

Cognitive deficits in Covid-19 survivors

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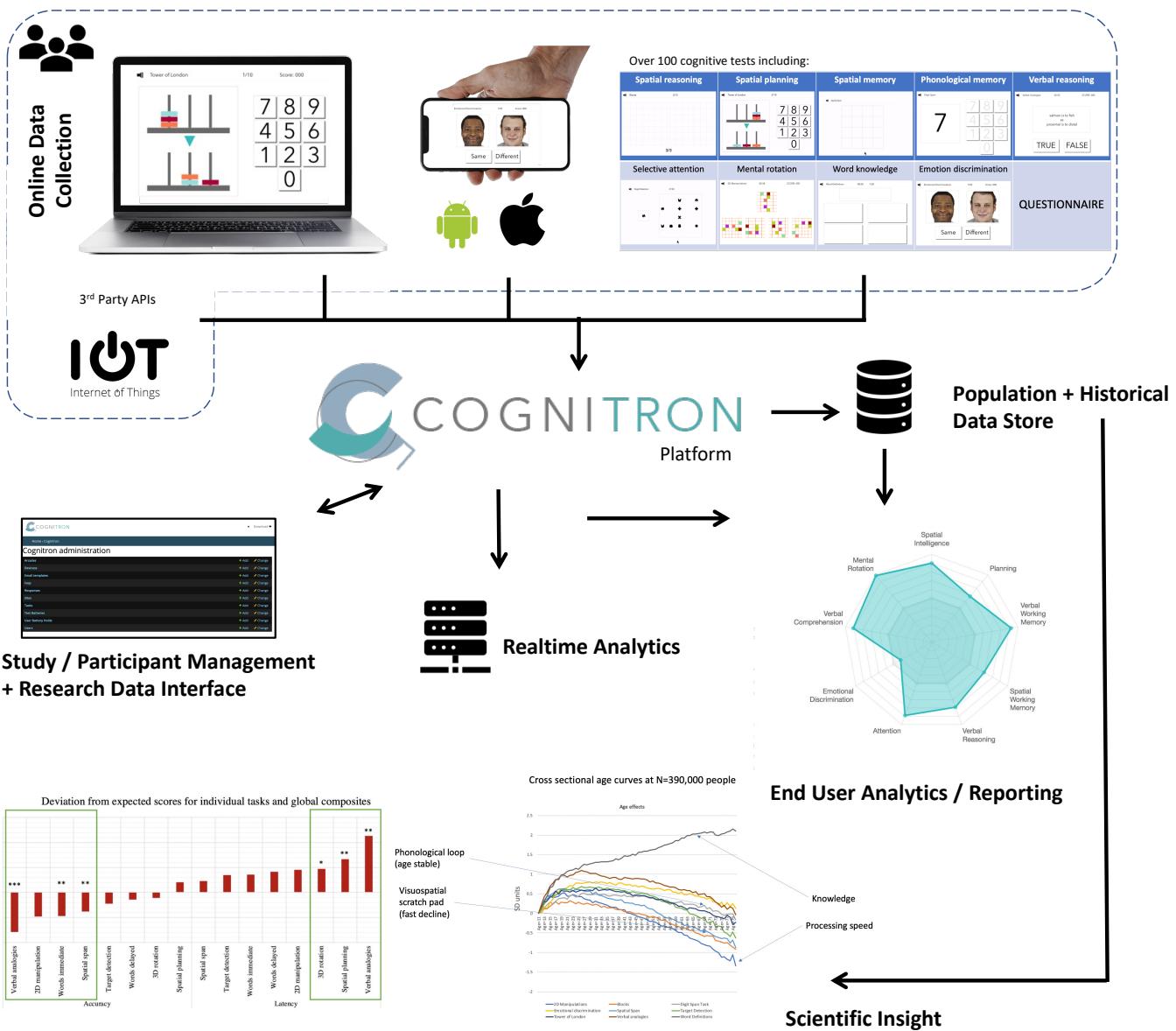


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Assessment platform - what is the Cognitron?

Flexible platform for developing & deploying cognitive assessments online and via custom Apps

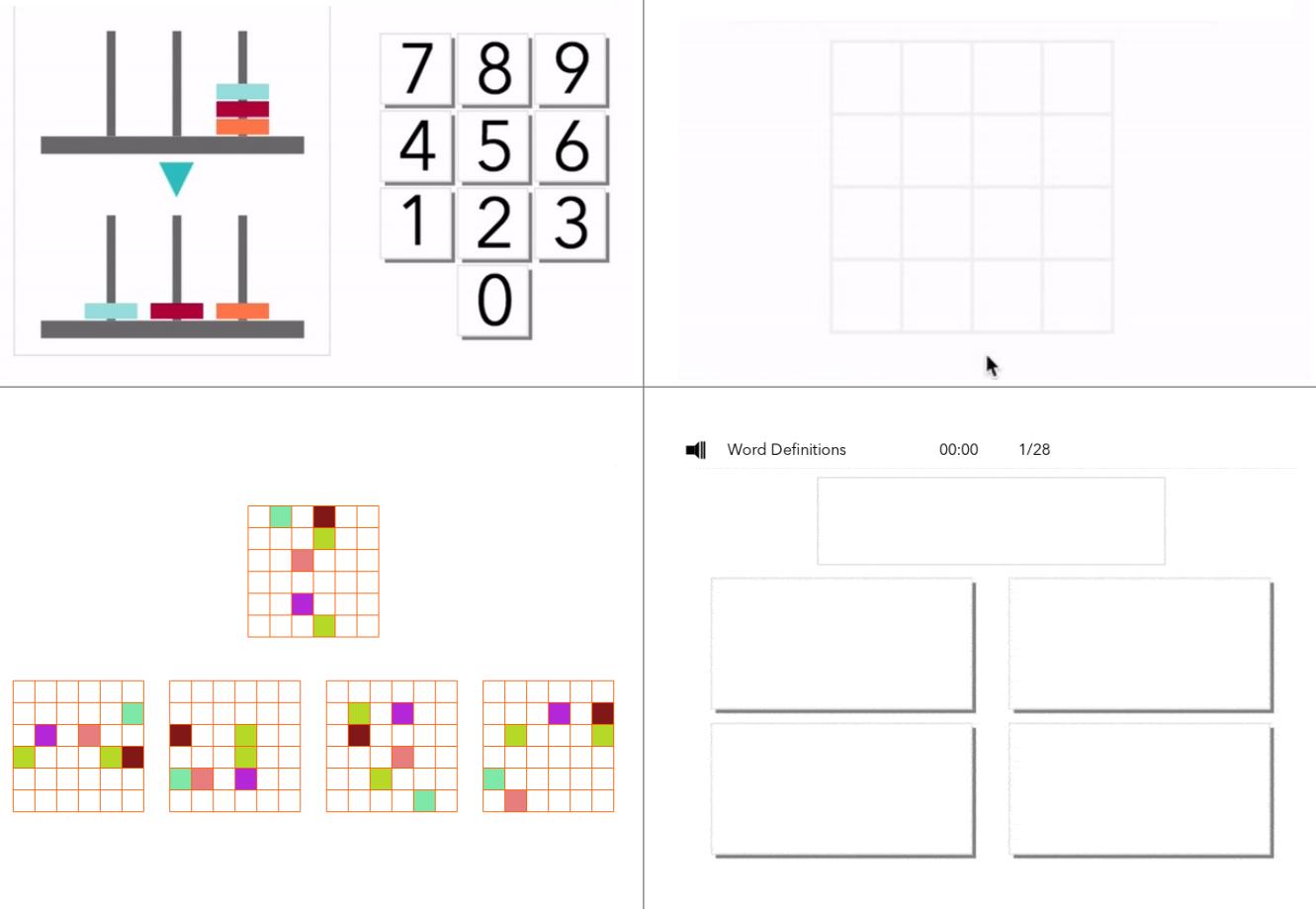
- >100 web-optimised cognitive paradigms
- Multi-language support
- Inbuilt questionnaire generator
- Easily extensible using libraries/templates
- Supports server-side optimisation studies
- Has handled up to ~36,000 concurrent users
- Supporting a growing body of studies, clinical cohorts, registers and trials
- Generates participant facing population standing graphs and clinician facing diagnostic reports



Cognitron task designs

Tasks are

- Build on established assessment paradigms but optimised for online deployment
- Run on smartphones, desktops and laptops in any modern browser
- Minimal sensitivity to device
- Public & Patient input with diverse clinical populations
- Ability to collect large normative datasets rapidly
- Brief (max 3 mins), minimally gamified and engaging, enabling custom batteries to be generated for specific purposes
- On the fly algorithms that generate stimuli, enabling deployment at many repeat timepoints



What was the Great British Intelligence Test?

