Standard Operating Procedures for Acquisition of Cognitive Measures

Accelerating Medicines Partnership® SCHIZOPHRENIA
An observational study examining clinical trajectories and predictors of outcomes in the clinical high risk population.

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Procedure	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13	Visit 14	Visit 15	Visit 16	Conversion
Month	-3 to -1	0	1	2	3	4	5	6	7	8	9	10	11	12	18	24	-
Consent Form	■																
Interview/ Questionnaire	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Cognitive Tasks	■	■		■				■						■		■	■
MRI*		■		■													
EEG*		■		■													
Blood and Saliva Samples*		■		■													
Actigraphy (daily)		■	■	■	■	■	■	■	■	■	■	■	■	■			
Digital Data (daily passive sensing, EMA, audio diary)		■	■	■	■	■	■	■	■	■	■	■	■	■			
Free Speech Sampling (audio and facial recording)		■		■													
PSYCHS (audio recording)		■	■	■	■			■						■	■	■	■

* In-person visit

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Team E Training Plan for Cognition

Training will be provided to administer and score tests from the:

1 - WebCNP CNB Virtual (Survey / telehealth) Assessment

2 - WASI-II (Vocabulary and Matrix Reasoning tests, and IQ derived score)

3 - WRAT-5 Word Reading Test

A 'train the trainer' model may be implemented, such that the neuropsychology team leader will train at least one suitably qualified representative at each site in the cognition battery administration and scoring procedures. That person will then train others at their sites, with the process anticipated to take 2-3 weeks. Prior to test administration, training will cover general rapport, creating favorable test environments to the extent possible, and will discuss how REDCap/RPMS form should be used as a guide and completed. The qualified site representatives will need to familiarize themselves with the Penn CNB, WASI-II, and WRAT-5 manuals prior to training by the co-leads.

Specific measures in test administration

Penn Battery (WebCNP) training. Team E co-leads will be trained by a Penn CNB administrator. Once they are trained, they will train representatives from each site in their respective networks by Zoom. Training times will be established.

WASI-II training in general administration and scoring procedures, administration and scoring of Vocabulary and Matrix Reasoning, and derivation of IQ scores will be taught by Zoom to representatives of each Network by the Team E co-leads. This process will include learning rules of test administration, scoring principles, learning to score during test administration and deriving IQ scores. For sites speaking other languages and where the WASI-II is not available in their language, the Vocabulary and Matrix Reasoning subtests will be administered from substitute Wechsler batteries (WISC-V for ages 12-15 and WAIS-IV for ages 16-30) and training will be the same.

WRAT-5 Reading training will include administration rules and scoring. As with the WASI-II, not all sites will have access to this measure in their language and some may not have reading tests that are structured the same way as the WRAT-5 Reading tests. In these sites, substitute measures such as the NART or not administering a reading test will be acceptable. Again, training will be the same.

Training will take 2-3 weeks. After training from the co-leads, trainees will need to assess at least 2 mock subjects for training purposes and then successfully administer the battery over Zoom to either: 1) one of the Team E co-leads or their delegated site associates, or 2) to a designated bilingual individual at their site who can communicate with the Team E lead about their performance, for certification. This process includes sending a pdf of the WASI-II and WRAT-5 (or substitute) record forms to the co-leads or to a designated bilingual individual at their site, for

inspection. The record forms need to be deemed 100% correct (i.e., no scoring errors) before certification can occur and so the process will be repeated as necessary until this criterion is met.

As a check on cross-network reliability, 3 sites in ProNET will be certified by the PRESCIENT co-lead and 3 in PRESCIENT will be certified by the ProNET co-lead.

