Cognitive impairment indicator for the CLSA: Development and evidence for validity

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Teamwork for this CLSA Project

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- Co-PIs of the 50,000 person 20 year long CLSA – Lauren Griffith, Christina Wolfson, Susan Kirkland, & Parminder Raina

Canadian Longitudinal Study on Aging (CLSA)

- Two cohorts - Tracking – telephone administered tests more geographically diverse (i.e., rural) (*N* = 21,241) was administered a wide range of questionnaires over the telephone (see https://www.clsa-elcv.ca/researchers/data-collection for the description of the data collection overview and tools).
- Participants in the Comprehensive cohort (*N* = 30,097) were assessed in person at one of eleven data collection sites across Canada. In addition to the same questionnaires asked of the Tracking cohort, participants in the Comprehensive cohort were also assessed physically (e.g., heart rate, blood pressure, electrocardiogram, spirometry, bone mineral density, hearing, visual acuity, hand grip strength).

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What are the Cognition Variables in CLSA?

Tracking –

Rey Auditory Verbal Learning test - immediate recall **REY I**,

5 min delayed recall **REY II**,

animal naming (scored two ways **AF1 & AF2**; we use AF2 for all composites),

Mental Alternation Test (**MAT**)

High scores = better performance

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What are the Cognition variables?

Comprehensive – REY I; REY II; AF 1; AF 2; MAT & controlled oral word fluency (**COWAT**) separated by F, A, and S; Victoria Stroop Test (**Stroop**) total time for dots, words, and colours

High scores = better performance
EXCEPT Stroop raw scores

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What is the Cognitive impairment indicator? **CII**

Tracking cohort (overall *N* = 21,241) – REY I, REY II, AF 2, MAT

Comprehensive cohort (overall *N* = 30,097) – 4 test REY I, REY II, AF 2, MAT &

6 test REY I, REY II, AF 2, MAT, FAS Total, Stroop Interference (colour/dot time; reversed)

Normed using hybrid approach; separate for EN/FR; stratified by sex, education, continuous for age

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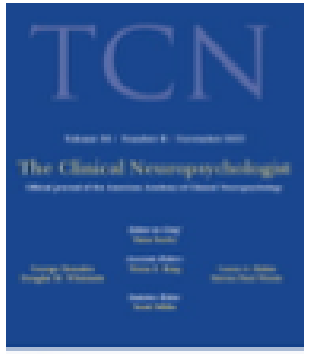
Why use the normed scores that are available from CLSA?

- remove measurement bias
- analysis at individual participant level

Fundamental differences in measurement in cognition scores

- Scores mean very different things in French (FR) and in English (EN)
- Low education creates spuriously low scores as can sex and age
- Corrections to scores using demographically adjusted normative comparison standards removes bias due to language of FR/EN (Taler et al., about to be submitted) and only specific models remove bias due to education and sex (O'Connell et al., 2021)



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Methodological considerations when establishing reliable and valid normative data: Canadian Longitudinal Study on Aging (CLSA) neuropsychological battery

Megan E. O'Connell, Helena Kadlec, Lauren E. Griffith, Geva Maimon, Christina Wolfson, Vanessa Taler, Martine Simard, Holly Tuokko, Stacey Voll, Susan Kirkland & Parminder Raina

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Full regression models did not remove bias due to education or sex; hybrid models were successful

If you do not use similar methods to adjust for language, sex, and education you might have biases in your cognition scores

Double correction for sex, education, age – might be the lesser challenge; clearly this depends on your statistical approach

Why use the normed scores that are available from CLSA?