- Collaboration with BBC2 Horizon in 2020
- Aimed to map cognitive abilities and mental health in fine detail across the British population
- High profile, advertised on BBC News and BBC Homepage
- Deployed using Cognitron platform, delivers objective cognitive tests & bespoke questionnaires via any device with a browser (PC/tablet/phone)
- Not advertised as a COVID-19 related study
- Covid related questions plus extended medical conditions and mental health scales added in May 2020

The image shows a grid-based user interface for the Cognitron platform. The top row contains five cognitive test modules: Spatial reasoning (Blocks task), Spatial planning (Tower of London task), Spatial memory (Spatial Span task), Phonological memory (Digit Span task), and Verbal reasoning (Verbal Analogies task). Below these are two rows of four modules each: Selective attention (Target Detection task), Mental rotation (2D Manipulations task), Word knowledge (Word Definitions task), and Emotion discrimination (Emotional Discrimination task). To the right of the Emotion discrimination module is a large, light-blue rectangular area labeled "QUESTIONNAIRE". Below the questionnaire area are three blue rectangular boxes labeled "Sociodemographics", "Lifestyle", and "Personality". At the bottom of the grid are three orange rectangular boxes labeled "Medical conditions", "Mental health", and "Pandemic impact".

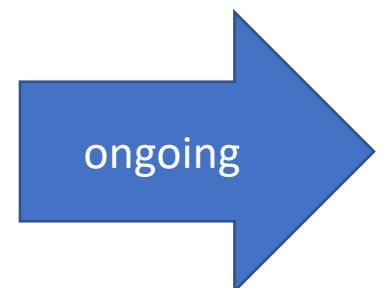
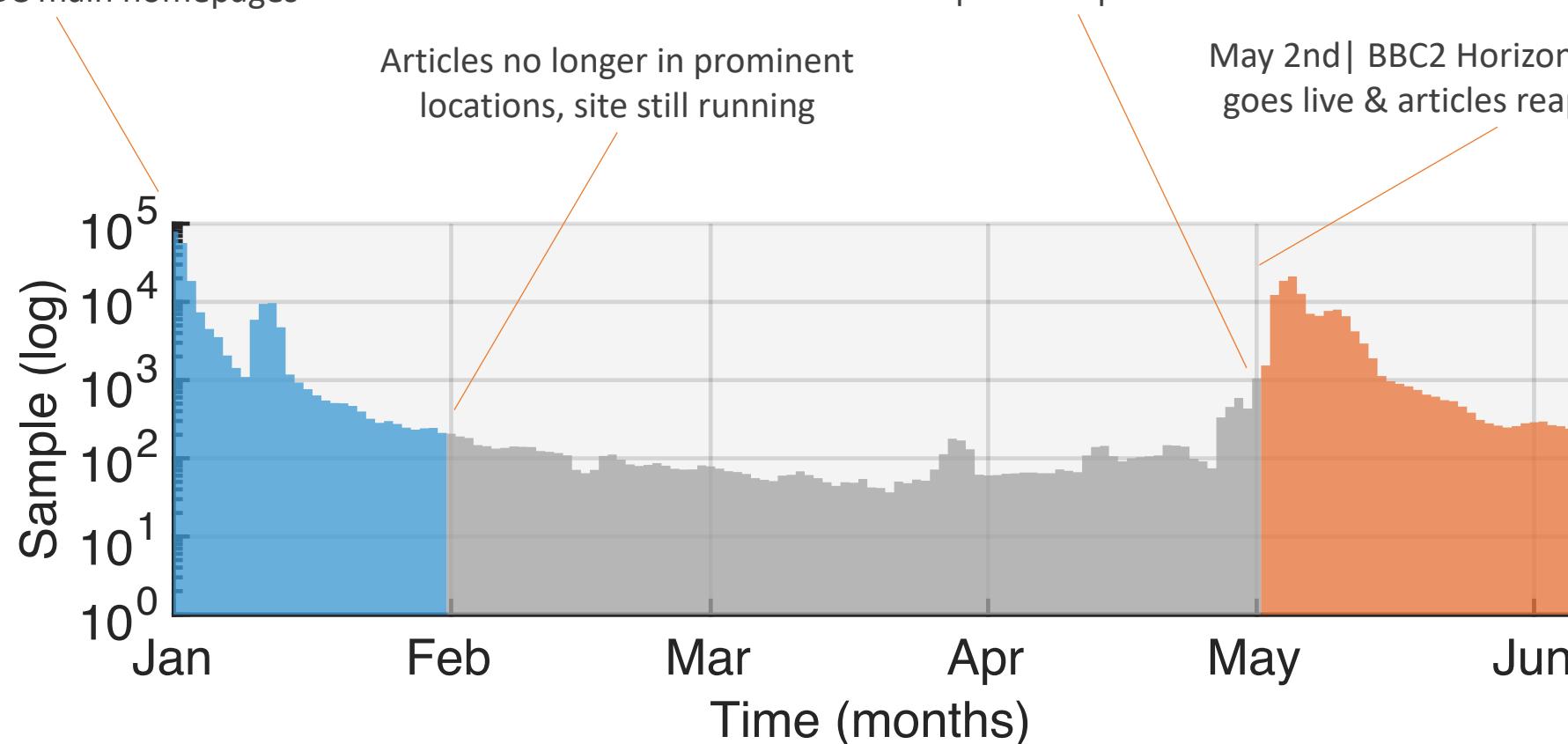
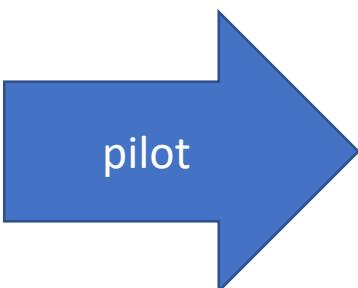
- *Mental health results - Hampshire et al., Nature Communications - 2021*
- *Covid-19 PTSD results - Chamberlain et al., BJP open - 2021*
- *Covid Cognition results – Hampshire et al., eClinicalHealth - 2021*
- *Free text analysis – Hampshire et al., Royal Society Interface Focus– in press*

Study timeline

January 1st | Articles appear on BBC news and BBC main homepages

May 1st | Questionnaire expanded in response to pandemic

May 2nd | BBC2 Horizon documentary goes live & articles reappear on BBC



Design considerations: decorrelation

Controversial what the main aspects of human cognitive ability are

Much research has focused on trying to identify latent variables by examining how peoples scores on different tests correlate with each other.