The Penn CNB and the IQ/reading tests are intended to be administered to participants remotely via the screen-share feature on Zoom. We are requesting that all sites employ the remote protocol to maintain procedural uniformity. Thus, while tests may be administered to a participant who is on-site, they should be done using two separate computer locations/rooms. For the Penn CNB, a link will be sent to the participant to access the tests (see the Penn CNB section for further details). For the WASI-II and WRAT-5, stimuli from Q-Global will be presented to the participant via screen-share. For a host of reasons, remote administration may not be feasible at some sites (e.g., non-English-speaking sites that do not have access to Q-Global or a comparable program). In these cases, in person/on-site administration may be permitted.

Quality Assurance Check

After certification, the Team E Co-leads will review for accuracy the first IQ/reading test record forms completed by each rater from a study participant. This will be done for each individual rater across sites for both networks. Feedback will be provided to the rater if errors are found, and if the rater has administered these tasks to more than one participant, they will be asked to check all of their completed record forms for accuracy and email the Team E Co-lead of their network to let them know they have completed this process.

As a check on cross-network reliability, records form from each site in ProNET will be reviewed by the PRESCIENT co-lead and records form from each site in PRESCIENT will be reviewed by the ProNET co-lead on an intermittent basis.

Calculating Chronological Age

Chronological age will need to be calculated for determining the WRAT5 Word Reading Standard Score and the WASI-II T-Scores (or WISC-V/WAIS-IV if applicable).

Use the space provided on the cover of the Record Form to calculate the participant's chronological age. Enter the test date and the participant's birth date in years, months, and days. Subtract the birth date from the test date to obtain the participant's age in years and months. If the testing occurred over multiple days, use the first test date to calculate the participant's chronological age. The figure below shows an example of the age calculation. For borrowing purposes, all months are set at 30 days. Once the calculation is completed, ignore the days. **Do not** round the age up to the next month or year. You could also use an online age calculator to ensure age is calculated accurately.

	Year	Month	Day
	2016	13 1̶	48

Date of Test	~~2017~~	~~2~~	~~18~~
Date of Birth	2000	2	20
Age	16	11	28

This participant's age is 16 years and 11 months.

The specific instructions for the WRAT5 and the WASI-II Vocabulary and Matrix Reasoning tests are described in the manuals. Brief instructions are presented below for each test.

WRAT5 – Word Reading

WRAT5 Word Reading is only administered once, at baseline, and is being used to estimate premorbid IQ.

Before administering the WRAT5 Word Reading, you should familiarise yourself thoroughly with the pronunciation of the words on the **Green Reading Word List** and you should be certified to administer this task as determined by the PRESCIENT or ProNET neuropsychologist/co-lead.

Materials

Equipment: Laptop or desktop computer
Green Word Reading List Card (digital)
WRAT5 Record form (paper)

General Administration Rules

Start Point Word Reading has two parts. In Part 1: Letter Reading, the participant reads from a list of letters. In Part 2: Word Reading, the participant reads from a list of words.

Reverse Rule If the Part 2 (Word Reading) raw score is below a cut-off, administer all of Part 1 (Letter Reading).

Discontinue Rule The test has a discontinue rule, but do not use it until it is clear that the discontinue criterion was met. This highlights the need for practice and familiarity with the words. See the WRAT5 Manual for additional instructions.

Test Administration
Note. Do not let the participant see your record form (scoresheet) because it contains the pronunciation guide.

Show the Green Reading Word List stimulus card on the screen to be viewed by the participant. Text to be read aloud to the participant is presented in bold below and is also on the Record Form. It is important to read the spoken text exactly as it is written. Do not paraphrase instructions, cue

or otherwise assist the participant unless the directions say to do so. Do not provide feedback on whether responses were correct or not. See the WRAT5 Manual and the Test Record form for additional instructions.

Recording and Scoring Responses

Score the participant's responses on the Green Reading Word List record form as the items are administered. Mark each administered item as correct or incorrect in a clear and consistent manner on the Record Form. Write down oral responses when the response differs from the correct response. This aids later scoring and quality control. Sometimes the participant will give more than one response for a given item. If the participant corrects a wrong answer spontaneously, use the corrected response. In any event, use the final response only, whether or not it is correct. If a participant gives several responses and you are unsure which one they intended, repeat back the responses and ask which one was the intended answer. Score only the indicated response. If the participant does not respond (NR), or says "I don't know," (DK) note this and mark the item as incorrect.

