Cognitive deficits in Covid-19 survivors

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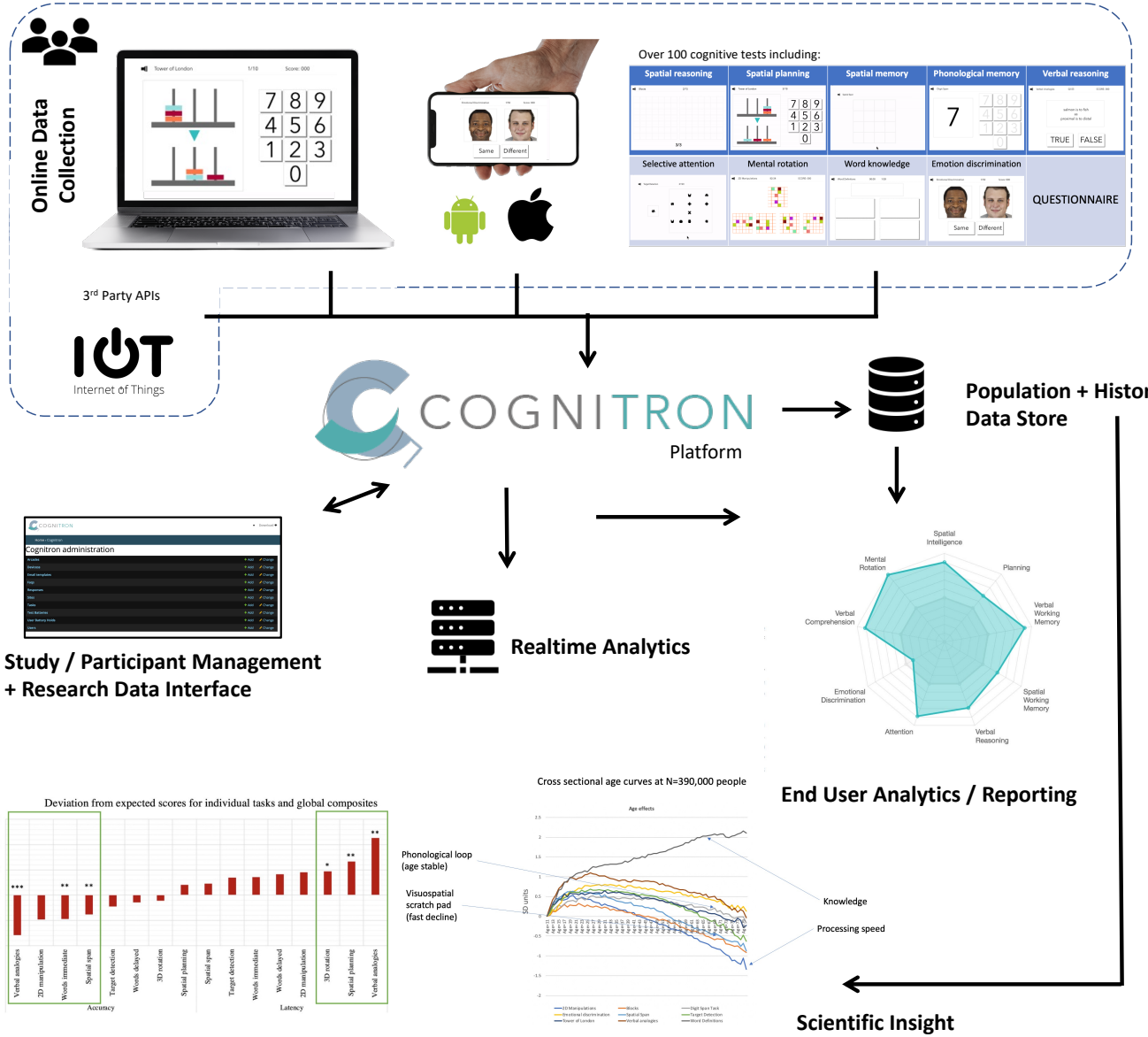
Assessment platform - what is the Cognitron?