Typically test scores have a positive correlation, although the strengths vary widely

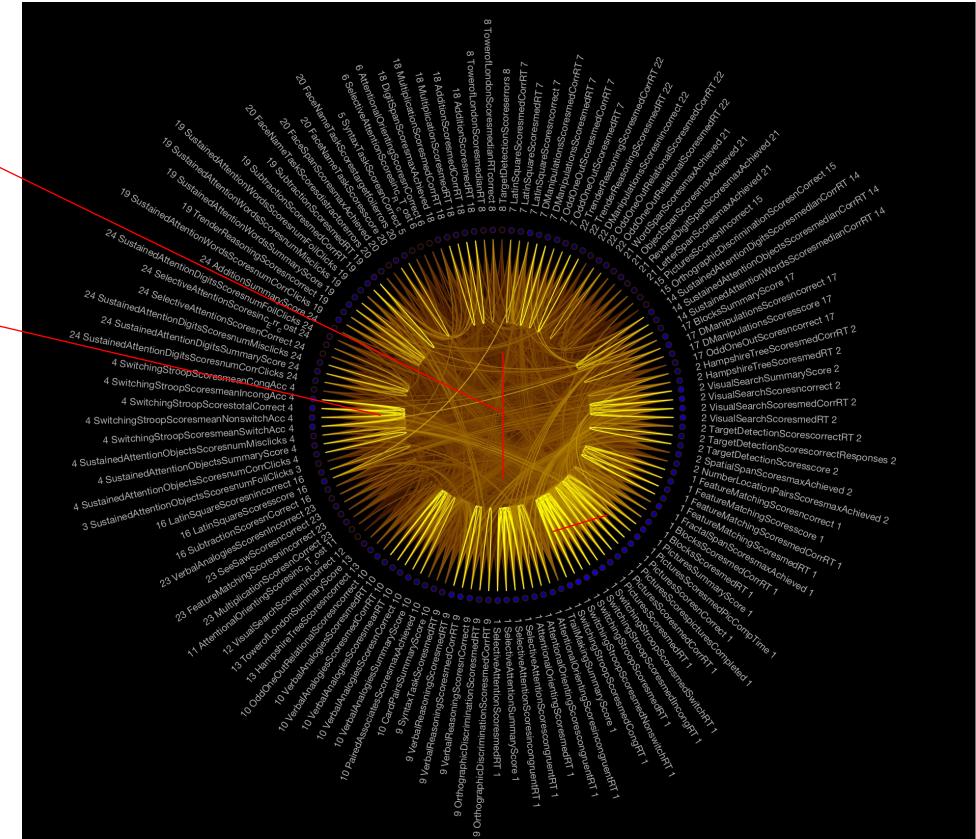
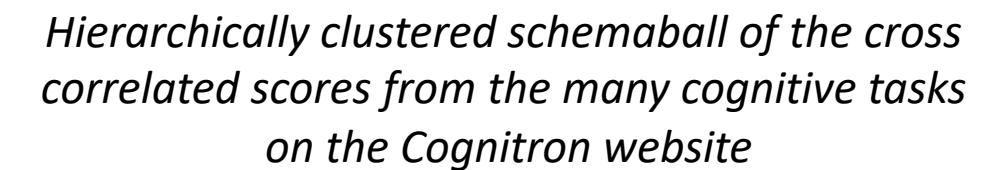
There also are clusters within this ‘positive correlation manifold’

This is the basis for a century old debate regarding how many different types of human intelligence there are ...

Diagnostically, for a battery of tests to be efficient, we want it to measure different aspects of cognition, i.e., to be *decorrelated*

Also important to consider the medium that a person is tested within. Browsers and Apps run on different devices in the wild.

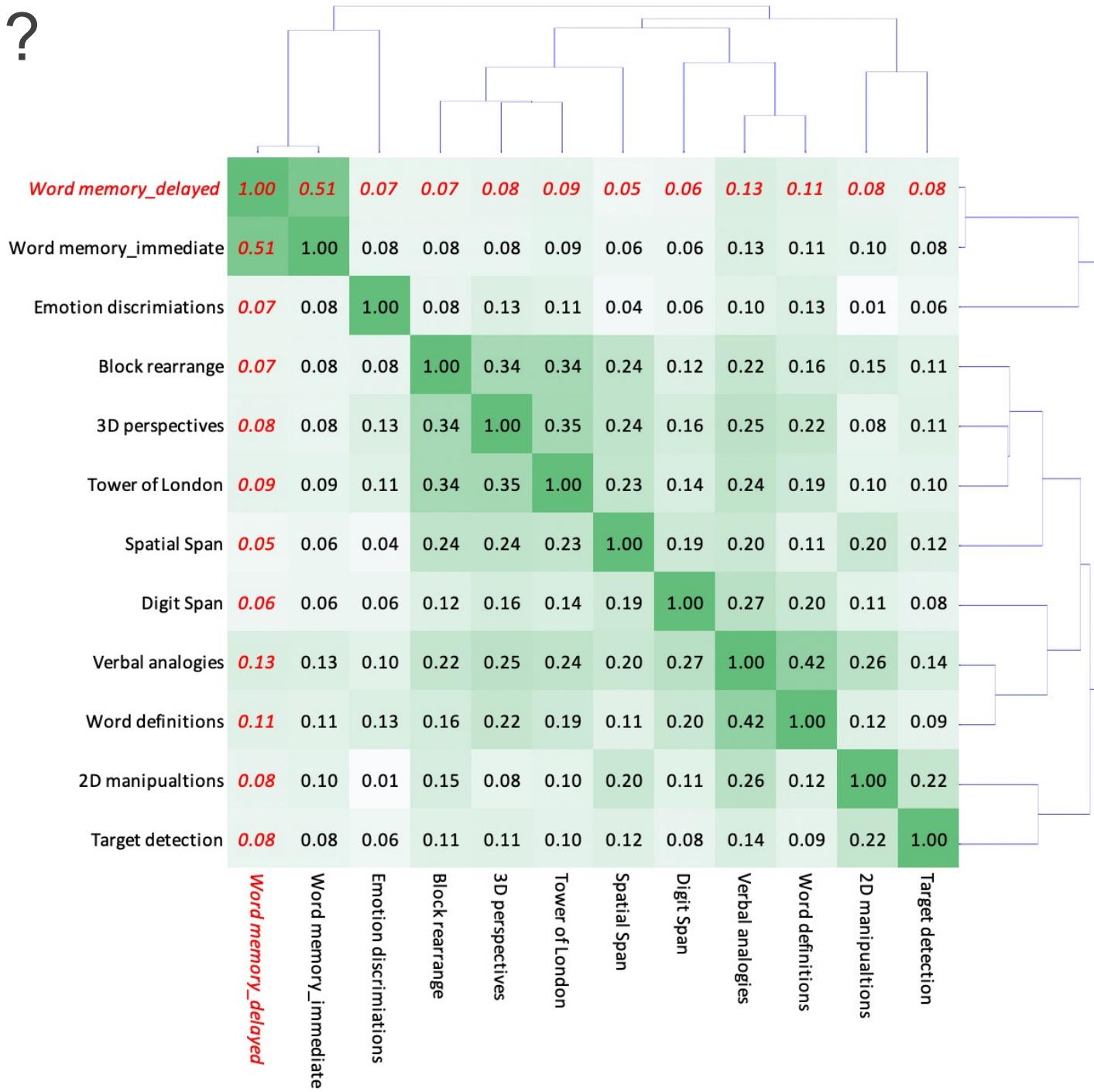
Plus there is not a one size fits all battery. Tests that are optimal for measuring subtle executive or reasoning deficits will be too complex for a dementia patient to understand what they are supposed to be doing.



How were the tasks selected?

- Low sensitivity to device (phone/tablet/PC)
- Partially decorrelated enabling multiple cognitive domains to be assessed
- Global cognition 'g' still measurable

% variance		Planning	Spatial WM	Word memory	Semantic problem solving
24.69					
11.77	Word memory_delayed	0.09	0.10	0.72	0.05
11.44	Word memory_immediate	0.08	0.08	0.69	0.07
9.18	Emotion discriminations	0.19	0.05	0.09	0.11
8.42	Digit Span	0.20	0.17	0.04	0.28
7.61	Verbal analogies	0.23	0.33	0.10	0.60
6.98	Word definitions	0.08	-0.12	0.04	0.60
5.60	Block rearrange	0.58	0.25	0.06	0.06
5.29	Tower of London	0.57	0.12	0.06	0.14
4.88	3D perspectives	0.60	0.11	0.05	0.18
4.12	2D manipulations	0.12	0.72	0.09	0.06
	Spatial Span	0.40	0.40	0.04	0.04
	Target detection	0.18	0.37	0.09	0.04



What was the Great British Intelligence Test?

