD conditions *continued...*					
		Condition	Present		Primary	Contributing	Non-contributing
15.	15.	Post-traumatic stress disorder (PTSD) (DSM-5-TR criteria*)	☐1	15a.	☐1	☐2	☐3
16.	16.	Developmental neuropsychiatric disorders (e.g., autism spectrum disorder (ASD), attention-deficit hyperactivity disorder (ADHD), dyslexia)	☐1	16a.	☐1	☐2	☐3
17.	17.	Delirium (DSM-5-TR criteria*)	☐1	17a.	☐1	☐2	☐3
18.	18.	Other psychiatric disorder (DSM-5-TR criteria*)	☐1	18a.	☐1	☐2	☐3

If the participant has cognitive impairment due to a psychiatric condition other than those described in Questions 10–17, select **1=Present** for Question 18, specify the psychiatric condition in the specify field, and indicate whether the psychiatric condition is the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the observed cognitive impairment.

18b.	18b.	If **present**, **(SPECIFY)** : _____					
19.	19.	Traumatic brain injury *(Distinct from TES and CTE, which are documented as a Clinical Syndrome and Etiologic Diagnosis, respectively)*	☐1	19a.	☐1	☐2	☐3

The definition of TBI below has been condensed from Menon et al. (2010):
TBI is defined as an alteration in brain function, or other evidence of brain pathology, caused by an external force.

A. Alteration in brain function is defined as 1 of the following clinical signs:
- Any period of loss of or a decreased LOC
- Any loss of memory for events immediately before (retrograde amnesia) or after the injury (PTA)
- Neurologic deficits (weakness, loss of balance, change in vision, dyspraxia paresis/plegia [paralysis], sensory loss, aphasia, etc.)
- Any alteration in mental state at the time of the injury (confusion, disorientation, slowed thinking, etc.)"

B. or other evidence of brain pathology: Such evidence may include visual, neuroradiologic, or laboratory confirmation of damage to the brain.

C. caused by an external force may include any of the following events:
- The head being struck by an object
- The head striking an object
- The brain undergoing an acceleration/deceleration movement without direct external trauma to the head
- A foreign body penetrating the brain
- Forces generated from events such as a blast or explosion
- Or other force yet to be defined

If the participant has had one or more TBIs as defined above, select **1=Present** for Question 19 and indicate whether the TBI is thought to be the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment in Question 19a.
If the participants has had no previous TBI, leave all boxes in Questions 19 and 19a blank and unchecked.

MENON, D. K., SCHWAB, K., WRIGHT, D. W. & MAAS, A. I. 2010. Position statement: definition of traumatic brain injury. Arch Phys Med Rehabil, 91, 1637-40.

20.	20.	Epilepsy	☐1	20a.	☐1	☐2	☐3

Refer to the paper by Fisher et al. (2014)[1] for clinical symptoms consistent with epilepsy.

If epilepsy is not present, leave all boxes in Questions 20 and 20a blank/unchecked. If epilepsy is present, select **1=Present**, and indicate whether it is thought to be the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment.

[1]*Epilepsia. 2014 Apr;55(4):475-82. doi: 10.1111/epi.12550. Epub 2014 Apr 14. ILAE official report: a practical clinical definition of epilepsy. Fisher RS1, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, Engel J Jr, Forsgren L, French JA, Glynn M, Hesdorffer DC, Lee BI, Mathern GW, Moshé SL, Perucca E, Scheffer IE, Tomson T, Watanabe M, Wiebe S.*

21.	21.	Normal-pressure hydrocephalus	☐1	21a.	☐1	☐2	☐3

If normal-pressure hydrocephalus is not present, leave all boxes in Questions 21 and 21a blank/unchecked. If normal-pressure hydrocephalus is present, select **1=Present**, and indicate whether it is thought to be the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment.

IVP	FVP	Section 3 – Primary or contributing non-degenerative or non-CVD conditions *continued...*					
22.	22.	CNS Neoplasm	☐1	22a.	☐1	☐2	☐3
22b.	22b.	If **present**, select one: ☐1 Benign ☐2 Malignant					

If CNS neoplasm (benign or malignant) is not present, leave all boxes for Questions 22, 22a, and 22b blank/unchecked. If CNS neoplasm is present,select **1=Present**, and indicate whether it is thought to be the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment.

23.	23.	Human immunodeficiency virus (HIV) infection	☐1	23.	☐1	☐2	☐3

Recent publications outline updated research criteria for determining the presence of an HIV-associated neurocognitive disorder — for instance, the paper by Antinori et al. (2007).

If HIV is present, select, and indicate whether it is thought to be the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment. If HIV is not present, leave all boxes for Questions 23 and 23a blank/unchecked.

Antinori A, Arendt G, Becker JT, et al. Updated research nosology for HIV-associated neurocognitive disorders. Neurology. 2007;69(18):1789-1799.

24.	24.	Post COVID-19 cognitive impairment	☐1	24a.	☐1	☐2	☐3
25.	25.	Sleep apnea *(i.e., obstructive, central, mixed or complex sleep apnea)*	☐1	25a.	☐1	☐2	☐3
26.	26.	Cognitive impairment due to other neurologic, genetic, infectious conditions (*not listed above*), or systemic disease/ medical illness (as indicated on Form A5/D2)	☐1	26a.	☐1	☐2	☐3
26b.	26b.	If **present**, **(SPECIFY):** _____					

If the participant has cognitive impairment due to a neurological, genetic, or infectious condition other than those described in Questions 10 – 25, or due to any systemic disease or medical illness not described, select **1=Present**, specify the condition or disease in the **Specify** field, and indicate whether the condition or disease is the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the observed cognitive impairment.

27.	27.	Cognitive impairment due to alcohol use or abuse	☐1	27a.	☐1	☐2	☐3
28.	28.	Cognitive impairment due to substance use or abuse	☐1	28a.	☐1	☐2	☐3
29.	29.	Cognitive impairment due to medications	☐1	29a.	☐1	☐2	☐3

Questions 30 – 32: If the participant has cognitive impairment due to a condition other than those described in Questions 10 – 29, select **1=Present**, enter the condition or disorder that is the cause in the **Specify** field, and indicate whether the condition or disorder is the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the observed cognitive impairment.

30.	30.	Cognitive impairment not otherwise specified (NOS)	☐1	30a.	☐1	☐2	☐3
30b.	30b.	If **present**, **(SPECIFY):** _____					
31.	31.	Cognitive impairment not otherwise specified (NOS)	☐1	31a.	☐1	☐2	☐3
31b.	31b.	If **present**, **(SPECIFY):** _____					
32.	32.	Cognitive impairment not otherwise specified (NOS)	☐1	32a.	☐1	☐2	☐3
32b.	32b.	If **present**, **(SPECIFY):** _____					

Coding Guidebook for **Form D1b:** Etiological Diagnosis and Biomarker Support

***INSTRUCTIONS**: This form is to be completed by the clinician for all participants, including cognitively unimpaired. Check only <u>one</u> box per question.*

The purpose of this form is to record when biomarkers are used to support an etiological diagnosis. This will allow future researchers to understand when a diagnosis is made on only clinical grounds versus when information from biomarkers that may reflect underlying pathological changes are used in addition to clinical information.

Given the rapidity of the development of biomarkers, this form is not meant to record biomarker values, methodological techniques, or to indicate availability of samples. Instead, this form has a very focused purpose to indicate when diagnoses are (or are not) supported by biomarker information. Sites should use their own internal methods to determine the relevance, presence or absence of a biomarker.

IVP	FVP		
1.	1.	Were any biomarker results used to support the current etiological diagnosis? *(Consider any biomarker results from any time that may be clinically relevant)*	☐ 0 No **(SKIP TO QUESTION 12)** ☐ 1 Yes **(CONTINUE TO QUESTION 2)**

Section 1 – Biomarkers and imaging

Complete this section if any of the following biomarker measures were used to **<u>support or exclude</u>** a presumed etiological diagnosis, including unimpaired individuals who have biomarker characterization. Please complete the checklist below for each data source available and the related questions for each supporting data. Then complete **Section 2: Etiological Diagnosis**. This section is not intended to capture actual data values or register sample availability; instead this section's purpose is to record what information was used by the clinician (or at consensus) to inform an etiological diagnosis.

Fluids

2.	2.	**Fluid Biomarkers** – Were fluid biomarkers used for assessing the etiological diagnosis?	☐ 0 No **(SKIP TO QUESTION 5)** ☐ 1 Yes, only blood-based biomarkers were used **(CONTINUE TO QUESTION 3, and SKIP QUESTIONS 4 – 4d)** ☐ 2 Yes, only CSF-based biomarkers were used **(SKIP TO QUESTION 4)** ☐ 3 Yes, both blood- and CSF-based biomarkers were used

Please use the following questions to indicate the results of the fluid biomarker test(s) used by the clinician (or at consensus) to determine the etiological diagnosis at this visit.

If a fluid biomarker was used to exclude an etiological diagnosis, select **0=Not consistent**. If a fluid biomarker was found to be consistent with a diagnosis, select **1=Yes, consistent**. If a fluid biomarker was found to be indeterminate, select **9**. In cases where one or more of the etiologies listed were not assessed using fluid biomarkers, select **8**.

3.	3.	**Blood-based biomarkers**	**No, inconsistent**	**Yes, consistent**	**Indeterminate**	**Not assessed**
		9=Indeterminate should reflect situations where clinical judgment about interpreting the result of a biomarker result is unclear. The "indeterminate" category is specifically about clinical confidence in cases where the biomarker is not or cannot be interpreted to support or refute a diagnosis. Examples of where this uncertainty can arise include, • A borderline result that's interpreted as being too close to the established cut point • A technical issue that prevents clear interpretation of the biomarker • Use of an unvalidated or insufficiently validated biomarker				
3a.	3a.	Consistent with AD	☐ 0	☐ 1	☐ 9	☐ 8
		Based on your center's standards, were blood-based biomarkers interpreted as supporting an etiological diagnosis of AD?				
3b.	3b.	Consistent with FTLD	☐ 0	☐ 1	☐ 9	☐ 8
		Based on your center's standards, were blood-based biomarkers interpreted as supporting an etiological diagnosis of FTLD?				
3c.	3c.	Consistent with LBD	☐ 0	☐ 1	☐ 9	☐ 8
		Based on your center's standards, were blood-based biomarkers interpreted as supporting an etiological diagnosis of LBD?				

3d.	3d.	Consistent with other etiology (**SPECIFY**): _____	☐0	☐1	☐9	☐8

Based on your center's standards, were blood-based biomarkers interpreted as supporting an etiological diagnosis of another etiology?

		CSF-based biomarkers	**No, inconsistent**	**Yes, consistent**	**Indeterminate**	**Not assessed**
4a.	4a.	Consistent with AD	☐0	☐1	☐9	☐8

Based on your center's standards, were CSF-based biomarkers interpreted as supporting an etiological diagnosis of AD?

4b.	4b.	Consistent with FTLD	☐0	☐1	☐9	☐8

Based on your center's standards, were CSF-based biomarkers interpreted as supporting an etiological diagnosis of FTLD?

4c.	4c.	Consistent with LBD	☐0	☐1	☐9	☐8

Based on your center's standards, were CSF-based biomarkers interpreted as supporting an etiological diagnosis of LBD?

4d.	4d.	Consistent with other etiology (**SPECIFY**): _____	☐0	☐1	☐9	☐8

Based on your center's standards, were CSF-based biomarkers interpreted as supporting an etiological diagnosis of another etiology?