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

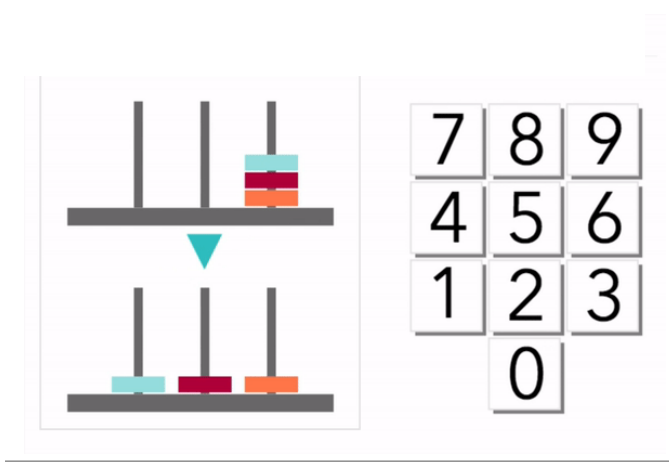
- >100 web-optimised cognitive paradigms
- Multi-language support
- Inbuilt questionnaire generator
- Easily extensible using libraries/templates
- Supports server-side optimisation studies
- Has handled up to ~36,000 concurrent users
- Supporting a growing body of studies, clinical cohorts, registers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