- remove measurement bias
- analysis at individual participant level

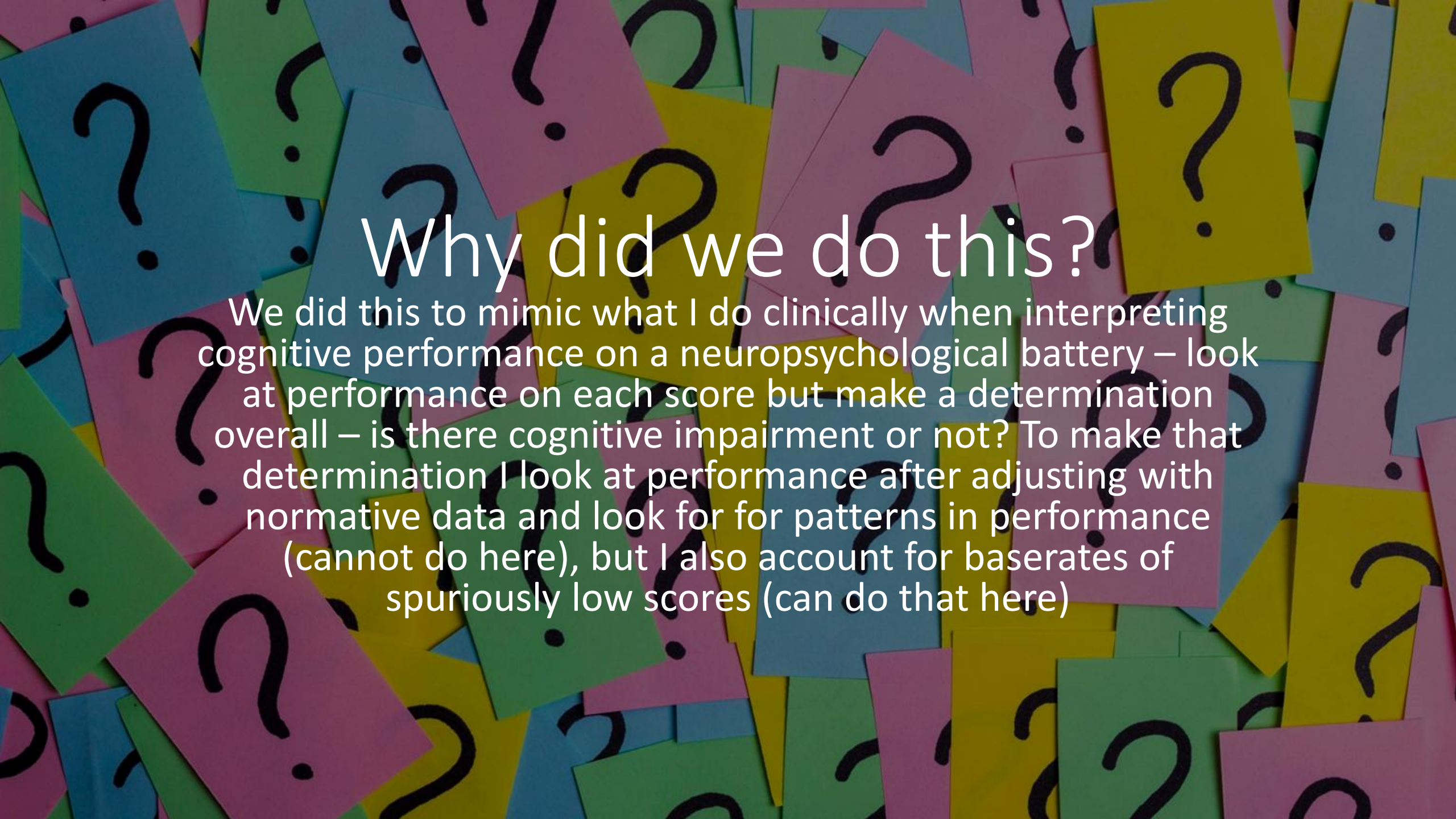
What is the Cognitive impairment indicator? CII?

- Each test score has an impairment indicator
- Cut-off is the 5th percentile of the normative distribution (empirical not theoretical distribution)

What is the Cognitive impairment indicator? CII?

- Across the battery of tests – 4 tests in the Tracking cohort and 6 in the Comprehensive cohort
- How many scores need to be impaired to say they are cognitively impaired?

- Base rate analyses of expected low scores based on (Crawford et al., 2007)
  - Intercorrelation of test performance in cognitively healthy sample
  - In the CII it is based on 5th percentile as low scores



Why did we do this?

We did this to mimic what I do clinically when interpreting cognitive performance on a neuropsychological battery – look at performance on each score but make a determination overall – is there cognitive impairment or not? To make that determination I look at performance after adjusting with normative data and look for for patterns in performance (cannot do here), but I also account for baserates of spuriously low scores (can do that here)

What is the Cognitive impairment indicator? CII?

- Tracking cohort - percentage of a cognitively healthy population presenting with at least one abnormally low score (at or below 5th percentile) on the four-test battery =
  - 15.9% of the English-speaking
  - 15.7% of the French-speaking subsamples
- 3.7% of the cognitively healthy population English-speaking subsample and 3.8% of the cognitively healthy population French-speaking subsample were estimated to present with at least two abnormally low scores

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What is the Cognitive impairment indicator? CII?

Comprehensive battery – 6CO – the estimated percentage of the population presenting with at least one abnormally low score was 22.6% (22.56% in English and 22.60% in French),

5.8% were estimated to present with **two or more low** scores (5.81% in English and 5.78% in French)

1.4% of the population were estimated to present with **three or more** abnormally low scores.