Imaging

5.	5.	**Imaging** – Was imaging used for assessing etiological diagnosis?	☐0 No **(SKIP TO QUESTION 8)** ☐1 Yes, only PET/SPECT imaging was used **(CONTINUE TO QUESTION 6, and SKIP QUESTIONS 7 – 7a3f)** ☐2 Yes, only MR/CT imaging was used **(SKIP TO QUESTION 7)** ☐3 Yes, both PET/SPECT and MR/CT imaging were used

Please use the following questions to indicate the results of the imaging used by the clinician (or at consensus) to determine the etiological diagnosis at this visit.

If imaging was used to exclude an etiological diagnosis, select **0=Not consistent**. If imaging was found to be consistent with a diagnosis, select **1=Yes, consistent**. If imaging was found to be indeterminate, select **9**. In cases where one or more of the etiologies listed were not assessed using imaging, select **8**.

6. PET/SPECT

9=Indeterminate should reflect situations where clinical judgment about interpreting the result of a biomarker result is unclear. The "indeterminate" category is specifically about clinical confidence in cases where the biomarker is not or cannot be interpreted to support or refute a diagnosis. Examples of where this uncertainty can arise include,

- A borderline result that's interpreted as being too close to the established cut point
- A technical issue that prevents clear interpretation of the biomarker
- Use of an unvalidated or insufficiently validated biomarker

6a.	6a.	**Tracer-based PET** - Were tracer-based PET measures used in assessing an etiological diagnosis?	☐0 No **(SKIP TO QUESTION 6b)** ☐1 Yes, results were normal or abnormal ☐2 Yes, results were indeterminate

		If used in diagnosis, indicate the results:	**No**	**Yes**	**Indeterminate**	**Not assessed**
6a1.	6a1.	Elevated Amyloid	☐0	☐1	☐9	☐8

Based on your center's standards, were there evidence of elevated cerebral amyloid on PET imaging?

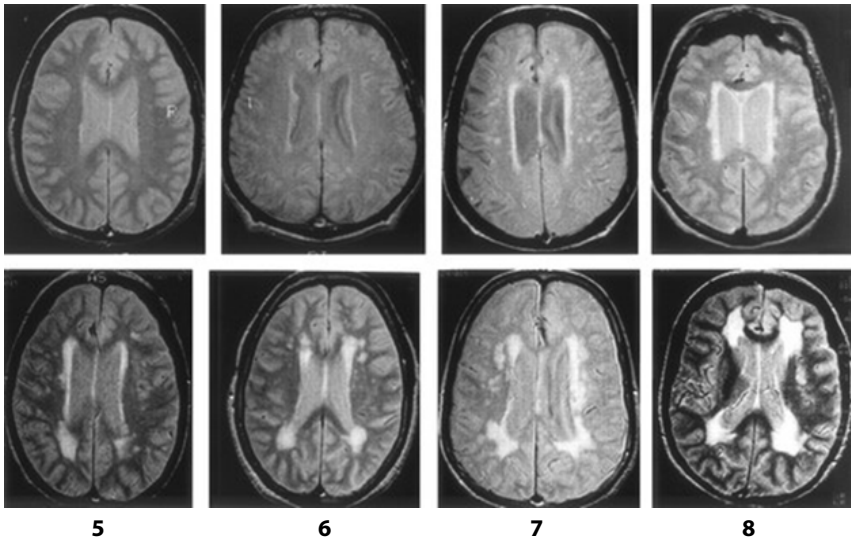
6a2.	6a2.	Elevated tau pathology	☐0	☐1	☐9	☐8

Based on your center's standards, were there evidence of elevated cerebral tau on PET imaging?

IVP	FVP	Section 1 – Biomarkers and imaging *continued...*				
6b.	6b.	**FDG PET** - Was FDG PET data or information used to support an etiological diagnosis?	☐0 No **(SKIP TO QUESTION 6c)** ☐1 Yes, results were normal or abnormal ☐2 Yes, results were indeterminate			
			No, inconsistent	**Yes, consistent**	**Indeterminate**	**Not assessed**
6b1.	6b1.	Consistent with AD	☐0	☐1	☐9	☐8
		Based on your center's standards, was an FDG PET scan interpreted as being consistent with an underlying etiology of AD?				
6b2.	6b2.	Consistent with FTLD	☐0	☐1	☐9	☐8
		Based on your center's standards, was an FDG PET scan interpreted as being consistent with an underlying etiology of FTLD?				
6b3.	6b3.	Consistent with LBD	☐0	☐1	☐9	☐8
		Based on your center's standards, was an FDG PET scan interpreted as being consistent with an underlying etiology of LBD?				
6b4.	6b4.	Consistent with other etiology (**SPECIFY**): _____	☐0	☐1	☐9	☐8
		Based on your center's standards, was an FDG PET scan interpreted as being consistent with an underlying etiology of another etiology?				
6c.	6c.	**Dopamine Transporter (DAT) Scan** - Was DAT Scan data or information used to support an etiological diagnosis?	☐0 No ☐1 Yes, results were normal or abnormal ☐2 Yes, results were indeterminate			
		Based on your center's standards, was a DAT scan interpreted as being consistent with an underlying etiology of a Parkinson's disorder?				
6d.	6d.	**Other tracer-based imaging** - Were other tracer-based imaging used to support an etiological diagnosis? **(SPECIFY):** _____	☐0 No **(SKIP TO QUESTION 7a)** ☐1 Yes, results were normal or abnormal ☐2 Yes, results were indeterminate			
			No, inconsistent	**Yes, consistent**	**Indeterminate**	**Not assessed**
6d1.	6d1.	Consistent with AD	☐0	☐1	☐9	☐8
		Was another tracer-based imaging assessment interpreted as being consistent with AD?				
6d2.	6d2.	Consistent with FTLD	☐0	☐1	☐9	☐8
		Was another tracer-based imaging assessment interpreted as being consistent with FTLD?				
6d3.	6d3.	Consistent with LBD	☐0	☐1	☐9	☐8
		Was another tracer-based imaging assessment interpreted as being consistent with LBD?				
6d4.	6d4.	Consistent with other etiology (**SPECIFY**): _____	☐0	☐1	☐9	☐8
		Was another tracer-based imaging assessment interpreted as being consistent with another etiology?				
7.	7.	**Structural Imaging**				
7a.	7a.	**Structural Imaging (i.e., MRI or CT)** – Was structural imaging data or information used to support an etiological diagnosis?	☐0 No **(SKIP TO QUESTION 8)** ☐1 Yes, results were normal or abnormal ☐2 Yes, results were indeterminate			

				No, inconsistent	Yes, consistent	Indeterminate	Not assessed
7a1.	7a1.		Atrophy pattern consistent with AD	☐0	☐1	☐9	☐8
			Based on your center's standards, was an atrophy pattern interpreted as supporting an etiology of AD?				
7a2.	7a2.		Atrophy pattern consistent with FTLD	☐0	☐1	☐9	☐8
			Based on your center's standards, was an atrophy pattern interpreted as supporting an etiology of FTLD?				
7a3.	7a3.		Consistent with Cerebrovascular disease (CVD)	☐0	☐1	☐9	☐8
			Based on your center's standards, was an atrophy pattern interpreted as supporting an etiology of cerebrovascular disease as a cause for the cognitive disorder?				

			If there is evidence for CVD on imaging, indicate the findings:	No	Yes	Indeterminate	Not assessed
			QUESTIONS 7a3a – 7a3f: Use your Center's local standards to determine whether the participant had imaging evidence for each of the Questions 7a3a – 7a3f. If there is no evidence or ambiguous evidence for each particular CVD listed according to your Center's standards, select **0=No** for the corresponding question. Although each Center's local standards should be used to determine whether the participant has imaging evidence for CVD, clinicians are welcome to refer to the following paper: *Wardlaw JM, et al. Neuroimaging standards for research into small vessel disease and its contribution to ageing and neurodegeneration. Lancet Neurol 2013;12:822-38.*				
7a3a.	7a3a.		Large vessel infarct(s)	☐0	☐1	☐9	☐8
7a3b.	7a3b.		Lacunar infarct(s)	☐0	☐1	☐9	☐8
7a3c.	7a3c.		Macrohemorrhage(s)	☐0	☐1	☐9	☐8
7a3d.	7a3d.		Microhemorrhage(s)	☐0	☐1	☐9	☐8
7a3e.	7a3e.		White matter hyperintensity	☐0	☐1	☐9	☐8
7a3e1.	7a3e1.		If **Yes**, choose the severity: ☐1 Moderate white-matter hyperintensity (CHS score 5-6) ☐2 Extensive white-matter hyperintensity (CHS score 7-8+)				



Examples of single slices from complete scans that were used by the study neuroradiologists to grade white matter. Grade 1 was described as discontinuous periventricular rim with minimal dots of subcortical disease; grade 2,thin, continuous periventricular rim with a few patches of subcortical disease; grade 3, thicker, continuous periventricular rim with scattered patches of subcortical disease; grade 4, thicker, shaggier periventricular rim with mild subcortical disease, may have minimal confluent periventricular lesions; grade 5, mild periventricular confluence surrounding the frontal and occipital horns; grade 6, moderate periventricular confluence surrounding the frontal and occipital horns; grade 7, periventricular confluence with moderate involvement of the centrum semiovale; and grade 8, periventricular confluence involving most of the centrum semiovale. Studies with no white matter findings were graded 0, and those with findings more remarkable than grade 8 were scored 9.

If the participant has a white matter grade of 5, 6, 7, 8, or 9, select **1= Yes** for Question 7a3e. If the participant has a score of 0, 1, 2, 3, or 4, select **0=No** for Question 7a3e.

If the participant has a white matter grade of 5 or 6, select **1= Moderate white-matter hyperintensity (CHS score 5-6)** for Question 7a3e1. If the participant has a white matter grade of 7, 8, or 9, select **2=Extensive white-matter hyperintensity (CHS score 7-8+)** for Question 7a3e1**.**

_____

Longstreth WT Jr1 , Manolio TA, Arnold A, Burke GL, Bryan N, Jungreis CA, Enright PL, O'Leary D, Fried L. Clinical correlates of white matter findings on cranial magnetic resonance imaging of 3301 elderly people. The Cardiovascular Health Study. Stroke. Stroke, 27(8):1274-82, 1996.

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IVP **FVP** **Section 1 – Biomarkers and imaging** ***continued...***

Other biomarker modalities *(e.g., tissues, skin, retinal imaging, etc.)*

Please use the following questions to indicate the results of any additional biomarker modalities used by the clinician (or at consensus) to support the etiological diagnosis at this visit.

If a biomarker modality was used to exclude an etiological diagnosis, select **0=Not consistent**. If a biomarker modality was found to be consistent with a diagnosis, select **1=Yes, consistent**. If a biomarker was found to be indeterminate, select **9**. In cases where one or more of the etiologies listed were not assessed using a biomarker modality, select **8**.

9=Indeterminate should reflect situations where clinical judgment about interpreting the result of a biomarker result is unclear. The "indeterminate" category is specifically about clinical confidence in cases where the biomarker is not or cannot be interpreted to support or refute a diagnosis. Examples of where this uncertainty can arise include,

- A borderline result that's interpreted as being too close to the established cut point
- A technical issue that prevents clear interpretation of the biomarker
- Use of an unvalidated or insufficiently validated biomarker

This section is included to accommodate for the expected rapid changes in the biomarker field. When a biomarker not accounted for above (for example, skin biopsies to confirm LBD) is used to support an etiological diagnosis, please use these fields to account for it. This section is not designed to collect information on values, types, or availability of biomarkers but instead is here to indicate when a biomarker is being used by the clinician or at consensus (using local standards) to support an etiological diagnosis.