Do not penalize responses for errors in speech, diction, foreign or other geographically-based accent. See the WRAT5 Manual for additional details.

Completing the Record Form

After the administration is complete, see the WRAT5 Manual for instructions on how to complete the record form and to determine the raw and the age-based standard scores.

Uploading the Record Form

When entering the data into REDCap/RPMS, upload the record form (including the WRAT5 Summary Page and Word Reading subtest page) so that all raw data (i.e., participant responses and scoring procedures) is saved for future reference and quality assurance check.

Specific instructions for non-English speaking sites

For non-English speaking sites the WRAT5 is not being used. Instead, each site will liaise with the Team E co-leads to identify an equivalent reading task in their local language. For example, the local version of the NART will be used instead (e.g., French NART (fNART) in French-speaking countries). In some cases (e.g., Chinese), such a task is unavailable and premorbid IQ will not be measured.

The administration of the various forms of the NART is very similar to the WRAT5, except for the NART there is no Discontinue rule, which means the whole test needs to be administered. There is also no letter reading component and so the Reverse rule does not apply. The general test administration, recording and scoring of responses is the same as for the WRAT5. Scoring involves tallying the number of words pronounced correctly (raw score) and then converting the raw score to an age-based standard score (IQ estimate) using the relevant conversion table/formula.

WASI-II (Two subtest version: Vocabulary and Matrix Reasoning)

Remote Testing Protocol

WASI-II is administered twice, at baseline and week 104, and is being used to estimate current IQ.

Before administering the WASI-II, you should familiarise yourself thoroughly with the words in the Vocabulary subtest and items in the Matrix Reasoning subtest and you should be certified to administer this task as determined by the PRESCIENT or ProNET neuropsychologist/co-lead.

Materials

- Equipment: Laptop or desktop computer
- WASI-II Digital Manual, Norms Tables and Stimuli
- WASI-II Record Form (paper)

General Testing Guidelines

- The Participant should take tests in a well-lit, quiet space as free of distractions as possible
- Establish rapport, stay attentive to the participant
- Say you are going ask them some questions and show them some pictures
- Allow bathroom breaks, if possible between tests rather than during them
- Show interest by praising <u>effort</u>, but <u>not performance</u>. Do not provide feedback as to whether the response was correct or incorrect. If the subject asks if they got an item correct or otherwise asks for feedback about their test performance, say you are sorry but you cannot provide answers.
- Neutral supportive statements are ok if the participant struggles, such as encouraging them to just try their best.
- See the WASI-II Manual for additional details

General Administration Rules
See the WASI-II Manual

Completing the Summary Page
See the WASI-II Manual

Administration

Vocabulary Test
Scoring is based on a 3-point scale. Consult the WASI-II Manual for details of administration and scoring.

Matrix Reasoning
Matrix Reasoning is a visual, multiple-choice test involving the identification of missing portions of designs. Consult the WASI-II Manual for administration and scoring instructions.

Uploading the Record Form
When entering the data into REDCap/RPMS, upload the record form (including the WASI-II Summary Page, Vocabulary subtest page, and Matrix Reasoning subtest page) so that all raw data (i.e., participant responses and scoring procedures) is saved for future reference and quality assurance check.

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Specific instructions for non-English speaking sites

For sites speaking languages other than English and where the WASI-II is not available in their language, the Vocabulary and Matrix Reasoning subtests will be administered from substitute Wechsler batteries (specifically, WISC-V for ages 12-15 and WAIS-IV for ages 16-30).

While the item content and number differ slightly from the WASI-II, the administration, recording and scoring of responses is exactly the same as described for the WASI-II.