- Resulted in ~390,000 datasets with ~120,000 in May
- Mean age=46yrs, 14% minority ethnic , ~1:1 male/female split & thousands non-binary, broad education range, tens of thousands with pre-existing neurologic or psychiatric conditions in May alone
- Data collected at 2 follow up time points
 - December2020-Jan2021
 - June-July 2021

The image shows a grid of 15 panels from the Great British Intelligence Test. The top row contains five cognitive tasks: Spatial reasoning (Blocks), Spatial planning (Tower of London), Spatial memory (Spatial Span), Phonological memory (Digit Span), and Verbal reasoning (Verbal Analogies). The second row contains five more tasks: Selective attention (Target Detection), Mental rotation (2D Manipulations), Word knowledge (Word Definitions), Emotion discrimination (Emotional Discrimination), and a Questionnaire section. The third row contains three blue boxes labeled Sociodemographics, Lifestyle, and Personality. The fourth row contains three orange boxes labeled Medical conditions, Mental health, and Pandemic impact.

Spatial reasoning	Spatial planning	Spatial memory	Phonological memory	Verbal reasoning
Blocks 2/15 3/3	Tower of London 2/10 7 8 9 4 5 6 1 2 3 0	Spatial Span	Digit Span 7 7 8 9 4 5 6 1 2 3 0	Verbal Analogies 02:55 SCORE: 000 salmon is to fish as proximal is to distal TRUE FALSE
Selective attention	Mental rotation	Word knowledge	Emotion discrimination	QUESTIONNAIRE
Target Detection 3/100	2D Manipulations 00:34 SCORE: 000	Word Definitions 00:00 1/28	Emotional Discrimination 1/50 Score: 000 Same Different	
Sociodemographics	Lifestyle	Personality		
Medical conditions	Mental health	Pandemic impact		

- Mental health results - Hampshire et al., Nature Communications - 2021*
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Covid-19 survivors – respiratory symptom severity and treatment

May subset - 81,337 usable cognitive datasets with optional Covid-19 questionnaire

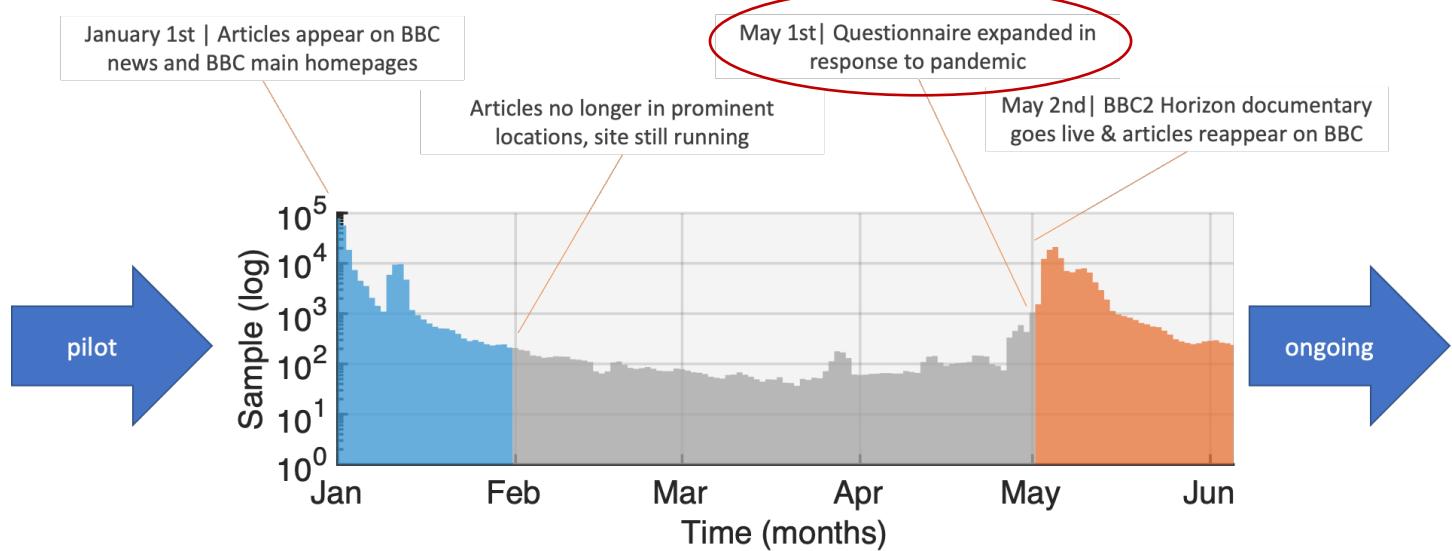
Participants organised by respiratory outcome as a proxy for severity

12,689 participants believed they'd had the virus

192 hospitalised, 44 on ventilators

386 positive biological tests (almost all of those who were in hospital)

	Not ill	III without respiratory symptoms	Respiratory symptoms without home assistance	Respiratory symptoms with home assistance	Hospitalised No ventilator	Hospitalised Ventilator
No/don't know/awaiting results	68648	8726	3286	159	126	6
Yes	0	212	100	14	22	38



Covid-19 survivors – age range

May subset - 81,337 usable cognitive datasets with optional Covid-19 questionnaire

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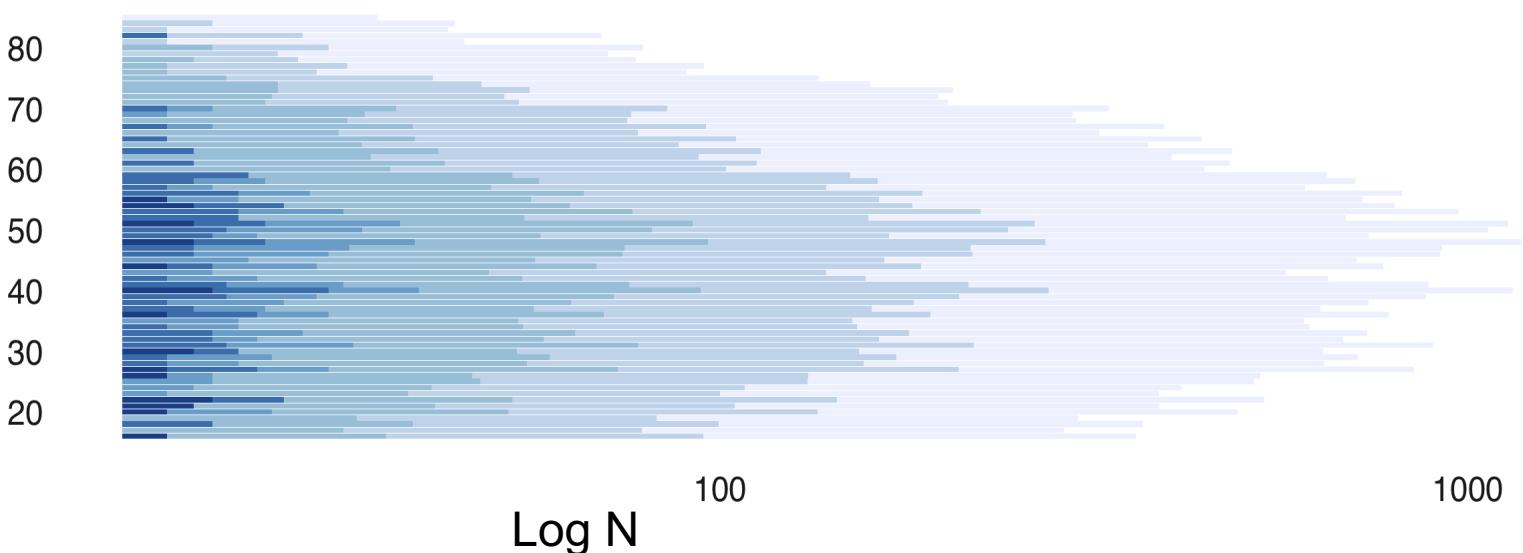
Those who were ill spanned a broad age (mean 44yrs) and demographic range