8.	**8.**	**Other biomarker modality** - Was another biomarker modality used to support an etiological diagnosis? **(SPECIFY):** _____	☐0 No **(SKIP TO QUESTION 11)** ☐1 Yes, results were normal or abnormal ☐2 Yes, results were indeterminate	

			No	**Yes**	**Indeterminate**
8a.	**8a.**	Consistent with AD	☐0	☐1	☐9
8b.	**8b.**	Consistent with FTLD	☐0	☐1	☐9
8c.	**8c.**	Consistent with LBD	☐0	☐1	☐9
8d.	**8d.**	Consistent with other etiology (**SPECIFY**): _____	☐0	☐1	☐9

IVP	FVP	Section 1 – Biomarkers and imaging *continued...*

9.	9.	**Other biomarker modality** - Was another biomarker modality used to support an etiological diagnosis? **(SPECIFY):** _____	☐0 No **(SKIP TO QUESTION 11)** ☐1 Yes, results were normal or abnormal ☐2 Yes, results were indeterminate

			No	Yes	Indeterminate
9a.	9a.	Consistent with AD	☐0	☐1	☐9
9b.	9b.	Consistent with FTLD	☐0	☐1	☐9
9c.	9c.	Consistent with LBD	☐0	☐1	☐9
9d.	9d.	Consistent with other etiology (**SPECIFY**): _____	☐0	☐1	☐9

10.	10.	**Other biomarker modality** - Was another biomarker modality used to support an etiological diagnosis? **(SPECIFY):** _____	☐0 No **(SKIP TO QUESTION 11)** ☐1 Yes, results were normal or abnormal ☐2 Yes, results were indeterminate

			No	Yes	Indeterminate
10a.	10a.	Consistent with AD	☐0	☐1	☐9
10b.	10b.	Consistent with FTLD	☐0	☐1	☐9
10c.	10c.	Consistent with LBD	☐0	☐1	☐9
10d.	10d.	Consistent with other etiology (**SPECIFY**): _____	☐0	☐1	☐9

Supportive genetics

11.	11.	Is there an autosomal dominant pathogenic variant to support an etiological diagnosis?	☐0 No ☐1 Yes ☐9 Unknown/Not disclosed

Section 2 – Etiological diagnoses

*Using all the available data (i.e. clinical, cognitive, biomarker, etc) please provide an etiological diagnosis. For those with no biomarker data, enter a **presumed** etiological diagnosis.*

Must be filled out for all participants. 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 etiological diagnoses 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 unimpaired participants: Proceed using your center's diagnostic philosophy to determine whether the etiology is present and primary, contributing, or non-contributing or leave the checkboxes blank.

		Etiological Diagnoses	Present		Primary	Contributing	Non-contributing
12.	12.	Alzheimer's disease	☐1	12a.	☐1	☐2	☐3

Indicate if the etiological diagnosis is suspected to be Alzheimer's disease using any combination of clinical criteria and biomarkers, per your center's standards. If Alzheimer's disease is not present, leave all boxes for Questions 12 and 12a unchecked. For reference, AD clinical criteria are excerpted and condense from the 2011 NIA-AA criteria for AD dementia (McKhann et al., 2011).

For participants with cognitive and/or behavioral impairment: If Alzheimer's disease is present, select **1=Present** and indicate whether it is thought to be the **1=Primary** or **2=Contributing** cause of the cognitive impairment.

Probable AD can be indicated as **1=Primary** or **2=Contributing**. On the contrary, Possible Alzheimer's disease (atypical course or seemingly mixed etiologies) should not be marked as **1=Primary**; the only exception is when there is an atypical course, positive biomarker evidence for AD, and no compelling clinical or biomarker evidence for another primary etiology.

For participants with normal cognition: If the participant has normal cognition and either sufficient biomarker evidence for Alzheimer's disease or a known genetic mutation, leave all checkboxes in Questions 12 and 12a blank/ unchecked.

For participants with normal cognition and behavior and positive biomarkers: For participants who exhibit normal cognitive function but have biomarker evidence consistent with Alzheimer's disease pathology (or possess a known genetic mutation associated with the disease), you have the flexibility to proceed according to your center's diagnostic philosophy:

Option 1: If your center's practice is to diagnose Alzheimer's disease in cognitively normal individuals with positive biomarkers, you may **check the appropriate boxes in Questions 12 and 12a** to reflect this diagnosis.

Option 2: If your center prefers not to assigne an Alzheimer's disease diagnosis to cognitively normal individuals despite positive biomarkers, you may **leave all checkboxes in Questions 12 and 12a blank/unchecked**. In this scenario, the biomarker and genetic information provided in **Section 1** can be utilized to determine the presence of preclinical or presymptomatic Alzheimer's disease.

A. Probable AD is diagnosed when the patient:

1. Meets criteria for dementia, and has the following characteristics:
2. Insidious onset. Symptoms have a gradual onset over months to years; and
3. Clear-cut history of worsening of cognition by report or observation; and
4. The initial and most prominent cognitive deficits are evident on history and examination in one of the following categories.
   (1) Amnestic disorder: The most common syndromic presentation of AD dementia.
   (2) Non-amnestic disorders:
   - Language disorder
   - Visuospatial disorder
   - Executive and behavioral disorder
5. Exclusions: The diagnosis of probable AD dementia should not be applied when there is evidence of:
   (a) substantial concomitant cerebrovascular disease or
   (b) core features of dementia with Lewy bodies other than dementia itself; or
   (c) prominent features of behavioral variant frontotemporal dementia; or
   (d) prominent features of semantic variant primary progressive aphasia or non-fluent/agrammatic variant primary progressive aphasia; or
   (e) evidence for another concurrent, active neurological disease, or a non-neurological medical co-morbidity or medication use that could have a substantial impact on cognition.

B. Possible AD is diagnosed when the patient meets one of the two following criteria:

1. Atypical course: Meets the core clinical criteria (1) and (4) (above) for probable AD dementia, but either had a sudden onset of cognitive impairment or demonstrates insufficient historical detail or objective cognitive documentation of progressive decline, or
2. Etiologically mixed presentation: Meets all core clinical criteria (1) through (4) (above) for probable AD dementia but has evidence of:
   (a) concomitant cerebrovascular disease or
   (b) features of dementia with Lewy bodies other than the dementia itself; or
   (c) evidence for another neurological disease or a non-neurological medical co-morbidity or medication use that could have a substantial impact on cognition.

McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement. 2011;7(3):263-269.

The following guidance is excerpted from the 2011 NIA-AA criteria for MCI due to AD (Albert et al., 2011):

Summary of clinical and cognitive evaluation for MCI due to AD

Establish clinical and cognitive criteria

- Cognitive concern reflecting a change in cognition reported by patient or informant or clinician (i.e., historical or observed evidence of decline over time)
- Objective evidence of impairment in one or more cognitive domains, typically including memory (i.e., formal or bedside testing to establish level of cognitive function in multiple domains)
- Largely preserved independence in functional abilities
- Not demented

Examine etiology of MCI consistent with AD pathophysiological process

- Rule out vascular, traumatic, medical causes of cognitive decline, where possible
- Provide evidence of longitudinal decline in cognition, when feasible
- Report history consistent with AD genetic factors, where relevant

Abbreviations: AD, Alzheimer's disease; MCI, mild cognitive impairment

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"Alzheimer's and Dementia, 7/3, Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, Fox NC, Gamst A, Holtzman DM, Jagust WJ, Petersen RC, Snyder PJ, Carrillo MC, Thies B, Phelps CH, The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease, 270-279, 2011, with permission from Elsevier http://www.sciencedirect.com/science/article/pii/S155252601100104X."

IVP	FVP						
13.	13.	Lewy body disease	☐1	13a.	☐1	☐2	☐3

Refer to the papers McKeith et al., 2017 (see DLB criteria on pages 99 – 100) and Litvan et al., 2003 (see criteria table below) to assess the presence of dementia with Lewy body disease. The following criteria refer for probably and possible MCI with Lewy bodies.

Summary of research criteria for the clinical diagnosis of the prodromal phase of dementia with Lewy Bodies (DLB) excerpted from McKeith et al., 2020[1].

RESEARCH CRITERIA for the clinical diagnosis of probable and possible MCI with Lewy bodies (MCI-LB):

1. **Essential for a diagnosis of MCI-LB is MCI defined by the presence of each of the following:**
   - Concern by the patient, informant, or clinician regarding cognitive decline.
   - Objective evidence of impairment in 1 or more cognitive domains. The cognitive impairment may include any domain, but is more likely to be associated with attention-executive and/or visual processing deficits.
   - Preserved or minimally affected performance of previously attained independence in functional abilities, which do not meet the criteria for dementia.
2. **Core clinical features:**
   - Fluctuating cognition with variations in attention and alertness.
   - Recurrent visual hallucinations.
   - REM sleep behavior disorder.
   - One or more spontaneous cardinal features of parkinsonism: these are bradykinesia (defined as slowness of movement and decrement in amplitude or speed), rest tremor, or rigidity.
3. **Supportive clinical features:**
   - Severe sensitivity to antipsychotic agents; postural instability; repeated falls; syncope or other transient episodes of unresponsiveness; prolonged or recurrent delirium not due to provoking factors such as surgery, infections, or other systemic illness; autonomic dysfunction, e.g., constipation, orthostatic hypotension, urinary incontinence; hypersomnia; hyposmia; REM sleep without atonia; hallucinations in other modalities including passage, and sense of presence phenomena; systematized delusions including Capgras syndrome; apathy, anxiety, and depression.
4. **Proposed biomarkers:**
   - Reduced dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET.
   - Polysomnographic confirmation of REM sleep without atonia.
   - Reduced meta-iodobenzylguanidine (MIBG) uptake on myocardial scintigraphy.
5. **Potential biomarkers:**
   - Quantitative EEG showing slowing and dominant frequency variability.
   - Relative preservation of medial temporal lobe structures on structural imaging.
   - Insular thinning and gray matter volume loss on MRI.
   - Low occipital uptake on perfusion/metabolism scan.
   - MCI plus supportive clinical features or potential biomarkers are insufficient to diagnose MCI-LB but may raise suspicion of it and prompt biomarker investigation and may add weight to an existing MCILB diagnosis.
   - MCI-LB is less likely in the presence of any other physical illness or brain disease including cerebrovascular disease, sufficient to account in part or in total for the clinical picture, although these do not exclude an MCI-LB diagnosis and may serve to indicate mixed or multiple pathologies contributing to the clinical presentation.
   - Skin biopsy[4]
6. **Probable MCI-LB can be diagnosed if:**
   a. Two or more core clinical features of DLB are present, with or without the presence of a proposed biomarker, or
   b. Only 1 core clinical feature is present, but with 1 or more proposed biomarkers.
7. **Probable MCI-LB should not be diagnosed based on biomarkers alone.**
8. **Possible MCI-LB can be diagnosed if:**
   a. Only 1 core clinical feature of DLB is present, with no proposed biomarkers, or
   b. One or more of the proposed biomarkers is present, but there are no core clinical features.

---

[1] McKeith IF, Ferman TJ, Thomas AJ, et al. Research criteria for the diagnosis of prodromal dementia with Lewy bodies, Neurology 2020; 94: 1-13

[2] McKeith IF, Boeve BF, Dickson DW, et al. Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium, Neurology 2017; 89: 88-100.