However, with reference to scoring, the age-based standard score for Vocabulary and Matrix Reasoning will be a Scaled Score (rather than T-score). To determine the Scaled Score, look up the relevant age-based scaled score table in the WISC-V or WAIS-IV manual and record the scaled score for Vocabulary and Matrix Reasoning on the front page of the record form.

Next, calculate the average of the two scaled scores by adding them together and dividing them by 2. For example, Vocab 12 + MR 10 = 22 / 2 Mean = 11. Please record this on the front of the record form.

Next, full-Scale IQ will be estimated using the following online calculator: https://www.psychometrica.de/normwertrechner_en.html. Enter the mean Scaled Score (e.g., 11) into the box that says, "Wechsler Subscale" and the IQ score will be shown in the box that says "IQ-Score" (e.g., 105). For decimal IQ scores, round up or down as appropriate (e.g., 107.5 = 108) because the IQ score must be a whole number. Please record the full-scale IQ on the front of the record form.

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Penn Computerized Neurocognitive Battery (PennCNB)

The PennCNB is administered at multiple time-points (baseline, week 8, week 26, week 52, week 104), and is being used to assess the cognitive domains most relevant to psychosis.

There are 8 tests in the battery and their order of administration is as follows:

Test Order	Test Acronym	Test Name	Length (mins)
1	SPLLT	Short Penn List Learning Test	3
2	MPRACT	Motor Praxis Test	2
3	SPCPTNL	Short Penn Continuous Performance Test	5
4	ER40	Penn Emotion Recognition Test	3.5

	~ break point~		
5	SFNB2	Short Fractal N-Back Test	10
6	DIGSYM	Digit-Symbol Test	3
7	SVOLT	Short Visual Object Learning Test	2.5
8	SCTAP	Short Computerized Finger-Tapping Test	3.5
		Total	32.5

The detailed and most up to date training SOP is kept on a publicly accessible wiki. The SOP serves as a reference to guide both individuals completing the CNB Training and Certification process. To access, simply click on the link below. Make sure to review both pages by clicking on the 'Training Procedures' hyperlink at the end of the first page below.

https://github.com/upenn/cnb-pub/wiki/CNB-Training-Procedures

You should also review the Administrator Manual, which is available on the WebCNB website. Use practice account credentials to log in. This should serve as a reference guide even post CNB certification once you have begun assessing for a project.
Administrator Manual: https://webcnp.med.upenn.edu/manuals.pl?name=manual

ProNET/PRESCIENT Training Procedures for PennCNB:

To initiate PennCNB training for a new rater at your site, please contact a CNB Project Manager to receive a link to the training modules.

After completing the modules 1-4, review the additional ProctTrack training video. Paste the link below on your browser's search bar as is, do not just click on it.
https://upenn.box.com/s/3iozwhgs0bt0ah5ygb44d3xj6vo244qi

Then, you are **strongly encouraged** to practice administering the full CNB a minimum of 4 times (start to finish) to a practice participant before you record your Standardized Assessment video. Use the practice account to practice and record your video.**The best way to record the video is to use a video conference software (ex: Zoom, Teams, GoTo Meeting, BlueJeans) as your "meeting room". **
Please note, you will need to administer **BOTH** batteries (administer the SPLLT battery first, followed by the NOSPLLT battery) to administer the "full CNB assessment". Please refer to the Full Assessment Video in the CNB Training and Certification Platform for procedures.

(The practice account is only for use in practice sessions and should NOT be used to assess participants upon completion of the CNB training process)

NOTE: You will need to create a unique SubjectID to register a session and administer the battery. For practice purposes, the unique SUBJECT ID should be your initials followed by the date in MMDDYYYY format.

For example, the test links for Allison Port's CNB Standardized Assessment session would have the subject ID of '=AMP08312021' for the assessment date of August 31, 2021

Please review the [Assessment Procedures](#) section for details on how to create the Subject ID if you are unsure of how to proceed.