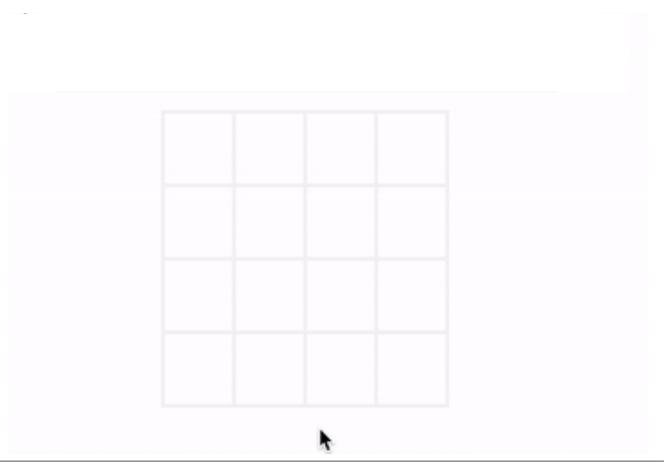


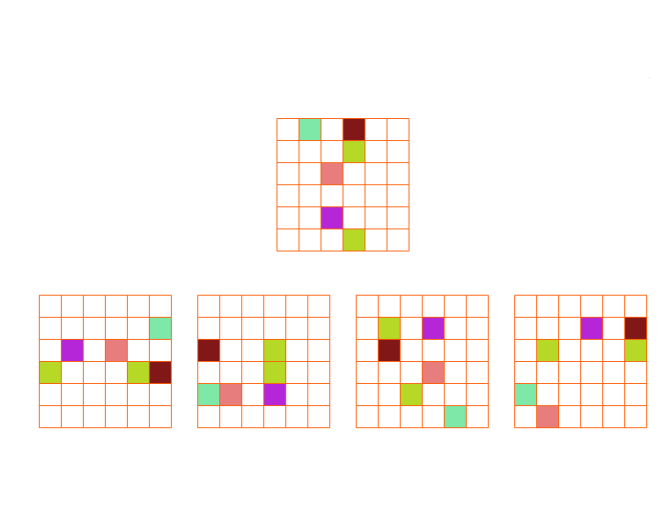
Cognitron task designs

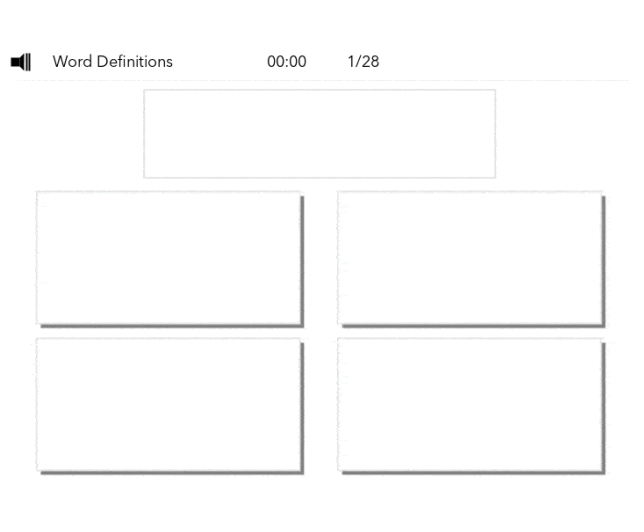
Tasks are

- 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



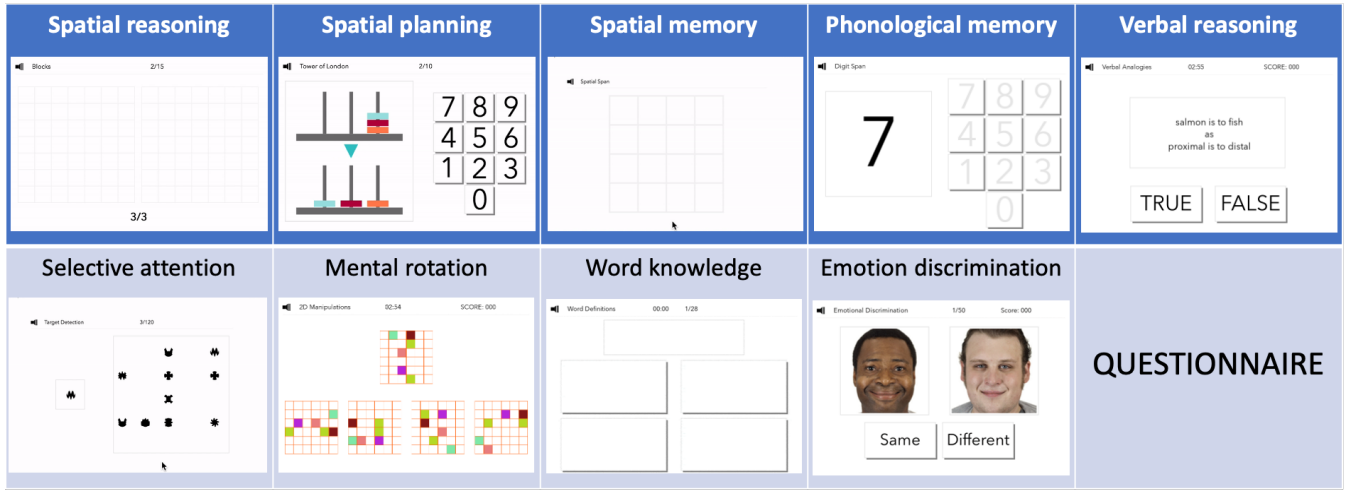






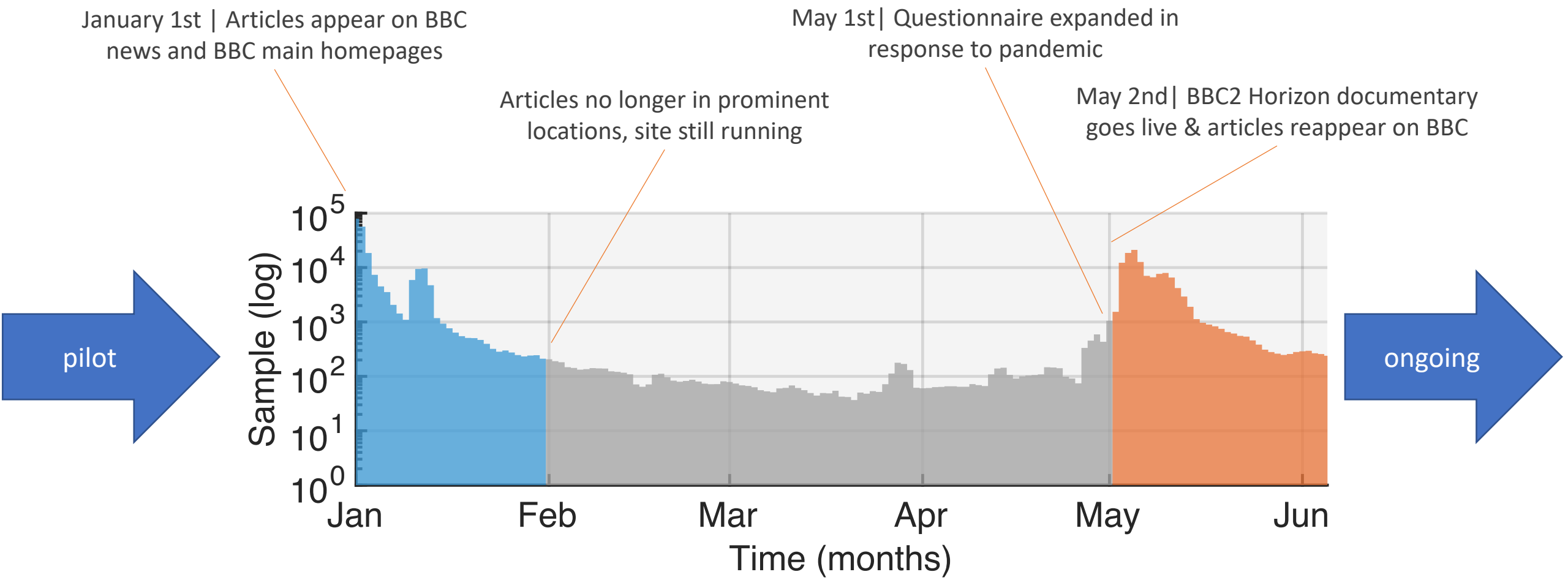
What was the Great British Intelligence Test?