- Symptoms without respiratory symptoms
- Respiratory symptoms/ No home assistance
- Respiratory symptoms/ Medical home assistance
- Hospitalised/ No Ventilator
- Hospitalised/ Ventilator

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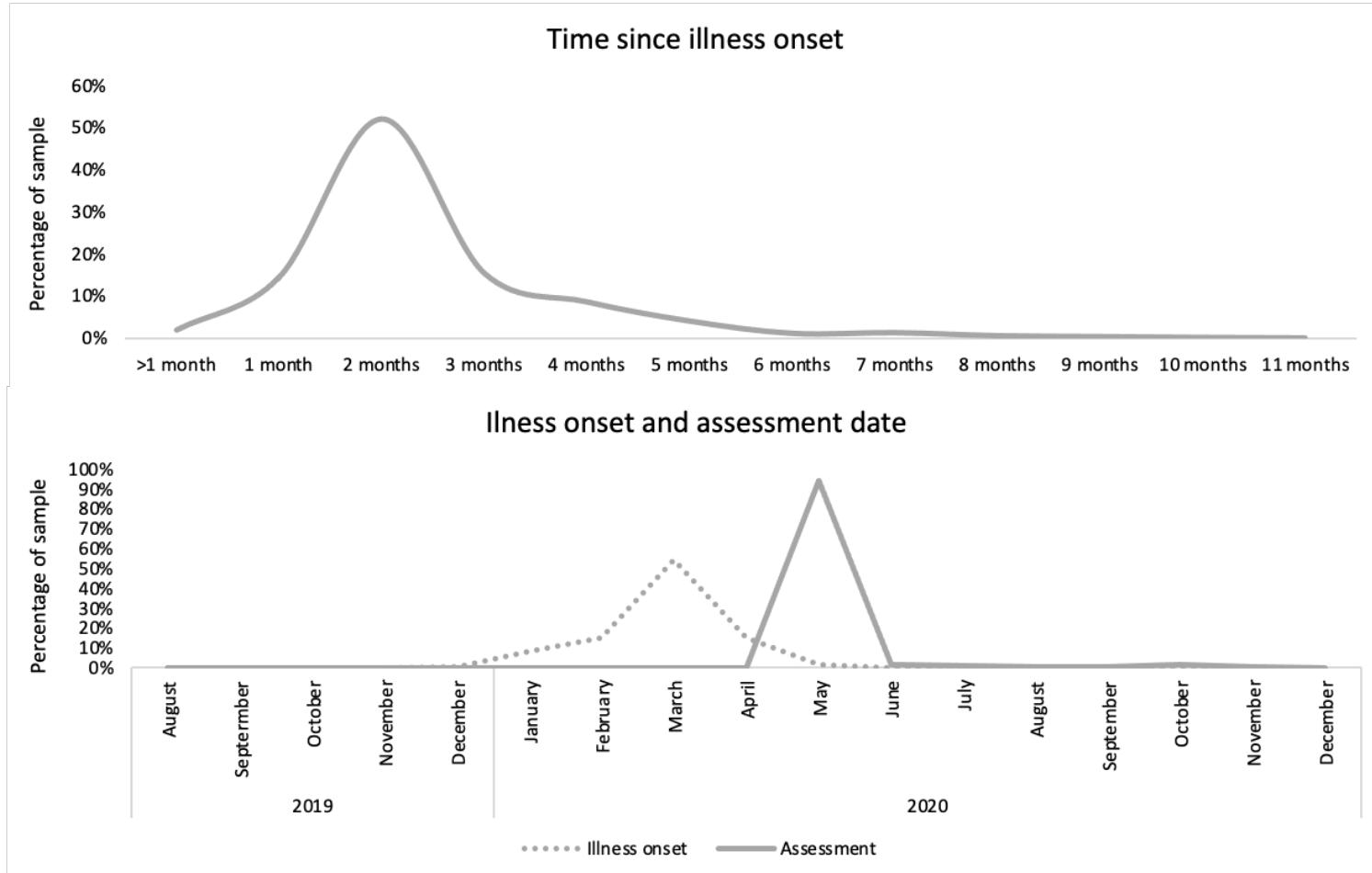
A I Count of each symptom group within each age division

Proportions within each age bracket have been scaled using a log10 function



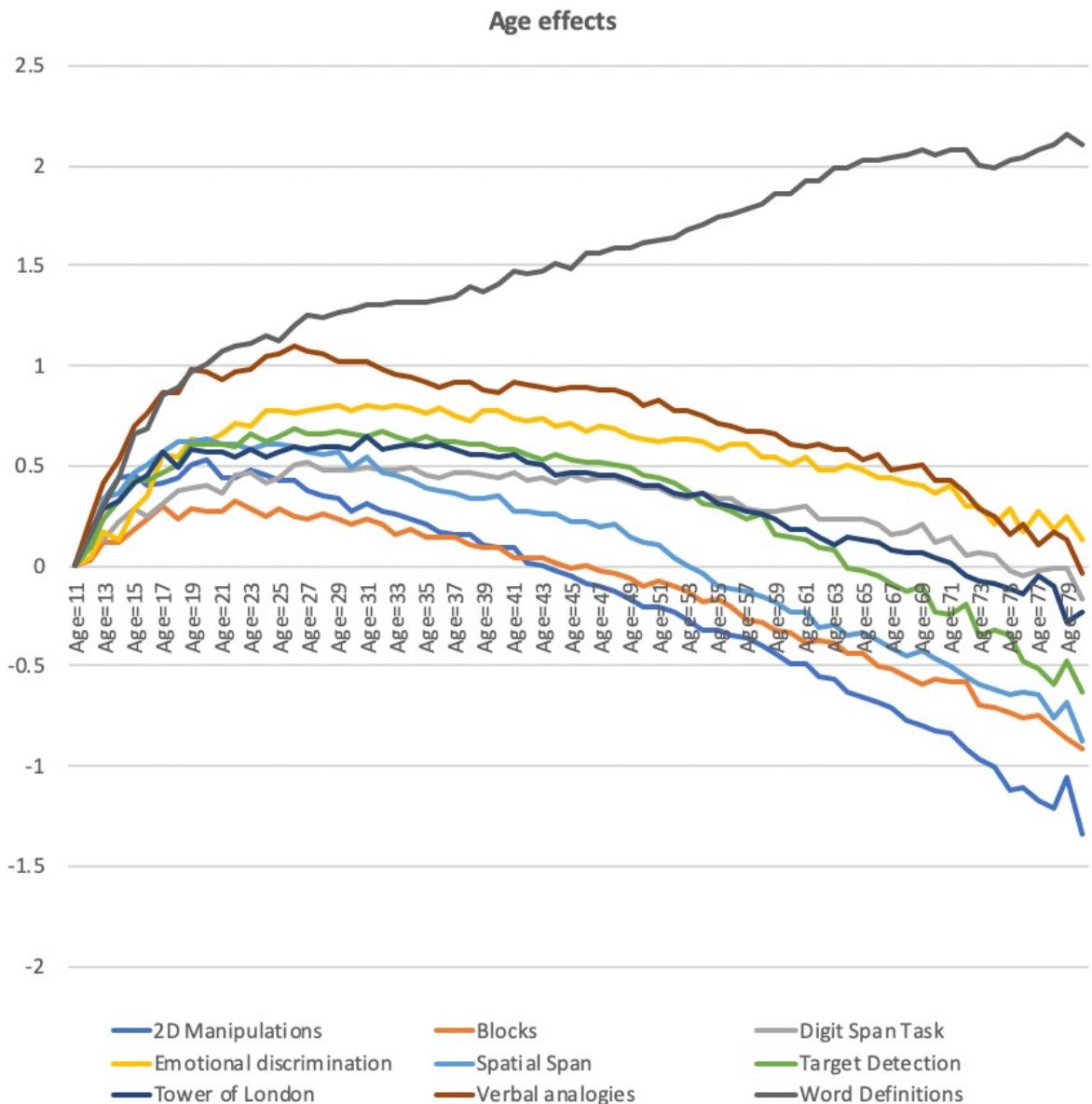
Covid-19 survivors – time from illness

- Reported time of illness vs time of cognitive assessment in bio-confirmed cases
- Illness onset coincides with first wave peak
- Assessment offset mode ~2 months post illness