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What is the Cognitive impairment indicator? CII?

- Tracking and Comprehensive cohorts,
  - participants who obtained two or more abnormally low test scores, whether in the four-test or the six-test battery, were classified as overall cognitively impaired (CII=1); otherwise, they were classified as not cognitively impaired (CII=0)
  - Had to have complete data

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Cognitive impairment indicator for the neuropsychological test batteries in the Canadian Longitudinal Study on Aging: definition and evidence for validity

Megan E. O'Connell[1*], Helena Kadlec[2], Lauren E. Griffith[3], Christina Wolfson[4], Geva Maimon[5], Vanessa Taler[6], Susan Kirkland[7] and Parminder Raina[8]

Tracking Cohort

Cognitive impairment on individual tests	Available *N*	# Imp	%[a]
Based on REY I immediate recall	19,488	1176	5.5
Based on REY II delayed recall	19,374	1026	5.3
Based on Animal Fluency	19,472	1100	5.6
Based on MAT score	18,246	1654	7.8
Based on Stroop Interference	-	-	-
Based on FAS total	-	-	-

Comprehensive Cohort

Cognitive impairment on individual tests	Available *N*	# Imp	%[a]
Based on REY I immediate recall	29,024	1671	5.8
Based on REY II delayed recall	28,715	1560	5.4
Based on Animal Fluency	28,804	1521	5.3
Based on MAT score	28,014	2122	7.6
Based on Stroop Interference	29,626	1602	5.4
Based on FAS total	27,724	1512	5.5

Tracking Cohort at Baseline - CII

Cognitive impairment on overall 4-test battery [b]	Total *N* possible	*n*	%
Cognitively impaired	16,371	664	3.1
Not impaired		15,707	95.9
Unclassified due to missing data — out of total *N*		(4870)	(22.9)

Comprehensive Cohort at Baseline - CII

	Total *N* possible	*n*	%
Cognitive impairment on overall 4-test battery[b]			
Cognitively impaired	27,203	983	3.6
Not impaired		26,220	96.4
Unclassified due to missing data — out of total *N*		(2894)	(9.6)
Cognitive impairment on overall 6-test battery[c]			
Cognitively impaired	25,168	1528	6.1
Not impaired		23,640	93.9
(Unclassified due to missing data — out of total *N*)		(4929)	(16.4)

Is this associated with anything?

- Self-reported chronic conditions – has a doctor ever told you that you have (list of chronic conditions)…

- Although we did associate the CII with each of the 30+ conditions we summarized them as well

Chronic conditions - summary

- Neurological
  - AD or dementia
  - Memory problems
  - Stroke
  - TIA
  - MS
  - Parkinsonism or PD
  - Epilepsy

Chronic conditions - summary

- Risk of neurological disease
  - Diabetes
  - Hypertension
  - Any one of the multiple cardiac diseases
  - Peripheral vascular disease
  - Depression
  - Kidney disease
  - Thyroid dysfunction
- Not neurological – none of the above but had conditions like osteoarthritis etc.