[3] Mov Disord. 2003 May; 18(5):467-86. Movement Disorders Society Scientific Issues Committee report: SIC Task Force appraisal of clinical diagnostic criteria for Parkinsonian disorders. Litvan I1, Bhatia KP, Burn DJ, Goetz CG, Lang AE, McKeith I, Quinn N, Sethi KD, Shults C, Wenning GK; Movement Disorders Society Scientific Issues Committee.

[4] Gibbons CH, Levine T, Adler C, Bellaire B, Wang N, Stohl J, Agarwal P, Aldridge GM, Barboi A, Evidente VGH, Galasko D, Geschwind MD, Gonzalez-Duarte A, Gil R, Gudesblatt M, Isaacson SH, Kaufmann H, Khemani P, Kumar R, Lamotte G, Liu AJ, McFarland NR, Miglis M, Reynolds A, Sahagian GA, Saint-Hillaire MH, Schwartzbard JB, Singer W, Soileau MJ, Vernino S, Yerstein O, Freeman R. Skin Biopsy Detection of Phosphorylated α-Synuclein in Patients With Synucleinopathies. JAMA. 2024 Apr 16;331(15):1298-1306. doi: 10.1001/jama.2024.0792. PMID: 38506839; PMCID: PMC10955354.

For participants with cognitive and/or behavioral impairment: If Lewy body disease (DLB or Parkinson's disease) is present, select **1=Present**, and indicate whether it is thought to be the **1=Primary** or **2=Contributing** cause of the cognitive impairment. If Lewy body disease is not present, leave all boxes for Questions 13 and 13a unchecked

For participants with normal cognition: If the participant has normal cognition but has a clinical diagnosis of Lewy body disease, select **1=Present** and leave checkbox 13a blank/unchecked.

For participants with normal cognition and behavior and positive biomarkers: For participants who exhibit normal cognitive function but have biomarker evidence consistent with Neuronal Synuclein disease pathology (or possess a known genetic mutation associated with the disease), you have the flexibility to proceed according to your center's diagnostic philosophy:

Option 1: If your center's practice is to diagnose Neuronal Synuclein disease in cognitively normal individuals with positive biomarkers, you may **check the appropriate boxes in Questions 13 and 13a** to reflect this diagnosis.

Option 2: If your center prefers not to assign a Neuronal Synuclein disease diagnosis to cognitively normal individuals despite positive biomarkers, you may **leave all checkboxes in Questions 13 and 13a blank/unchecked**. In this scenario, the biomarker and genetic information provided in **Section 1** can be utilized to determine the presence of preclinical or presymptomatic Neuronal Synuclein disease.

IVP	FVP	Section 2 – Etiological diagnoses *continued...*					
14.	14.	Frontotemporal lobar degeneration	☐1				
		If **present**, select all that apply:					
14a.	14a.	Progressive supranuclear palsy (PSP)	☐1	14a1.	☐1	☐2	☐3

Excerpted from Höglinger et al. (2017):

B1: Mandatory inclusion criteria

1. Sporadic occurrence*
2. Age 40 or older at onset** of first PSP-related symptom***
3. Gradual progression of PSP-related symptoms***

Core Features: We propose four core functional domains as characteristic clinical manifestations of PSP (ocular motor dysfunction **[O]**, postural instability **[P]**, akinesia **[A]**, and cognitive dysfunction **[C]**. In each domain, we propose three characteristic core clinical features, stratified by presumed levels of certainty (1 [highest], 2 [mid], and 3 [lowest]) that they contribute to the diagnosis of PSP.

LEVELS OF CERTAINTY	OCULAR MOTOR DYSFUNCTION	POSTURAL INSTABILITY	AKINESIA	COGNITIVE DYSFUNCTION
LEVEL 1	O1: Vertical supranuclear gaze palsy	P1: Repeated unprovoked falls within 3 years	A1: Progressive gait freezing within 3 years	C1: Speech/language disorder (i.e., nonfluent/ agrammatic variant of primary progressive aphasia or progressive apraxia of speech)
LEVEL 2	O2: Slow velocity of vertical saccades	P2: Tendency to fall on the pull-test within 3 years	A2: Parkinsonism, akinetic-rigid predominantly axial, and levodopa resistant	C2: Frontal cognitive/ behavioral presentation
LEVEL 3	O3: Frequent macro square wave jerks or "eyelid opening apraxia"	P3: More than two steps backward on the pull-test within 3 years	A3: Parkinsonism, with tremor and/or asymmetric and/or levodopa responsive	C3: Corticobasal syndrome

Levels with lower numbers are considered to contribute higher certainty to a diagnosis of PSP that levels with higher numbers.

B2: Mandatory exclusion criteria

Clinical findings

1. Predominant, otherwise unexplained impairment of episodic memory, suggestive of AD
2. Predominant, otherwise unexplained autonomic failure, e.g., orthostatic hypotension (orthostatic reduction in blood pressure after 3 minutes standing 30mm Hg systolic or15mm Hg diastolic), suggestive of multiple system atrophy or Lewy body disease
3. Predominant, otherwise unexplained visual hallucinations or fluctuations in alertness, suggestive of dementia with Lewy bodies
4. Predominant, otherwise unexplained multisegmental upper and lower motor neuron signs, suggestive of motor neuron disease (pure upper motor neuron signs are not an exclusion criterion)
5. Sudden onset or step-wise or rapid progression of symptoms, in conjunction with corresponding imaging or laboratory findings, suggestive of vascular etiology, autoimmune encephalitis, metabolic encephalopathies, or prion disease
6. History of encephalitis
7. Prominent appendicular ataxia
8. Identifiable cause of postural instability, e.g., primary sensory deficit, vestibular dysfunction, severe spasticity, or lower motor neuron syndrome

Imaging findings

1. Severe leukoencephalopathy, evidenced by cerebral imaging
2. Relevant structural abnormality, e.g., normal pressure or obstructive hydrocephalus; basal ganglia, diencephalic,mesencephalic, pontine or medullary infarctions, hemorrhages, hypoxic-ischemic lesions, tumors, or malformation

For participants with cognitive and/or behavioral impairment: If PSP is present, select **1=Present** and indicate whether it is thought to be the **1=Primary** cause, a **2=Contributing** cause or a **3=Non-contributing** cause of the cognitive impairment.

For participants with normal cognition and behavior: If the participant has normal cognition but clinical symptoms sufficient for a diagnosis of PSP, select PSP as **1=Present** and leave the checkboxes about whether it is primary or contributing in Question 14a1 blank/unchecked.

For participants with normal cognition and behavior and positive biomarkers: For participants who exhibit normal cognitive function but have biomarker evidence consistent with PSP pathology (or possess a known genetic mutation associated with the disease), you have the flexibility to proceed according to your center's diagnostic philosophy:

> **Option 1:** If your center's practice is to diagnose PSP in cognitively normal individuals with positive biomarkers, you may **check the appropriate boxes in Questions 14a and 14a1** to reflect this diagnosis.
>
> **Option 2:** If your center prefers not to assign a PSP diagnosis to cognitively normal individuals despite positive biomarkers, you may **leave all checkboxes in Questions 14a and 14a1 blank/unchecke**d. In this scenario, the biomarker and genetic information provided in Section 1 can be utilized to determine the presence of preclinical or presymptomatic PSP.

If PSP is not present leave the checkboxes in Questions 14a and 14a1 blank/unchecked.

Höglinger GU, Respondek G, Stamelou M, Kurz C, Josephs KA, Lang AE, Mollenhauer B, Müller U, Nilsson C, Whitwell JL, Arzberger T, Englund E, Gelpi E, Giese A, Irwin DJ, Meissner WG, Pantelyat A, Rajput A, van Swieten JC, Troakes C, Antonini A, Bhatia KP, Bordelon Y, Compta Y, Corvol JC, Colosimo C, Dickson DW, Dodel R, Ferguson L, Grossman M, Kassubek J, Krismer F, Levin J, Lorenzl S, Morris HR, Nestor P, Oertel WH, Poewe W, Rabinovici G, Rowe JB, Schellenberg GD, Seppi K, van Eimeren T, Wenning GK, Boxer AL, Golbe LI, Litvan I; Movement Disorder Society-endorsed PSP Study Group. Clinical diagnosis of progressive supranuclear palsy: The movement disorder society criteria. Mov Disord. 2017 Jun;32(6):853-864. doi: 10.1002/mds.26987. Epub 2017 May 3. PMID: 28467028; PMCID: PMC5516529.

14b.	**14b.**		Corticobasal degeneration (CBD)	☐1	**14b2.**	☐1	☐2	☐3

Refer to diagnostic criteria by Armstrong et al. (2013) when assessing the presence of CBD.

For participants with cognitive and/or behavioral impairment: If CBD is present, select **1=Present** and indicate whether it is thought to be the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment.

For participants with normal cognition and behavior: If the participant has normal cognition but clinical symptoms sufficient for a diagnosis of CBD, select CBD as **1=Present** and leave the checkboxes about whether it is primary or contributing in Question 14b1 blank/unchecked.

For participants with normal cognition and behavior and positive biomarkers: For participants who exhibit normal cognitive function but have biomarker evidence consistent with CBD pathology (or possess a known genetic mutation associated with the disease), you have the flexibility to proceed according to your center's diagnostic philosophy:

> **Option 1:** If your center's practice is to diagnose CBD in cognitively normal individuals with positive biomarkers, you may **check the appropriate boxes in Questions 14b and 14b1** to reflect this diagnosis.
>
> **Option 2:** If your center prefers not to assign a CBD diagnosis to cognitively normal individuals despite positive biomarkers, you may **leave all checkboxes in Questions 14b and 14b1 blank/unchecked**. In this scenario, the biomarker and genetic information provided in **Section 1** can be utilized to determine the presence of preclinical or presymptomatic CBD.

If CBD is not present, leave all boxes for Questions 14b and 14b1 blank/unchecked.

Proposed clinical phenotypes (syndromes) associated with the pathology of corticobasal degeneration (CBD)

Syndrome	Features
Probable corticobasal syndrome	**Asymmetric presentation of TWO OF:** a) limb rigidity or akinesia, b) limb dystonia, c) limb myoclonus; **PLUS TWO OF:** d) orobuccal or limb apraxia, e) cortical sensory deficit, f) alien limb phenomena (more than simple levitation)
Possible corticobasal syndrome	**May be symmetric; ONE OF:** a) limb rigidity or akinesia, b) limb dystonia, c) limb myoclonus; **PLUS ONE OF:** d) orobuccal or limb apraxia, e) cortical sensory deficit, f) alien limb phenomena (more than simple levitation).

[1] *Armstrong, MJ, Litvan I, et al. Criteria for the diagnosis of corticobasal degeneration. Neurology 2013;80;496.*

14c.	**14c.**		FTLD with motor neuron disease	☐1	**14c1.**	☐1	☐2	☐3

Use the following criteria, adapted from El Escorial revisited: Revised criteria for the diagnosis of amyotrophic lateral sclerosis (Brooks et al., 2000)[1]:

Requirements for the diagnosis of amyotrophic lateral sclerosis

The diagnosis of ALS requires the PRESENCE of:

- Evidence of lower motor neuron (LMN) degeneration by clinical, electrophysiological or neuropathologic examination;
- Evidence of upper motor neuron (UMN) degeneration by clinical examination; and
- Progressive spread of symptoms or signs within a region or to other regions, as determined by history or examination, together with B1 and B2 in next column.