Age curves: N=~390,000

- Important to account for sociodemographic variables
 - Age especially associated with cognitive performance
 - Also education level, first language and other factors to varying degrees



Model-based approach to culture fair assessment

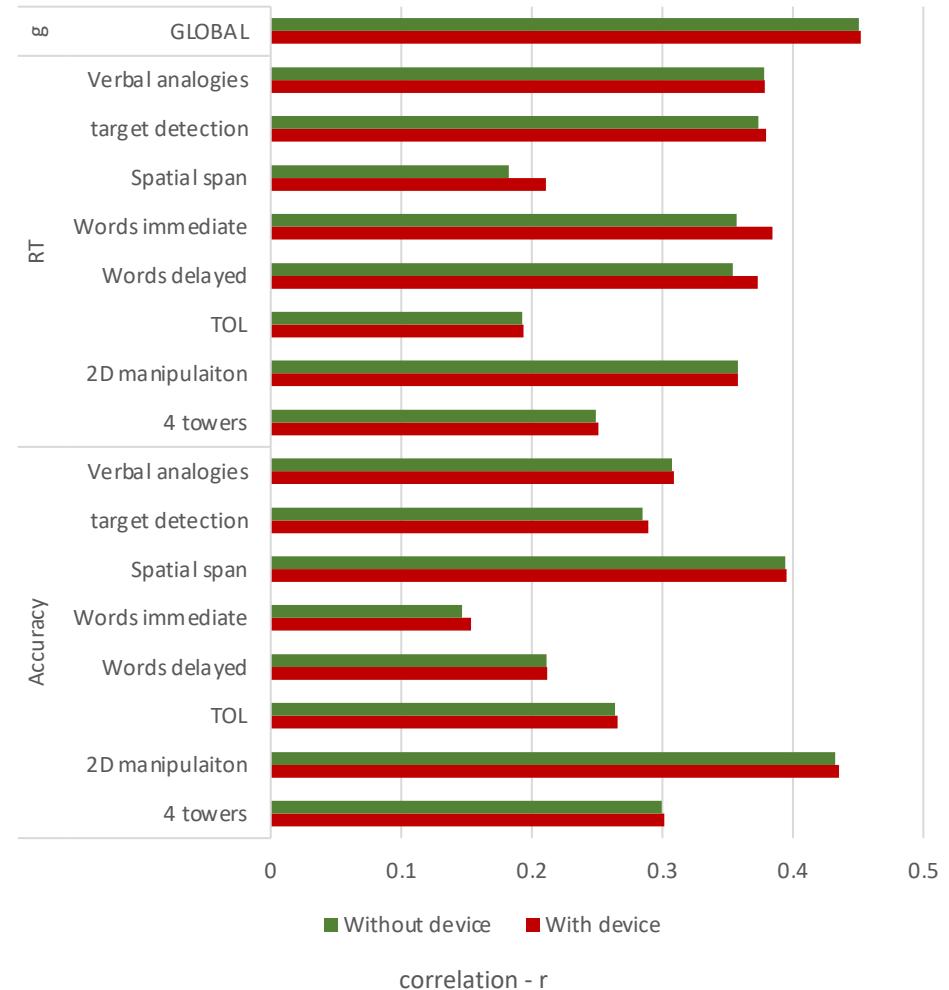
Population factor – cognitive score associations make interpretation of objective assessment results difficult

Simple linear modelling to predict performance on each task

- Train on one subset of individuals
- Predict task scores based on
 - **Age to third order**
 - Handedness
 - Sex
 - **Education level**
 - **English first language (binary)**
 - **Testing device**
- Explains held out data global composite at $r \approx 0.45$

The very large normative dataset can be used to enable culture fair assessment, calculating ***deviation from expected score*** for similar people

Observed vs predicted score



Covid-19 survivors – global cognitive deficits

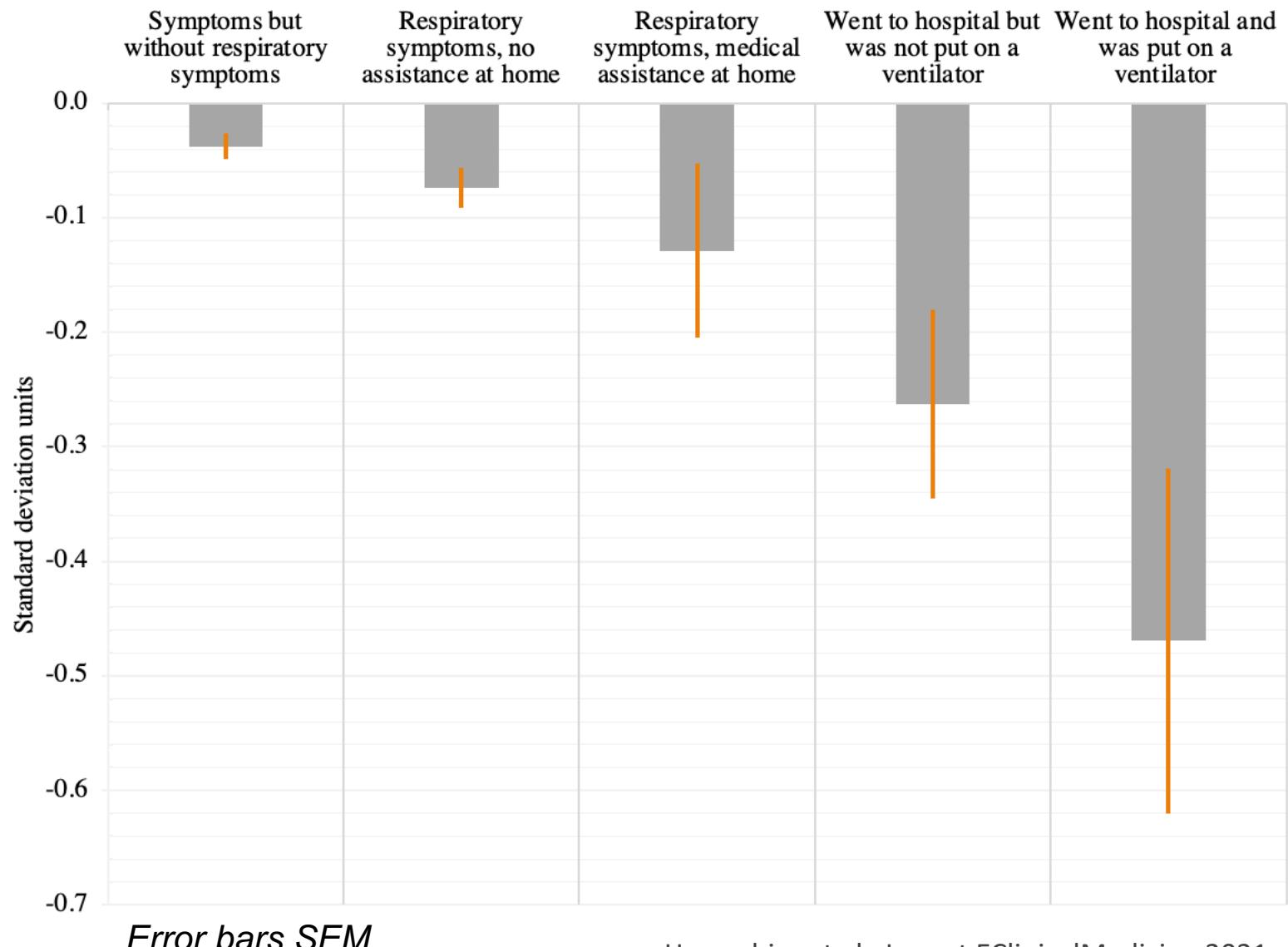
After accounting for

- age,
- gender,
- ethnicity,
- handedness
- country of residence
- first language
- pre-existing conditions
- occupational status
- economic status
- depression
- anxiety
- insomnia
- tiredness