Helpful advice from the CNB Team:

- Make sure both your camera is on AND the participant's camera is on before you start the CNB.
    - The person who is "completing the battery" (aka clicking the buttons to respond to the trials) will be sharing their screen for that portion of the assessment.
    - So, for example, you would start by registering a session for the practice participant with the SPLLT task battery ONLY.
    - Instead of sending them the link once you register the session, you open the link for the SPLLT test on YOUR screen. (Remember, you don't send them the SPLLT link BECAUSE by sending the link to them, this action allows them to click on the buttons and effectively score their own data).
- **You SHOULD NOT share your screen during the SPLLT test administration.** The CNB Team will be able to determine the validity and the administration of the SPLLT based on the audio from the participant (in the video) and the scores entered in the database.
- When the SPLLT test is done (that's the only test part of that link), you will send them the link for the remainder battery, ask them to open the link on their computer, then share their screen. To do this, you will have to register another session (with the same subject ID) with the NOSPLLT battery.

Virtual CNB ProNET/PRESCIENT Order of Procedures

1. Welcome participant and introduce the CNB
2. Confirm cell phones are off
3. Administer SPLLT task
4. Update ProctTrack for SPLLT
5. Send participant the link for their battery in the chat feature of your video conference software
6. Ask participant to open the link on their computer
7. Ask participant to share their screen
8. As the participant is opening the link, pull up the ProctTrack page. As a reminder, you are expected to use ProctTrack live, as the session unfolds, to track the assessment.
9. Administer all tasks in the remainder CNB battery, making sure to update ProctTrack as the battery progresses
10. Make sure to offer the break point at the halfway mark!
11. When CNB is completed, thank the participant for their efforts!
12. When you have a moment without the participant present, enter any remaining notes into the virtual platform ([ProctTrack](#)).

PennCNB Mock Data Upload:

1. Go to https://webcnp.med.upenn.edu and click "start testing".
2. Log in with the practice account information.
3. For the SPLLT:
   a. Select the SPLLT-A battery from the dropdown.
   b. Select the PRACTICE site.
   c. Enter one of your site's test IDs.
4. Practice with a colleague/ friend or you can run through this on your own to enter answers.
5. After the SPLLT, repeat steps 3 & 4 but select the ProNET_NOSPLLT battery.
6. Once completed, please submit a run sheet (labeled "Penn CNB") in REDCap using the corresponding test ID.

For live participant testing:

a. *Site*:   Each site has its own unique site ID, which will appear in the dropdown. Once you are certified, your personal administrator account will be already loaded with the correct site ID you will need access to.
b. *Subject*:   Enter the subject's AMPSCZ ID which is the usual 2 letters then 5 numbers (e.g., XX12345).
c. *Visit*:   After the visit, go to Edit Sessions page[1] and complete the visit ID field with 1, 2, 3, 4, or 5 according to this chart below:

>   i. Baseline = 1
>   ii. Month 2 = 2
>   iii. Month 6 = 3
>   iv. Month 12 = 4
>   v. Month 24 = 5

After Certification:
Email Eirini Zoupou to obtain your personal administrator account. In your email, include your full name and site. Your personal account will have access to all 6 relevant batteries. If you are administering the CNB in a non-English site, you will have access to the translated batteries. See mapping below for which batteries should be administered at which visit.

ProNET:

Visit #	Battery 1	Battery 2
1	SPLLT-A	NOSPLLT
2	SPLLT-B	NOSPLLT_b
3	SPLLT-C	NOSPLLT

4	SPLLT-D	NOSPLLT_b
5	SPLLT-A	NOSPLLT

Prescient:

Visit #	Battery 1	Battery 2
1	SPLLT-A	NOSPLLT_C1
2	SPLLT-B	NOSPLLT_b
3	SPLLT-C	NOSPLLT_C1
4	SPLLT-D	NOSPLLT_b
5	SPLLT-A	NOSPLLT_C1