The diagnosis of ALS requires the ABSENCE of:

- Electrophysiological or pathological evidence of other disease processes that might explain the signs of LMN and/or UMN degeneration; and
- Neuroimaging evidence of other disease processes that might explain the observed clinical and electrophysiological signs.

[1] *Brooks BR, Miller RG, Swash M, Munsat TL, Diseases WFoNRGoMN. El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord. 2000;1(5):293-299.*

For participants with cognitive and/or behavioral impairment: If FTLD with motor neuron disease is present, select **1=Present** and indicate whether it is thought to be the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment.

For participants with normal cognition and behavior: If the participant has normal cognition but clinical symptoms sufficient for a diagnosis of FTLD with motor neuron disease, select **1=Present** and leave the checkboxes about whether it is primary or contributing in Question 14c1 blank/unchecked.

For participants with normal cognition and behavior and positive biomarkers: For participants who exhibit normal cognitive function but have biomarker evidence consistent with FTLD with motor neuron disease pathology (or possess a known genetic mutation associated with the disease), you have the flexibility to proceed according to your center's diagnositc philosophy:

Option 1: If your center's practice is to diagnose FTLD with motor neuron disease in cognitively normal individuals with positive biomarkers, you may **check the appropriate boxes in Questions 14c and 14c1** to reflect this diagnosis.

Option 2: If your center prefers not to assign a FTLD with motor neuron disease diagnosis to cognitively normal individuals despite positive biomarkers, you may **leave all checkboxes in Question 14c and 14c1 blank/unchecked**. In this scenario, the biomarker and genetic information provided in **Section 1** can be utilized to determine the presence of preclinical or presymptomatic FTLD with motor neruon disease.

If FTLD with motor neuron disease is not present, leave the checkboxes in Question 14c blank/unchecked.

IVP	FVP	Section 2 – Etiological diagnoses							*continued...*
14d.	14d.		FTLD - not otherwise specified (NOS)	☐1	14d1.	☐1	☐2	☐3	

Select **1=Present** if FTLD not otherwise specified (NOS) is present (e.g., Pick's disease). This diagnosis should not be selected if PSP, CBD, or FTLD with motor neuron disease is present. If FTLD NOS is present, indicate whether it is thought to be the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment.

If FTLD NOS is not present, leave all checkboxes for Questions 14d and 14d1 blank/unchecked.

14e.	14e.		If FTLD **(QUESTION 14)** is **present**, specify FTLD subtype: ☐1 Tauopathy ☐2 TDP-43 proteinopathy ☐3 Other **(SPECIFY):** _____ ☐9 Unknown

Select **1=Tauopathy**, **2=TDP-43 proteinopathy**, or **3=Other (specify)** if specific evidence (e.g., genetics) beyond the clinical syndrome is available to indicate the FTLD subtype. If a subtype other than Tauopathy or TDP43 proteinopathy is present, select **3=Other** and specify the subtype. Select **9=Unknown** if there is no evidence beyond the clinical syndrome to specify the FTLD subtype.

15.	15.		Vascular brain injury (based on clinical and imaging evidence according to your Center's standards)	☐1	15a.	☐1	☐2	☐3

If there is evidence of significant vascular brain injury confirmed by clinical or neuroimaging studies, select **1=Present** for Question 15. Significant vascular brain injury includes either:

- CLINICAL EVIDENCE of symptomatic stroke (i.e., abrupt onset of focal neurological signs) – OR –
- NEUROIMAGING EVIDENCE of one or more of the following:
  - cystic infarcts (large or small)
  - significant white matter changes (Grade 7–8+ on Cardiovascular Health Study Scale)
  - intraparenchymal hemorrhage
  - multiple microbleeds

If the participant has no clinical evidence of symptomatic stroke and neuroimaging studies do not indicate evidence of significant vascular brain injury, leave the checkboxes in Question 15 and 15a blank/unchecked.

For participants with cognitive impairment: Indicate whether vascular brain injury is thought to be the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment.

If there is clinical evidence of a symptomatic stroke with temporal relationship to cognitive decline but no available supporting neuroimaging, select **1=Primary** or **2=Contributing** based on clinical judgment.

If there is significant vascular brain injury but no clear temporal or anatomical relationship with cognitive impairment, select **2=Contributing** or **3=Non-contributing** based on clinical judgment.

If there is a history of gradually progressive cognitive decline preceding a symptomatic stroke in the absence of extensive confluent white matter changes (thereby suggesting an underlying neurodegenerative etiology), select **2=Contributing** or **3=Non-contributing** based on clinical judgment.

For participants with normal cognition: If the participant has normal cognition but has evidence of significant vascular brain injury, select **1=Present** for Question 15 and leave the primary and contributing boxes in Question 15a blank/ unchecked.

For participants with normal cogntition and behavior and positive biomarkers: For participants who exhibit normal cognitive function but have biomarker evidence consistent with Vascular brain injury (or possess a known genetic mutation associated with the disease), you have the flexibility to proceed according to your center's diagnostic philosophy:

> **Option 1:** If your center's practice is to diagnose Vascular brain injury in cognitively normal individuals with positive biomarkers, you may **check the appropriate boxes in Questions 15 and 15a** to relfect this diagnosis.
>
> **Option 2:** If your center prefers not to assign a Vascular brain injury diagnosis to cognitively normal individuals despite positive biomarkers, you may **leave all checkboxes in Questions 15 and 15a blank/unchecked**. In this scenario the biomarker and genetic information provided in Section 1 can be utilized to determine the presence of preclinical or presymptomatic Vascular brain injury.

IVP FVP Section 2 – Etiological diagnoses *continued...*

16.	**16.**	Multiple system atrophy	☐ 1	**16a.**	☐ 1	☐ 2	☐ 3

Excerpted from Wenning et al. (2022):

Diagnostic criteria for clinically established and clinically probable multiple system atrophy

Division into clinically established MSA-P or MSA-C according to predominant motor syndrome		
Essential features	A sporadic, progressive adult (>30 years) onset disease	
	Clinically established MSA	**Clinically probable MSA**
Core clinical features	1. Autonomic dysfunction defined as (at least one is required) • Unexplained voiding difficulties with post-void urinary residual volume≥100 mL • Unexplained urinary urge incontinence • Neurogenic OH (≥20/10 mmHg blood pressure drop) within3 minutes of standing or head-uptilt test and at least one of 1. Poorly L-dopa-responsive parkinsonism 2. Cerebellar syndrome (at least two of gait ataxia, limb ataxia, cerebellar dysarthria, or oculomotor features)	At least two of: 1. Autonomic dysfunction defined as (at least one is required): • Unexplained voiding difficulties with post-void urinary residual volume • Unexplained urinary urge incontinence • Neurogenic OH (≥20/10 mmHg blood pressure drop) within 10 minutes of standing or head-up tilt test 2. Parkinsonism 3. Cerebellar syndrome (at least one of gait ataxia, limb ataxia, cerebellar dysarthria, or oculomotor features)
Supportive clinical (motor or non-motor) features	At least two	At least one
MRI marker	At least one	Not required
Exclusion criteria	Absence	Absence

Supportive clinical features	
Supportive motor features	**Supportive non-motor features**
• Rapid progression within 3 years of motor onset • Moderate to severe postural instability within 3 years of motor onset • Craniocervical dystonia induced or exacerbated by L-dopa in the absence of limb dyskinesia • Severe speech impairment within3 years of motor onset • Severe dysphagia within 3 years of motor onset • Unexplained Babinski sign • Jerky myoclonic postural or kinetic tremor • Postural deformities	• Stridor • Inspiratory sighs • Cold discolored hands and feet • Erectile dysfunction (below age of 60 years for clinically probable MSA) • Pathologic laughter or crying

[a] Excluding erectile dysfunction as an isolated feature.

Abbreviations: MSA = multiple system atrophy; MSA-P = MSA-parkinsonian type; MSA-C = MSA-cerebellar type; OH = orthostatic hypotension; MRI = magnetic resonance imaging.

For participants with cognitive and/or behavioral impairment: If MSA is present, select **1=Present** and indicate whether it is thought to be the **1=Primary** cause, a **2=Non-contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment.

For participants with normal cognition and behavior: If the participant has normal cognition but clinical symptoms sufficient for a diagnosis of MSA, select MSA as **1=Present** and leave the checkboxes about whether it is primary or contributing in Question 16a blank/unchecked.

For participants with normal cognition and behavior and positive biomarkers: For participants who exhibit normal cognitive function but have biomarker evidence consistent with MSA (or possess a known genetic mutation associated with the disease), you have the flexibility to proceed according to your center's diagnostic philosophy:

> **Option 1:** If your center's practice is to diagnose MSA in cognitively normal individuals with positive biomarkers, you may c**heck the appropriate boxes in Questions 16 and 16a** to reflect this diagnosis.
>
> **Option 2:** If your center prefers not to assign a MSA diagnosis to cognitively normal individuals despite positive biomarkers, you may **leave all checkboxes in Questions 16 and 16a blank/unchecked**. In this scenario, the biomarker and genetic information provided in **Section 1** can be utilized to determine the presence of preclinical or presymptomatic MSA.

If MSA is not present, leave the checkboxes in Question 16 blank/unchecked.

Wenning GK, Stankovic I, Vignatelli L, Fanciulli A, Calandra-Buonaura G, Seppi K, Palma JA, Meissner WG, Krismer F, Berg D, Cortelli P, Freeman R, Halliday G, Höglinger G, Lang A, Ling H, Litvan I, Low P, Miki Y, Panicker J, Pellecchia MT, Quinn N, Sakakibara R, Stamelou M, Tolosa E, Tsuji S, Warner T, Poewe W, Kaufmann H. The Movement Disorder Society Criteria for the Diagnosis of Multiple System Atrophy. Mov Disord. 2022 Jun;37(6):1131-1148. doi: 10.1002/mds.29005. Epub 2022 Apr 21. PMID: 35445419; PMCID: PMC9321158.

IVP	FVP						
17.	17.	Chronic traumatic encephalopathy (CTE)	☐1	17a.	☐1	☐2	☐3

Excerpted from Katz et al. (2021):

Primary Diagnostic Criteria for TES: Substantial Exposure to Repetitive Head Impacts [1]

History of substantial exposure to repetitive impacts to the head is required. These impacts may or may not have been associated with clinical symptoms or signs of concussion or TBI. Individuals should be screened for multiple possible sources of exposure over a lifetime. Examples or sources of substantial exposure to RHIs include the following:

- **Involvement in high-exposure contact or collision sports** such as (but not limited to) boxing, American (tackle) football, ice hockey, soccer, rugby, professional wrestling, mixed martial arts, and some other sports with high risk of exposure to RHIs (e.g., motocross and bull riding).
  - For American football, a minimum of 5 y of organized play is required. This minimum should include ≥ 2 y at the high school level or beyond. [The inclusion of level of play (i.e., high school) is based on clinical judgement, with limited evidence]. Nearly all of the participants in a published study establishing the 5-y threshold played at least high school level football[2]
  - Exposure risk thresholds for other contact or collision sports, or combinations or contact/collision sports, have not yet been established but should be a substantial number of years (e.g., ≥ 5 y) at a level of play involving routing RHIs.
- **Military service involving RHIs**, including (but not limited to) combat exposure to multiple blast and other explosions, noncombatant exposure to explosions (including breacher training – blasting and forced opening of locked doors), or multiple blows to the head over an extended period of time (e.g., pugil stick training – repeated blows with padded military training weapon.
  - Exposure risk thresholds for military service have not yet been established.
- **Other sources involving multiple head impacts** over an extended period of time, including (but not limited to) domestic violence (or intimate partner violence), head banging, and vocational activities such as breaching locked doors and other barriers by first responders.
  - Exposure risk thresholds for other sources have not yet been established.