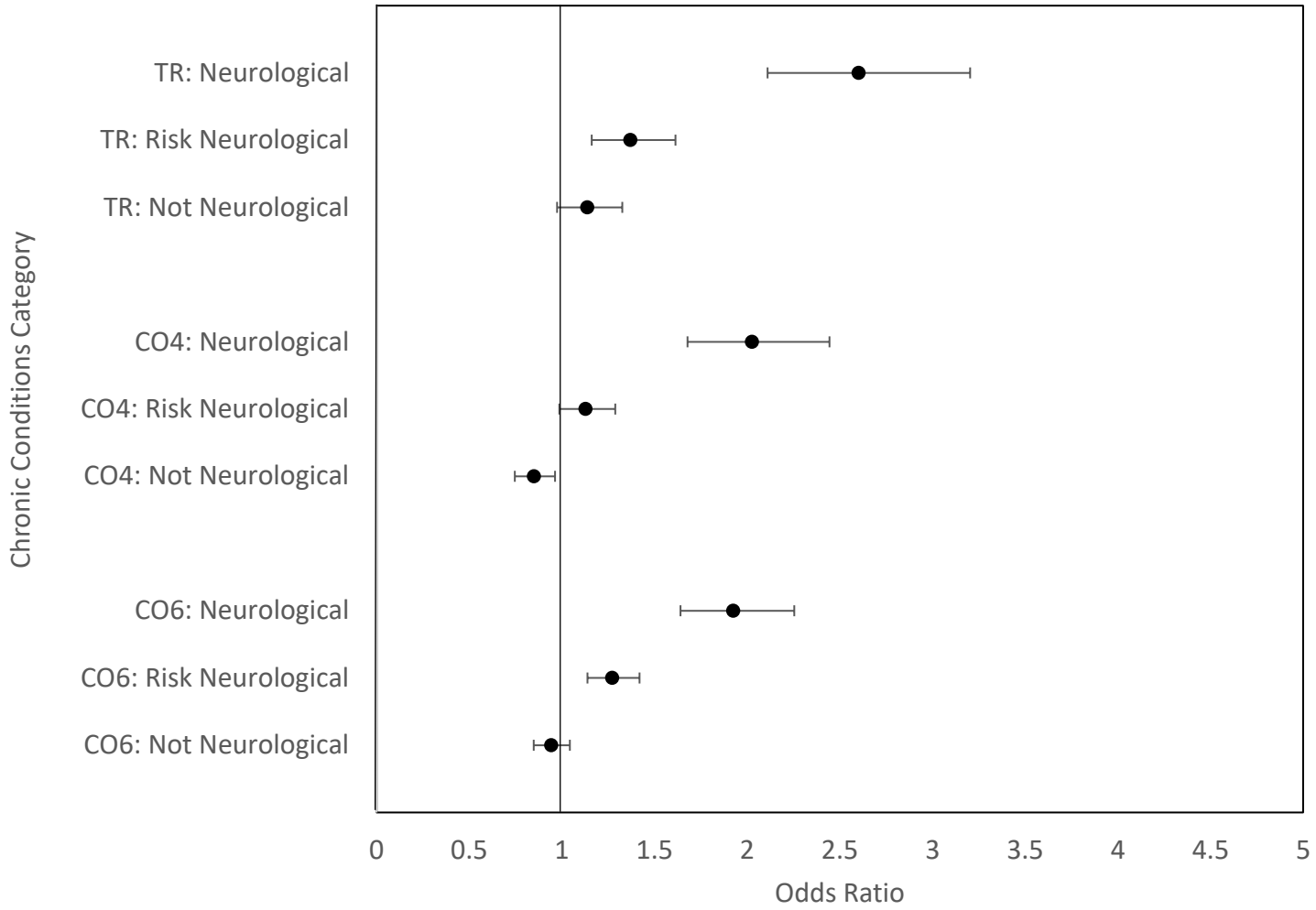

Figure 1. Odds Ratios and confidence intervals for Tracking (TR) and Comprehensive (CO) cohorts (4 test CO4 and 6 test CO6 for groups with neurological conditions (Neurological), conditions that are risk factors for cognitive impairment (Risk Neurological), and conditions that we would not expect to be linked to cognition (Not Neurological).