Global cognitive performance varied as a function of respiratory severity

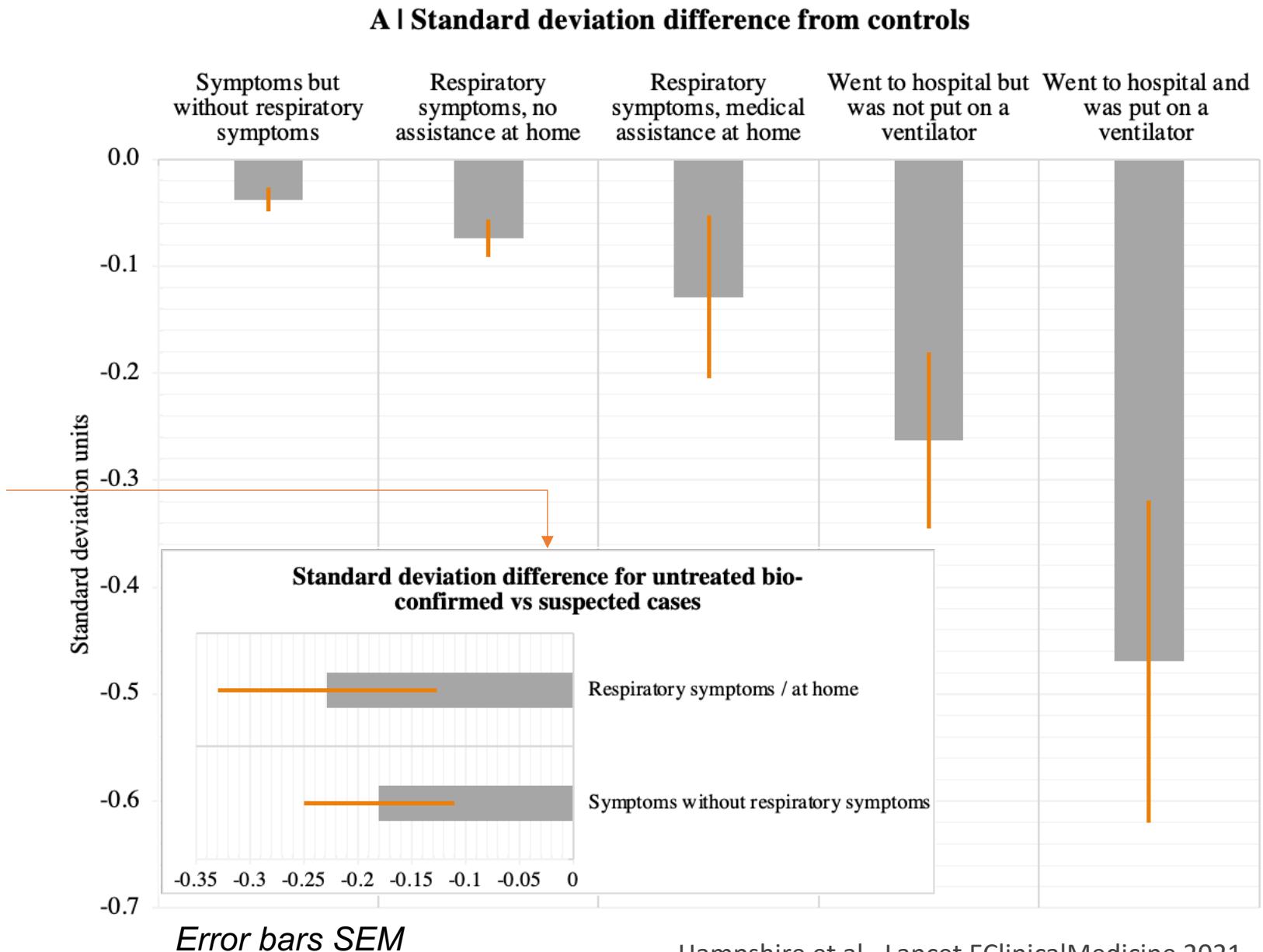
Even the least severe group shows a very small cognitive disadvantage