- 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



- *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



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’

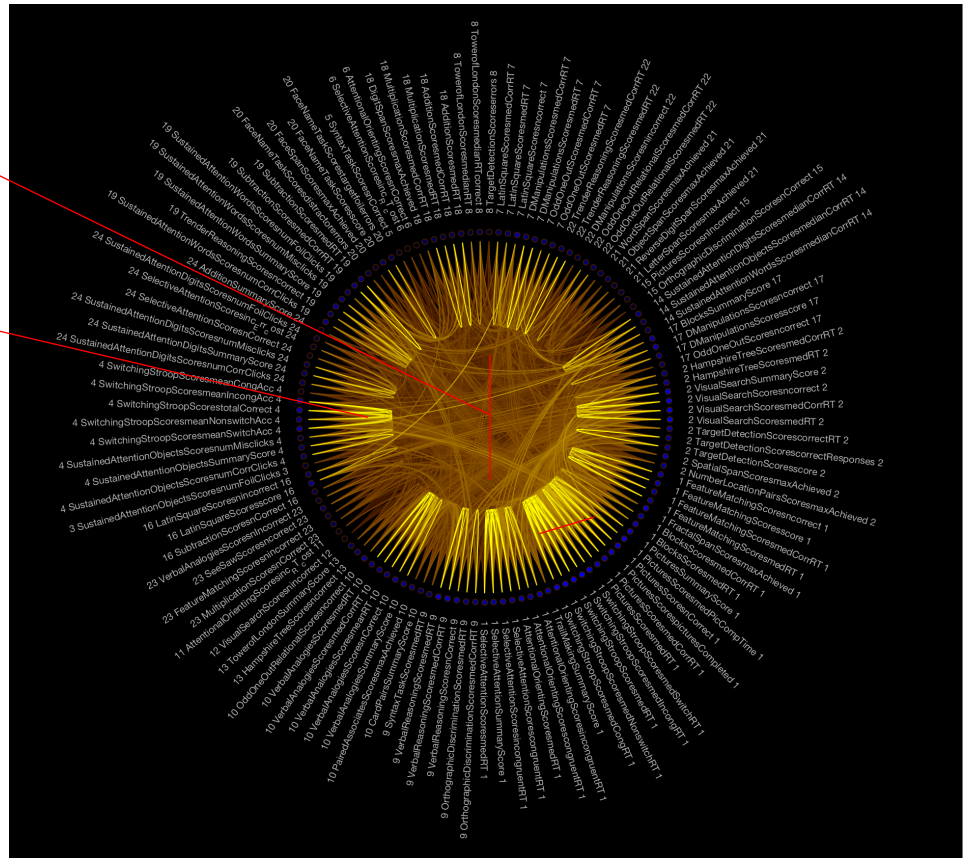
This is the basis for a century old debate regarding how many different types of human intelligence there are …

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.