Abbreviations: RHI = repeated head impact; TBI = traumatic brain injury; TES = traumatic encephalopathy syndrome

Primary Diagnostic Criteria for TES: Core Clinical Features[1]

Cognitive impairment or neurobehavioral dysregulation, or both, is required to meet TES criteria. A progressive course is also required to meet TES criteria.

Cognitive impairment (all 4 are required):

1. As reported by self or informant, or by clinician's report.
2. Representing a significant decline from baseline functioning. The determination of baseline level of functioning may be challenging and require clinical judgment in cases where decline may have begun during the period of RHI exposure.
3. With deficits in episodic memory and/or executive functioning (additional domains may be impaired in addition to these). Substantiated by impaired performance on formal neuropsychological testing (if available), as defined by performance at a level of at least 1.5 SDs below appropriate norms, accounting for the individual's estimated for premorbid functioning.
4. If formal neuropsychological testing is not available, there should be substantial evidence of impairment below expected norms and/or a person's estimated baseline in episodic memory and/or executive functioning on a standardized mental status examination (e.g., Montreal Cognitive Assessment and Mini-Mental State Examination) by a clinician experienced in the evaluation of cognition.

Neurobehavioral dysregulation (all 3 are required)

1. As reported by self or informant, or by clinician's report.
2. Representing a significant change from baseline functioning may require clinical judgment in cases where change may have begun during the period of RHI exposure.
3. With symptoms and/or observed behaviors representing poor regulation or control of emotions and/or behavior, including (but not limited to) explosiveness, impulsivity, rage, violent outbursts, having a short fuse (exceeding what might be described as periodic episodes or minor irritability), or emotional lability (often reported as mood swings), preferable substantiated by standardized measures that demonstrate clinical impairment in these domains. In most cases, standardized measures of neurobehavioral dysregulation will not be available, but there should be substantial evidence of change from a person's baseline. These symptoms and/or observed behaviors do not appear to represent a transient response to life events, e.g., divorce, death of a loved one, and financial problems.

Progressive course

There is evidence of progressive worsening of these clinical features over a period of at least 1 year in the absence of continued exposure to RHIs or TBI. The evidence should be supported by serial standardized testing (if available) or clear history supporting a change in functioning over time (e.g., clinician reports, job performance, evaluations, or self- or informant report).

[1] *Katz DI, Bernick C, Dodick DW, Mez J, Mariani ML, Adler CH, Alosco ML, Balcer LJ, Banks SJ, Barr WB, Brody DL, Cantu RC, Dams-O'Connor K, Geda YE, Jordan BD, McAllister TW, Peskind ER, Petersen RC, Wethe JV, Zafonte RD, Foley ÉM, Babcock DJ, Koroshetz WJ, Tripodis Y, McKee AC, Shenton ME, Cummings JL, Reiman EM, Stern RA. National Institute of Neurological Disorders and Stroke Consensus Diagnostic Criteria for Traumatic Encephalopathy Syndrome. Neurology. 2021 May 4;96(18):848-863. doi: 10.1212/WNL.0000000000011850. Epub 2021 Mar 15. PMID: 33722990; PMCID: PMC8166432.*

For participants with cognitive and/or behavioral impairment: If CTE is present, select **1=Present** and indicate whether it is thought to be the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment.

For participants with normal cognition and behavior: If the participant has normal cognition but clinical symptoms sufficient for a diagnosis of CTE, select CTE as **1=Present** and leave the checkboxes about whether it is primary or contributing in Question 17a blank/unchecked.

For participants with normal cognition and behavior and positive biomarkers: For participants who exhibit normal cognitive function but have biomarker evidence consistent with CTE (or possess a known genetic mutation associated with the disease), you have the flexibility to proceed according to your center's diagnostic philosophy:

> **Option 1:** If your center's practice is to diagnose CTE in cognitively normal individuals with positive biomarkers, you may c**heck the appropriate boxes in Questions 17 and 17a** to reflect this diagnosis.
>
> **Option 2:** If your center prefers not to assign a CTE diagnosis to cognitively normal individauls, despite positive biomarkers, you may **leave all checkboxes in Questions 17 and 17a blank/unchecked**. In this scenario, the biomarker and genetic information provided in Section 1 can be utilized to determine the presence of preclinical or presymptomatic CTE.

If CTE is not present, leave the checkboxes in Question 17 blank/unchecked.

[2] *Mez J, Daneshvar DH, Abdolmohammadi B, Chua AS, Alosco ML, Kiernan PT, Evers L, Marshall L, Martin BM, Palmisano JN, Nowinski CJ, Mahar I, Cherry JD, Alvarez VE, Dwyer B, Huber BR, Stein TD, Goldstein LE, Katz DI, Cantu RC, Au R, Kowall NW, Stern RA, McClean MD, Weuve J, Tripodis Y, McKee AC. Duration of American Football Play and Chronic Traumatic Encephalopathy. Ann Neurol. 2020 Jan;87(1):116-131. doi: 10.1002/ana.25611. Epub 2019 Nov 23. PMID: 31589352; PMCID: PMC6973077.*

IVP | FVP | Section 2 – Etiological diagnoses *continued...*

IVP	FVP						
17b.	17b.	If CTE **(QUESTION 17)** is **present**, specify certainty: ☐1 Suggestive CTE ☐2 Possible CTE ☐3 Probable CTE ☐4 Indeterminate					
18.	18.	Down syndrome	☐1	18a.	☐1	☐2	☐3

If Down syndrome is present, select 1=Present and indicate whether it is thought to be the **1=Primary** cause, a **2=Contributing cause**, or a **3=Non-contributing** cause of the cognitive impairment, if applicable.

If Down syndrome is not present, leave all boxes for Questions 18 and 18a blank/unchecked. If the participant has normal cognition and behavior but has Down syndrome, select **1=Present** for Question 18 and leave the primary and contributing boxes in Question 18a blank/unchecked.

19.	19.	Huntington's disease	☐1	19a.	☐1	☐2	☐3

If Huntington's disease is present, select **1=Present** for Question 19, and indicate whether it is thought to be the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment in Question 19a, if applicable.

If Huntington's disease is not present, leave all boxes for Questions 19 and 19a blank/ unchecked.

If the participant has normal cognition and behavior but has Huntington's disease features or a known mutation, select **1=Present** and leave the primary and contributing boxes in Question 19a blank/unchecked.

IVP	FVP	Section 2 – Etiological diagnoses						*continued...*
20.	20.	Prion disease (CJD, other)	☐1	20a.	☐1	☐2	☐3	

Refer to the paper by Puoti et al. (2012)[1] regarding the clinical diagnosis of prion disease.

If prion disease is not present, leave all checkboxes in Questions 20 and 20a blank/unchecked. Select **1=Present** if prion disease (Creutzfeldt-Jakob disease or other type) is present, and indicate whether it is thought to be the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment in Question 19a.

If the participant has normal cognition and behavior but has tested positive for prion disease, select **1=Present** for Question 20 and leave the primary, contributing, and non-contributing boxes in Question 20a blank/ unchecked.

[1] *Lancet Neurol. 2012 Jul;11(7):618-28. doi: 10.1016/S1474-4422(12)70063-7. Sporadic human prion diseases: molecular insights and diagnosis. Puoti G1, Bizzi A, Forloni G, Safar JG, Tagliavini F, Gambetti P.*

21.	21.	Cerebral amyloid angiopathy	☐1	21a.	☐1	☐2	☐3	

Excerpt from Charidimou et al. 2022:
Boston criteria version 2.0 for sporadic cerebral amyloid angiopathy

1. Definite CAA

Full brain post-mortem examination demonstrating:

- Spontaneous intracerebral hemorrhage, transient focal neurological episodes, convexity subarachnoid hemorrhage, or cognitive impairment or dementia
- Severe CAA with vasculopathy
- Absence of other diagnostic lesion

2. Probable CAA with supporting pathology

Clinical data and pathological tissue (evacuated hematoma or cortical biopsy) demonstrating:

- Presentation with spontaneous intracerebral hemorrhage, transient focal neurological episodes, convexity subarachnoid hemorrhage, or cognitive impairment or dementia
- Some degree of CAA in specimen
- Absence of other diagnostic lesion

3. Probable CAA

For participants aged 50 years and older, clinical data and MRI demonstrating:

- Presentation with spontaneous intracerebral hemorrhage, transient focal neurological episodes, or cognitive impairment or dementia
- At least two of the following strictly lobar hemorrhagic lesions on T2*-weighted MRI, in any combination: intracerebral hemorrhage, cerebral microbleeds, or foci of cortical superficial siderosis or convexity subarachnoid hemorrhage

OR

- One lobar hemorrhagic lesion plus one white matter feature (severe perivascular spaces in the centrum semiovale or white matter hyperintensities in a multispot pattern)†
- Absence of any deep hemorrhagic lesions (i.e., intracerebral hemorrhage or cerebral microbleeds) on T2*-weighted MRI
- Absence of other cause of hemorrhagic lesions*
- Hemorrhagic lesion in cerebellum not counted as either lobar or deep hemorrhagic lesion

4. Possible CAA

For participants aged 50 years and older, clinical data and MRI demonstrating:

- Presentation with spontaneous intracerebral hemorrhage, transient focal neurological episodes, or cognitive impairment or dementia
- Absence of other cause of hemorrhage*
- One strictly lobar hemorrhagic lesion on T2*-weighted MRI: intracerebral hemorrhage, cerebral microbleeds, or foci of cortical superficial siderosis or convexity subarachnoid hemorrhage

OR

- One white matter feature (severe visible perivascular spaces in the centrum semiovale or white matter hyperintensities in a multispot pattern)†
- Absence of any deep hemorrhagic lesions (i.e., intracerebral hemorrhage or cerebral microbleeds) on T2*-weighted MRI
- Absence of other cause of hemorrhagic lesions*
- Hemorrhagic lesion in cerebellum not counted as either lobar or deep hemorrhagic lesion

*Other causes of hemorrhagic lesion: antecedent head trauma, hemorrhagic transformation of an ischemic stroke, arteriovenous malformation, hemorrhagic tumor, central nervous system vasculitis. Other causes of cortical superficial siderosis and acute convexity subarachnoid hemorrhage should also be excluded.

Abbreviations: CAA = cerebral amyloid angiopathy, MRI = magnetic resonance imaging, ICH = intracerebral hemorrhage, TFNE = transient focal neurologic episodes, CI = cognitive impairment, CMB = cerebral microbleed, cSS = cortical superficial siderosis, cSAH = convexity subarachnoid hemorrhage, CSO-PVS = visible perivascular spaces in the centrum semiovale, WMH-MS = white matter hyperintensities in a multispot pattern

For participants with cognitive and/or behavioral impairment: If CAA is present, select **1=Present** and indicate whether it is thought to be the **1=Primary** cause, a **2= Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment.

For participants with normal cognition and behavior: If the participant has normal cognition but clinical symptoms sufficient for a diagnosis of CAA, select CAA as **1=Present** and leave the checkboxes about whether it is primary or contributing in Question 21a blank/unchecked.