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Follow-up CII

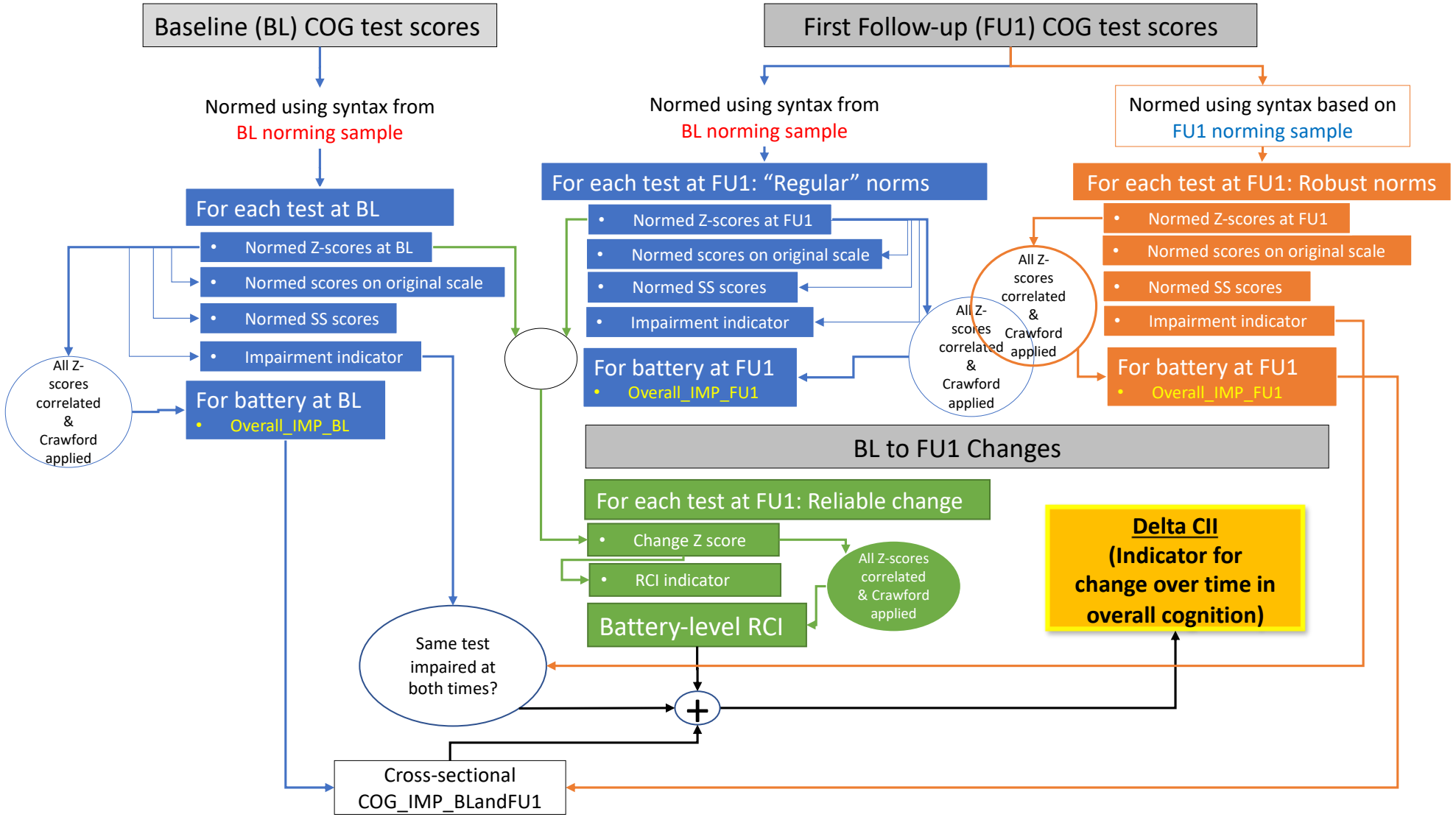
- We computed a **Δ**CII for first follow-up

- This was similar to the CII but differed in 3 main ways
  - Used new follow-up norms for cross-sectional impairment at each test score level
  - Used reliable change indices which adjust for error in measurement and expected practice effects
  - Analyzed patterns of consistently low scores – if spuriously low should not be consistently low

ΔCII – what is it?

COG_OVERALL _IMP at BL	COG_OVERALL _IMP at FU1 _robust	Results on individual cog tests (using ROBUST COG_ IMP indicators for FU1)	ΔCII
0	0	zero tests <5% at <u>both</u> time points; OR zero tests <5% at one time and one test <5% at the other time; OR 1 test <5% at both time points on DIFFERENT tests	0 = Not impaired
		1 test <5% at <u>both</u> time points on SAME test; OR RCI (sig decline) on 2 or more tests (i.e., Battery_RCI = -1)	2 = at risk
	1	0 or 1 test <5% at BL and 2+ <5% at FU1	1 = Impaired
1	0	2+ <5% at BL & 1 SAME test at FU1; OR RCI (sig decline) on 2 or more tests (i.e., Battery_RCI = -1	2 = at risk
		2+ <5% at BL & none at FU1; OR 2+ <5% at BL & 1 <5% at FU1 on DIFFERENT test	? Likely spuriously classified at BL? Thankfully only 1.6% of the TRM and 1.9% of COM are in this group – will re-code as 0
	1	Below 5% on 2+ tests at both time points	1 = Impaired

ΔCII – what is it?



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Can we use the ΔCII?

- Not yet do not know what the scores mean

What about CII or ΔCII for future waves?

- Cannot use method for BL CII – practice effects

- Problems with change in mode of delivery – small portion of the Comprehensive cohort did follow-up testing by phone as a retention technique but at follow-up 2 about half of Comprehensive did due to the pandemic
- Despite norming appropriately – Telephone and in-Person cognitive tests differ fundamentally (O'Connell et al., in preparation) but you should still use the appropriate norms based on mode of delivery
- Missing data is an increasing issue

What we are working on

- As part of the Memory Study work and led by Griffith et al. – CII for follow-up 3 with Memory Study diagnosis as reference standard
- Will move to follow-up 2
- Worries we have – increasingly select healthy sample have complete data – impacts our cross-sectional norms and potentially our reliable change scores* and will bias the **Δ**CII
  - * is why we do not plan to re-create RCIs for each wave rather will apply them as we use them clinically in neuropsychology
- Working on methods to adjust for the loss to attrition