A | Standard deviation difference from controls



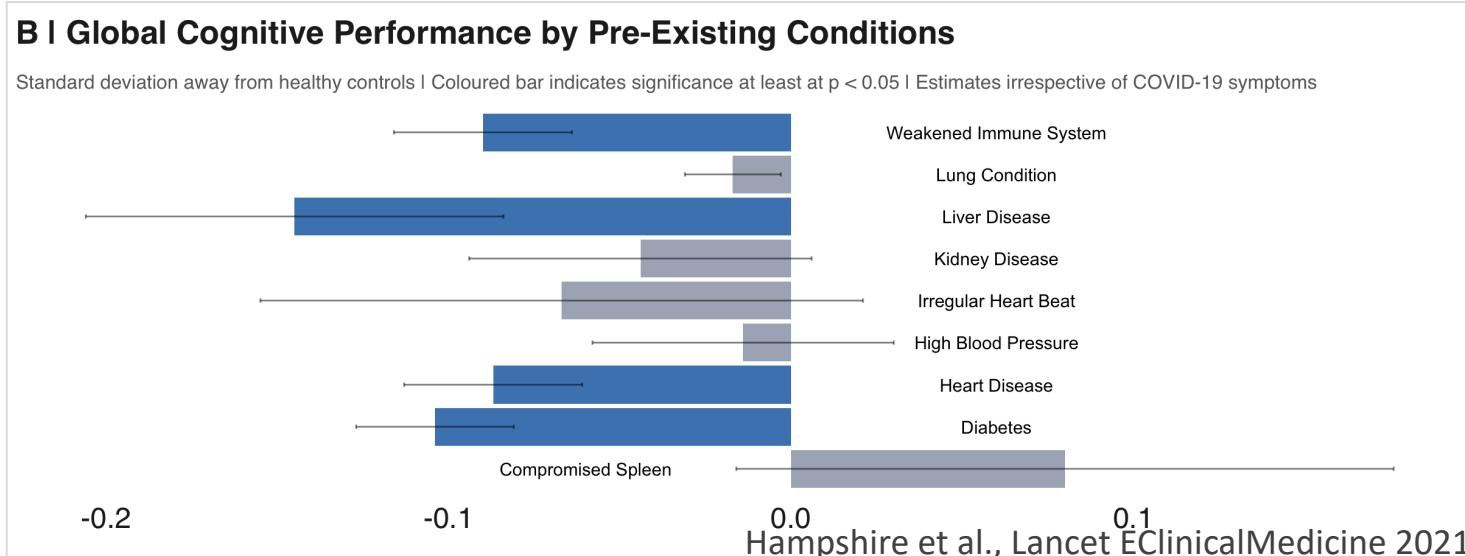
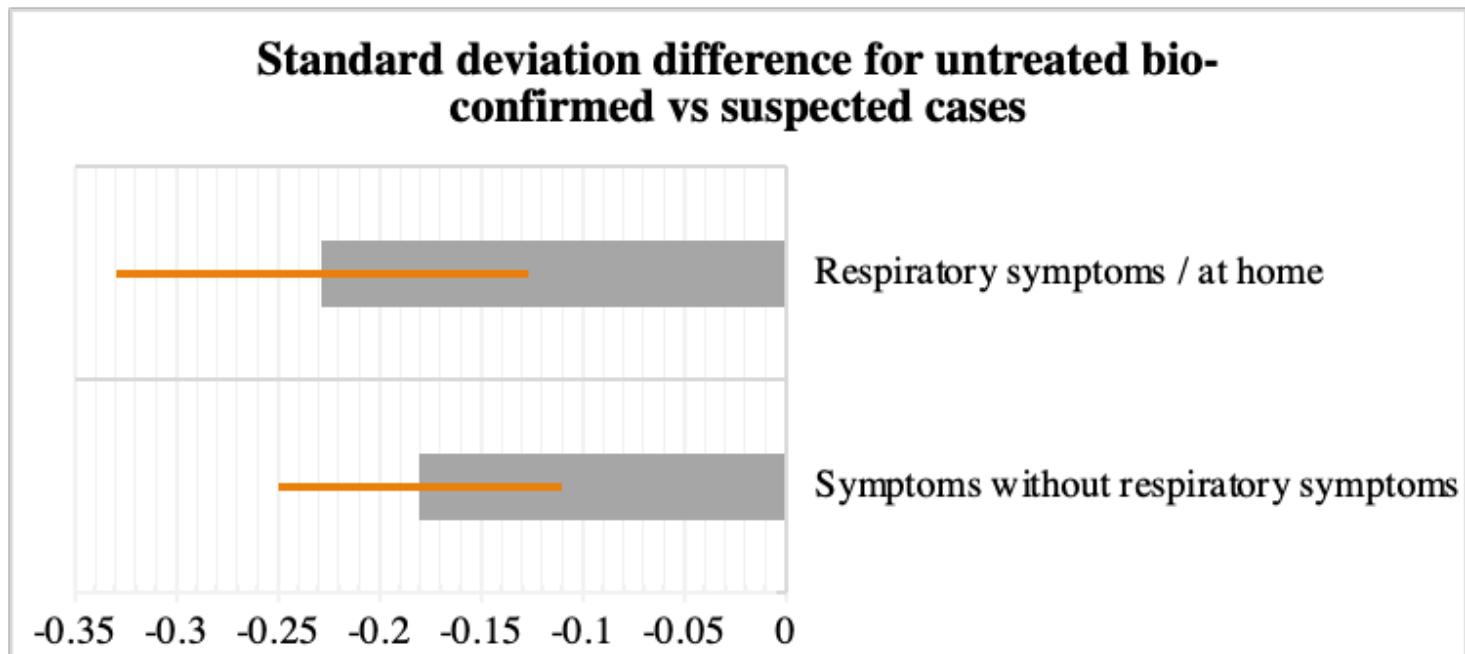
Covid-19 survivors – global cognitive deficits

- Global cognitive performance examined in mild bio-confirmed cases only
- More substantial cognitive underperformance evident in those with and without respiratory symptoms



Covid-19 survivors – global cognitive deficits

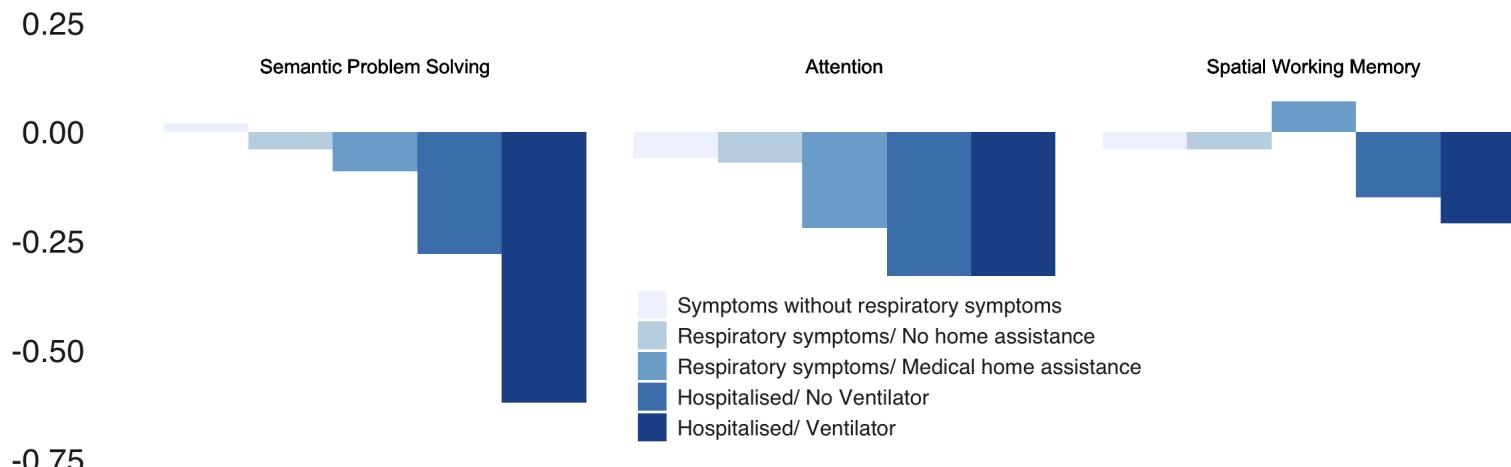
- Global cognitive performance examined in mild bio-confirmed cases only
- More substantial cognitive underperformance evident in those with and without respiratory symptoms
- Scale of deficit even amongst mild cases greater than for conditions predisposing to Covid-19 vulnerability
- *Also, correlation with time since illness was statistically non significant – though note, most participants in the sub-acute / early chronic phase*



Covid-19 survivors – domain specificity of cognitive deficits

A | Principal Component Analysis Estimates

Estimates are standard deviations away from healthy controls



- At a finer grain cognitive deficits appeared to be greatest for certain cognitive domains
- Especially semantic problem solving and attention

B | Individual Test Performance by Symptom Severity

Estimates are standard deviations away from healthy controls | Colour gradient equates to coefficient strength

	0	-0.04	-0.09	-0.22	-0.53
Word definitions	0	-0.04	-0.09	-0.22	-0.53
Verbal Analogies	-0.02	-0.06	-0.03	-0.38	-0.42
Target Detection	-0.02	-0.04	-0.13	-0.16	-0.35
Tower of London	-0.03	-0.03	-0.01	-0.11	-0.29
Blocks	-0.04	-0.04	-0.15	-0.23	-0.24
2D manipulations	-0.04	-0.02	0.04	-0.15	-0.17
Spatial Span	-0.04	-0.06	-0.1	-0.06	-0.1
Emotional Discrimination	0.04	-0.02	-0.07	-0.18	-0.01
Digit Span	0.01	-0.04	-0.02	0	0.32
	1	2	3	4	5

Symptoms without respiratory symptoms = 1 | Respiratory symptoms/ No home assistance = 2
Respiratory symptoms/ Medical home assistance = 3 | Hospitalised/ No Ventilator = 4
Hospitalised/ Ventilator = 5

Today's workshop

Citizen science projects have the strength of numbers but also limitations

- Self report
- Not controlled conditions

The above work was followed on with hospital and epidemiological cohort research. We will analyse some of that data today.

Tutorial

Walk through how to handle behavioural data

1. Data cleaning
2. Preprocessing

Walk through how to leverage big normative data in order to examine cognitive deficits in people who were hospitalized with COVID-19

Challenge

Apply this approach to examine the nature of cognitive deficits in people with dementia