For participants with normal cognition and behavior and positive biomarkers: For participants who exhibit normal cognitive function but have biomaker evidence consistent with CAA (or possess a known genetic mutation associated with the disease), you have the flexibility to proceed according to your center's diagnostic philosophy:

> **Option 1:** If your center's practice is to diagnose CAA in cognitively normal individuals with positive biomarkers, you may **check the appropriate boxes in Questions 21 and 21a** to reflect this diagnosis.
>
> **Option 2:** If your center prefers not to assign a CAA diagnosis to cognitively normal individuals despite positive biomarkers, you may **leave all checkboxes in Question 21 and 21a blank/unchecked**. In this scenario, the biomarker and genetic information provided in **Section 1** can be utilized to determine the presence of preclinical or presymptomatic CAA.

If CAA is not present, leave the checkboxes in Question 21 blank/unchecked.

Charidimou A, Boulouis G, Frosch MP, Baron JC, Pasi M, Albucher JF, Banerjee G, Barbato C, Bonneville F, Brandner S, Calviere L, Caparros F, Casolla B, Cordonnier C, Delisle MB, Deramecourt V, Dichgans M, Gokcal E, Herms J, Hernandez-Guillamon M, Jäger HR, Jaunmuktane Z, Linn J, Martinez-Ramirez S, Martínez-Sáez E, Mawrin C, Montaner J, Moulin S, Olivot JM, Piazza F, Puy L, Raposo N, Rodrigues MA, Roeber S, Romero JR, Samarasekera N, Schneider JA, Schreiber S, Schreiber F, Schwall C, Smith C, Szalardy L, Varlet P, Viguier A, Wardlaw JM, Warren A, Wollenweber FA, Zedde M, van Buchem MA, Gurol ME, Viswanathan A, Al-Shahi Salman R, Smith EE, Werring DJ, Greenberg SM. The Boston criteria version 2.0 for cerebral amyloid angiopathy: a multicentre, retrospective, MRI-neuropathology diagnostic accuracy study. Lancet Neurol. 2022 Aug;21(8):714-725. doi: 10.1016/S1474-4422(22)00208-3. PMID: 35841910; PMCID: PMC9389452.

IVP	FVP	Section 2 – Etiological diagnoses						
								continued...
22.	22.	LATE: Limbic-predominant age-related TDP-43 encephalopathy	☐1	22a.	☐1	☐2	☐3	

Excerpted from Wolk et. al (submission under review at journal)*:

LATE as the Primary Diagnosis

I. Core Clinical Syndrome* (1 and 2 required) 1. Primary amnestic syndrome with tempero-limbic memory loss 2. Other cognitive domains largely spared until much later in the course 3. May have mild semantic memory impairment 4. Indolent course with predominant amnestic syndrome present for at least 2 years 5. Age generally > 75 years old	**Probable LATE**	**Possible LATE**
II. Required Imaging Significant hippocampal atrophy (out of proportion to global atrophy)		
III. Required Supportive Features for Probable LATE A negative test of one of the following to rule out β-amyloid: a. Amyloid PET b. CSF Aβ42/40 c. CSF ptau181/Aβ42 or t-tau/Aβ42		
IV. Required Additional Measures if Amyloid-Positive If amyloid-positive based on III, a negative measure of one of the following Tau biomarkers is required: a. MTL Tau PET (preferred measure) b. CSF ptau181		**Possible LATE**

*Core clinical syndrome differs from typical AD, which is generally defined as an amnestic, multi-domain syndrome, but the overlap is significant making a purely clinical diagnosis challenging. Overlap with limbic-predominant AD is even greater.

Additional supportive neuroimaging features:

1. FDG PET without the stereotypical posterior temporo-parietal hypometabolism seen in AD or anterior temporal/frontoinsular pattern seen in temporal variant FTLD
2. FDG-PET with elevated inferior temporal/MTL ratio and absence of other degenerative patterns
3. Structural MTL changes suggestive of LATE (severe atrophy particularly hippocampal head and anterior ERC/PRC; elevated inferior temporal/MTL ratio)

*Criteria used prior to publication with consent from David Wolk as the lead author on the LATE clinical consensus criteria.

For participants with cognitive and/or behavioral impairment: If LATE is present, select **1=Present** and indicate whether it is thought to be the **1=Primary** cause, a **2=Contributing** cause, or a **3=Non-contributing** cause of the cognitive impairment.

For participants with normal cognition and behavior: If the participant has normal cognition but clinical symptoms sufficient for a diagnosis of LATE, select LATE as **1=Present** and leave the checkboxes about whether it is primary or contributing in Question 22a blank/unchecked.

For participants with normal cognition and behavior and positive biomarkers: For participants who exhibit normal cognitive fuction but have biomarker evidence consistent with LATE (or possess a known genetic mutation associated with the disease), you have the flexibility to proceed according to your center's diagnostic philosophy:

Option 1: If your center's practice is to diagnose LATE in cognitively normal individuals with positive biomarkers, you may **check the appropriate boxes in Questions 22 and 22a** to reflect this diagnosis.

Option 2: If your center prefers not to assign a LATE diagnosis to cognitively normal individuals despite positive biomarkrers, you may **leave all checkboxes in Questions 22 and 22a blank/unchecked.** In this scenario, the biomarker and genetic information provided in **Section 1** can be utilized to determine the presence of preclinical or presymptomatic LATE.

If LATE is not present, leave the checkboxes in Question 22 blank/unchecked.

Wolk DA, Nelson, PT, Apostolova LG, Arfanakis K, Boyle PA, Carlsson CM, Corriveau-Lecavalier N, Dacks PA, Dickerson BC, Domoto-Reilly K, Dugger BN, Edelmayer RM, Fardo DW, Grothe MJ, Hohman TJ, Irwin DJ, Jicha GA, Jones DT, Kawas CH, Lee EB, Lincoln KD, Maestre GE, Mormino EC, Onyike CU, Petersen RC, Rabinovici GD, Rademakers R, Raman R, Rascovsky K, Rissman RA, Rogalski E, Scheltens P, Sperling RA, Yang HS, Yu L, Zetterberg H, Schneider JA (2024). Clinical Criteria for Limbic-Predominant Age-Related TDP-43 Encephalopathy. Manuscript submitted for publication.

IVP	FVP	Section 2 – Etiological diagnoses						*continued...*
23.	23.	Other **(SPECIFY):** _____	☐1	23a.	☐1	☐2	☐3	

Coding Guidebook for **Form D1c:** Biological and Clinical Staging

***INSTRUCTIONS**: This form is based on the Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup (2024). This form is to be completed by the clinician for all participants, including cognitively unimpaired.*

The purpose of this form is to record the results of the biomarkers used in the new AA criteria for Alzheimer's disease. This will allow future researchers to classify who does or does not meet AD biomarker criteria, enable biological and clinical staging of AD, and test the new AA criteria in future studies. The data on this form is meant to operationalize the AA criteria, not to capture details on all possible biomarkers used to establish the etiological diagnosis. Refer to D1b to capture information on additional biomarkers.

Given the rapidity of the development of biomarkers, this form is not meant to record biomarker values, methodological techniques, or to indicate availability of samples. Instead, this form has a very focused purpose to indicate the results of the biomarker that was used in the etiological diagnosis and gather information on whether these were obtained at a central institution or study such as NCRAD, CLARiTI, LEADS, SCAN, etc., or whether they were obtained locally or elsewhere.

Section 1 – Categorization of fluid analyte and imaging biomarkers

Biomarkers are categorized in this section based on four criteria:

1. Identify three broad mechanistic groupings
2. Subclassify based on the proteinopathy or pathophysiologic pathway that each biomarker measures (e.g., A,T,N, etc.)
3. Within the Core category, distinguish between Core 1 and Core 2 biomarkers
4. Imaging and fluid analyte biomarkers are listed separately within each category

Core Biomarkers

Core 1

A (Aβ proteinopathy) and **T_1** (phosphorylated and secreted AD tau)

CSF or plasma analytes

Plasma

1.	Were plasma biomarkers used in the etiologic diagnosis?	☐ 0 No **(SKIP TO QUESTION 2)**	☐ 1 Yes
	If yes, select all plasma biomarkers that were used:		

If plasma biomarker results were considered when the D1b form was filled out, please report them here. Note that the assay does not need to be available widely, it just needs to have been used locally in the diagnosis.

1a.	☐ 1 p-tau 217		
	If checked:		
1a1.	p-tau 217 result	☐ 0 Normal	☐ 1 Abnormal

Use established cutoffs for your Center or provided by NCRAD if run at NCRAD. If the result is borderline or indeterminate, mark the result as "Abnormal".

1a2.	Where were the p-tau 217 values used in the diagnosis analyzed?	☐ 1 Analyzed by NCRAD ☐ 2 Analyzed in-house or elsewhere ☐ 9 Unknown

If a sample was analyzed both at NCRAD and elsewhere, please select the source that provided the analyses results that were used to determine whether the result was normal or abnormal

1a3.	Was the plasma p-tau 217 sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?	☐ 0 No ☐ 1 Yes ☐ 9 Unknown

1b.	☐ 1 %p-tau 217		
	If checked:		
1b1.	%p-tau 217 result	☐ 0 Normal	☐ 1 Abnormal

Use established cutoffs for your Center. If the result is borderline or indeterminate, mark the result as "Abnormal".

1b2.	Was the plasma %p-tau 217 sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?	☐ 0 No ☐ 1 Yes ☐ 9 Unknown
	*%p-tau values not currently analyzed by NCRAD; only available in-house or elsewhere	

1c. ☐ 1 Other plasma biomarker (**SPECIFY**): _____

If checked:

1c2.	Other plasma biomarker result	☐ 0 Normal	☐ 1 Abnormal

Note here any other plasma biomarkers used to evaluate amyloid status for which you have established cutoffs in your Center. NCRAD provides a p-tau 181 cutoff to use for data generated at NCRAD. Please enter the name of the biomarker in 1c (i.e., p-tau 181, ptau217/Aβ42/Aβ40). If the result is borderline or indeterminate, mark the result as "Abnormal".

1c3.	Where were the other plasma biomarker values used in the diagnosis analyzed?	☐ 1 Analyzed by NCRAD ☐ 2 Analyzed in-house or elsewhere ☐ 9 Unknown

If a sample was analyzed both at NCRAD and elsewhere, please select the source that provided the analyses results that were used to determine whether the result was normal or abnormal.

1c4.	Was the plasma sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?	☐ 0 No ☐ 1 Yes ☐ 9 Unknown

CSF or plasma analytes *continued...*

CSF

2. Were CSF biomarkers used in the etiologic diagnosis? ☐ 0 No **(SKIP TO QUESTION 3)** ☐ 1 Yes

If yes, select all CSF biomarkers that were used:

If CSF biomarker results were considered when the D1b form was filled out, please report them here. Note that the assay does not need to be available widely, it just needs to have been used locally in the diagnosis.

2a. ☐ 1 p-tau 181/ Aβ42

If checked:

2a1.	p-tau 181/ Aβ42	☐ 0 Normal	☐ 1 Abnormal

Use established cutoffs for your Center or provided by NCRAD if run at NCRAD. If the result is borderline or indeterminate, mark the result as "Abnormal".

2a2.	Where were the p-tau 181/ Aβ42 values used in the diagnosis analyzed?	☐ 1 Analyzed by NCRAD ☐ 2 Analyzed in-house or elsewhere ☐ 9 Unknown

If a sample was analyzed both at NCRAD and elsewhere, please select the source that provided the analyses results that were used to determine whether the result was normal or abnormal.

2a3.	Was the CSF p-tau 181/ Aβ42 sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?	☐ 0 No ☐ 1 Yes ☐ 9 Unknown

2b. ☐ 1 t-tau / Aβ42

If checked:

2b1.	t-tau / Aβ42	☐ 0 Normal	☐ 1 Abnormal

Use established cutoffs for your Center or provided by NCRAD if run at NCRAD. If the result is borderline or indeterminate, mark the result as "Abnormal".

2b2.	Was the CSF t-tau / Aβ42 sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?	☐ 0 No ☐ 1 Yes ☐ 9 Unknown
	*t-tau values not currently analyzed by NCRAD; only available in-house or elsewhere	

2c. ☐ 1 Aβ42 / 40

If checked:

2c1.	Aβ42 / 40	☐ 0 Normal	☐ 1 Abnormal

Use established cutoffs for your Center or provided by NCRAD if run at NCRAD. If the result is borderline or indeterminate, mark the result as "Abnormal".

2c2.	Where were the Aβ42 / 40 values used in the diagnosis analyzed?	☐ 1 Analyzed by NCRAD ☐ 2 Analyzed in-house or elsewhere ☐ 9 Unknown

If a sample was analyzed both at NCRAD and elsewhere, please select the source that provided the analyses results that were used to determine whether the result was normal or abnormal.

2c3.	Was the Aβ42 / 40 sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?	☐ 0 No ☐ 1 Yes ☐ 9 Unknown

2d. ☐ 1 Other CSF biomarker (**SPECIFY**): _____

If checked:

2d2.	Other CSF biomarker result	☐ 0 Normal	☐ 1 Abnormal

Note here any other CSF biomarkers used to evaluate amyloid status for which you have established cutoffs in your Center. Please enter the name of the biomarker in 2d. If the result is borderline or indeterminate, mark the result as "Abnormal".

2d3.	Where were the other CSF biomarker values used in the diagnosis analyzed?	☐ 1 Analyzed by NCRAD ☐ 2 Analyzed in-house or elsewhere ☐ 9 Unknown

If a sample was analyzed both at NCRAD and elsewhere, please select the source that provided the analyses results that were used to determine whether the result was normal or abnormal.

2d4.	Was the CSF sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?	☐ 0 No ☐ 1 Yes ☐ 9 Unknown

Imaging

Amyloid PET

3.	Was Amyloid PET used in the etiologic diagnosis?	☐ 0 No **(SKIP TO QUESTION 4)**	☐ 1 Yes

If amyloid PET results were considered when the D1b form was filled out, please report them here. Note that the assay does not need to be available widely, it just needs to have been used locally in the diagnosis.

3a.	Amyloid PET result:	☐ 0 Not elevated	☐ 1 Elevated

Use established cutoffs for your Center or provided by CLARiTI, ADNI, LEADS, or SCAN.

3b.	How were amyloid PET results obtained *(select all that apply)*?	☐ 1 Visual read	☐ 1 Quantitative
3c.	Where were amyloid PET results obtained?	☐ 1 Central (CLARiTI, ADNI, LEADS, SCAN) ☐ 2 Local or other interpretation (e.g., other clinical trials) ☐ 9 Unknown	
3d.	Was the amyloid PET scan used in the diagnosis from a date within +/- 12 months of the current UDS visit?	☐ 0 No ☐ 1 Yes ☐ 9 Unknown	

Core 2

T_2 (AD tau proteinopathy)

4.	Was tau PET used in the etiologic diagnosis?	☐ 0 No **(SKIP TO QUESTION 5)** ☐ 1 Yes

If tau PET results were considered when the D1b form was filled out, please report them here. Note that the assay does not need to be available widely, it just needs to have been used locally in the diagnosis.

MTL

4a.	Tau PET MTL result:	☐ 0 Not elevated ☐ 1 Elevated

Use established cutoffs for your Center or provided by CLARiTI, LEADS, or SCAN.

4b.	How were tau PET MTL results obtained (*select all that apply*)?	☐ 1 Visual read ☐ 1 Quantitative
4c.	Where were tau PET MTL results obtained?	☐ 1 Central (CLARiTI, ADNI, LEADS, SCAN) ☐ 2 Local or other interpretation (e.g., other clinical trials) ☐ 9 Unknown

Neocortical

4d.	Tau PET Neocortical result:	☐ 0 Not elevated ☐ 1 Elevated

Use established cutoffs for your Center or provided by CLARiTI, LEADS, or SCAN.

4e.	How were tau PET neocortical results obtained (*select all that apply*)?	☐ 1 Visual read ☐ 1 Quantitative
4f.	Where were tau PET neocortical results obtained?	☐ 1 Central (CLARiTI, ADNI, LEADS, SCAN) ☐ 2 Local or other interpretation (e.g., other clinical trials) ☐ 9 Unknown
4g.	Was the tau PET scan used in the diagnosis from a date within +/- 12 months of the current UDS visit?	☐ 0 No ☐ 1 Yes ☐ 9 Unknown

Biomarkers of non-AD co-pathology

V (vascular brain injury)

Infarction on MRI or WMH consistent with ischemia

5.	Was infarction on MRI or WMH consistent with ischemia or blood products consistent with CAA used in the etiologic diagnosis?	☐ 0 No **(SKIP TO QUESTION 6)** ☐ 1 Yes

If these results were considered when the D1b form was filled out, please report them here. Note that the assay does not need to be available widely, it just needs to have been used locally in the diagnosis.

5a.	Imaging result:	☐ 1 Infarction on MRI *(select all that apply below)* ☐ 1 Lacunar ☐ 1 Cortical ☐ 1 Microbleeds ☐ 1 WMH ☐ 1 Superficial siderosis ☐ 1 Other (**SPECIFY**): _____

These results are typically gleaned from local visual read, but you may use a central source such as SCAN or CLARiTI if available. When to report WMH: We recommend that you report WMH using a threshold of Fazekas score >=2.

5b.	Was the imaging scan used in the diagnosis from a date within +/- 12 months of the current UDS visit?	☐ 0 No ☐ 1 Yes ☐ 9 Unknown

S (α-synuclein)

αSyn-SAA*

6. Was αSyn-SAA used in the etiologic diagnosis: ☐0 No **(SKIP TO QUESTION 7)** ☐1 Yes

If αSyn-SAA results were considered when the D1b form was filled out, please report them here. Note that the assay does not need to be available widely, it just needs to have been used locally in the diagnosis.

6a. αSyn-SAA result: ☐0 Normal ☐1 Abnormal

Normal indicates a negative αSyn-SAA result and Abnormal indicates a positive αSyn-SAA result.

6b. αSyn-SAA assay:
☐1 CSF
☐2 Other (**SPECIFY**): _____

If "other" ensure it is an acceptable source for αSyn-SAA (e.g., skin biopsy)

6c. Where were αSyn-SAA values obtained? _____

Provide the commercial entity performing the assay, if selected. If in house, you may enter "in-house." ***Please do not provide potentially identifying information such as Center name or investigator/PI name.***

6d. Was the αSyn-SAA sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?
☐0 No
☐1 Yes
☐9 Unknown

** If a fluid analyte is presently informative only when measured in CSF this is denoted by (*), if informative with plasma or CSF then no specific notation added*

Biomarkers of non-AD co-pathology ***continued...***

7. Did the participant meet the AA biological biomarker criteria for Alzheimer's based on a positive Core 1 biomarker?
☐0 No **(END FORM HERE)**
☐1 Yes

The AA biomarker criteria only consider the subset of Core 1 biomarkers listed in Question 8 as sufficiently validated to establish a diagnosis of AD. In replying, please apply the same thresholds/criteria for positivity used in your responses to questions 1-3. If one or more of the listed biomarkers are positive respond **1=Yes**, if not answer **0=No**, even if other biomarkers are abnormal.

8. Which Core 1 biomarker was used to make this determination *(select all that apply)?*

Imaging:
☐1 Amyloid PET

Plasma:
☐1 p-tau217
☐1 %p-tau217

CSF:
☐1 p-tau181/Aβ42
☐1 t-tau/Aβ42
☐1 Aβ42/40

Other (SPECIFY):
_____

Please check all abnormal biomarkers that apply.

Section 2 – Biological staging for individuals on the Alzheimer's disease continuum

Use the information above to select the biological stage of the participant:

	Initial-stage biomarkers	Early-stage biomarkers	Intermediate- to advanced-stage biomarkers	
PET	Amyloid PET	Tau PET medial temporal region	Tau PET neocortical uptake	
	$A+T_{2-}$	$A+T_{2MTL+}$	$A+T_{2MOD+2HIGH+}$	
9. Select the biological stage of the participant:	☐ 1 (A)	☐ 2 (B)	☐ 3 (C-D)	☐ 9 Unable to determine stage (e.g., missing necessary biomarkers like tau PET)

Please complete staging based on tau PET results queried above. Please use your Center-specific standards for tau PET interpretation. Currently tau PET results are not available via CLARiTI, although we anticipate they will be in the future.

Section 3 – Clinical staging for individuals on the Alzheimer's disease continuum

Stage 0 Asymptomatic, deterministic gene

- No evidence of clinical change. Biomarkers in normal range.

  ** Participants with Down Syndrome may not be fully independent even in stage 0 because of underlying intellectual disability. In these participants, decline in functional independence from baseline may be a more appropriate indicator of stage.*

Stage 1 Asymptomatic, biomarker evidence only

- Performance within expected range on objective cognitive tests.
- No evidence of recent cognitive decline or new symptoms.

Stage 2 Transitional decline: Mild detectable change, but minimal impact on daily function

- Normal performance within expected range on objective cognitive tests.
- Decline from previous level of cognitive or neurobehavioral function that represents a change from individual baseline within the past 1 to 3 years, and has been persistent for at least 6 months.
- May be documented by evidence of subtle decline on longitudinal cognitive testing, which may involve memory or other cognitive domains but performance still within normal range.
- May be documented through subjective report of cognitive decline (SCD).
- May be documented with recent-onset change in mood, anxiety, motivation not explained by life events.
- Remains fully independent with no or minimal functional impact on activities of daily living (ADLs).

Stage 3 Cognitive impairment with early functional impact

- Performance in the impaired/abnormal range on objectives cognitive tests.
- Evidence of decline from baseline, documented by the individual's report or by an observer's (e.g., study partner) report or by change on longitudinal cognitive testing or neurobehavioral assessments.
- Performs daily life activities independently but cognitive difficulty may result in detectable functional impact on complex ADLs (i.e., may take more time or be less efficient but still can complete — either self-reported or corraborated by an observer).

Stage 4 Dementia with mild functional impairment

- Progressive cognitive and mild functional impairment on instrumental ADLs, with independence in basic ADLs.

Stage 5 Dementia with moderate functional impairment

- Progressive cognitive and moderate functional impairment on basic ADLs requiring assistance.

Stage 6 Dementia with severe functional impairment

- Progressive cognitive and functional impairment, and complete dependence for basic ADLs.

10. Clinical AD stage

☐ 0 Stage 0
☐ 1 Stage 1
☐ 2 Stage 2
☐ 3 Stage 3
☐ 4 Stage 4
☐ 5 Stage 5
☐ 6 Stage 6
☐ 9 Unable to determine stage

Determination of clinical staging should incorporate information provided by an informant who is close to the patient and able to provide objective assessment of their cognitive, behavioral, and daily functional abilities. Additionally, the informant should have the knowledge to track disease progression and associated functional decline over time.