Hierarchically clustered schemaball of the cross correlated scores from the many cognitive tasks on the Cognitron website

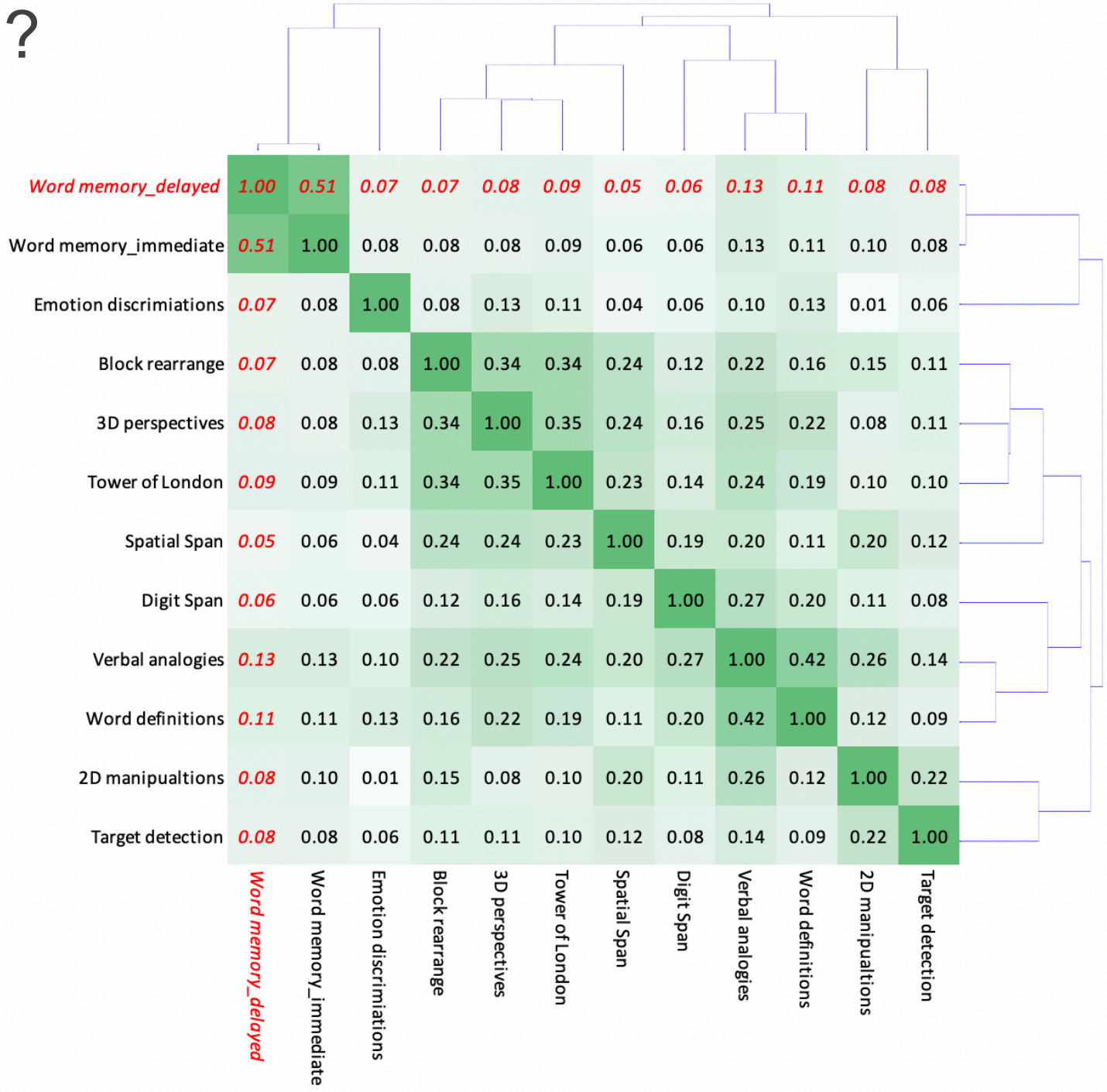


How were the tasks selected?

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

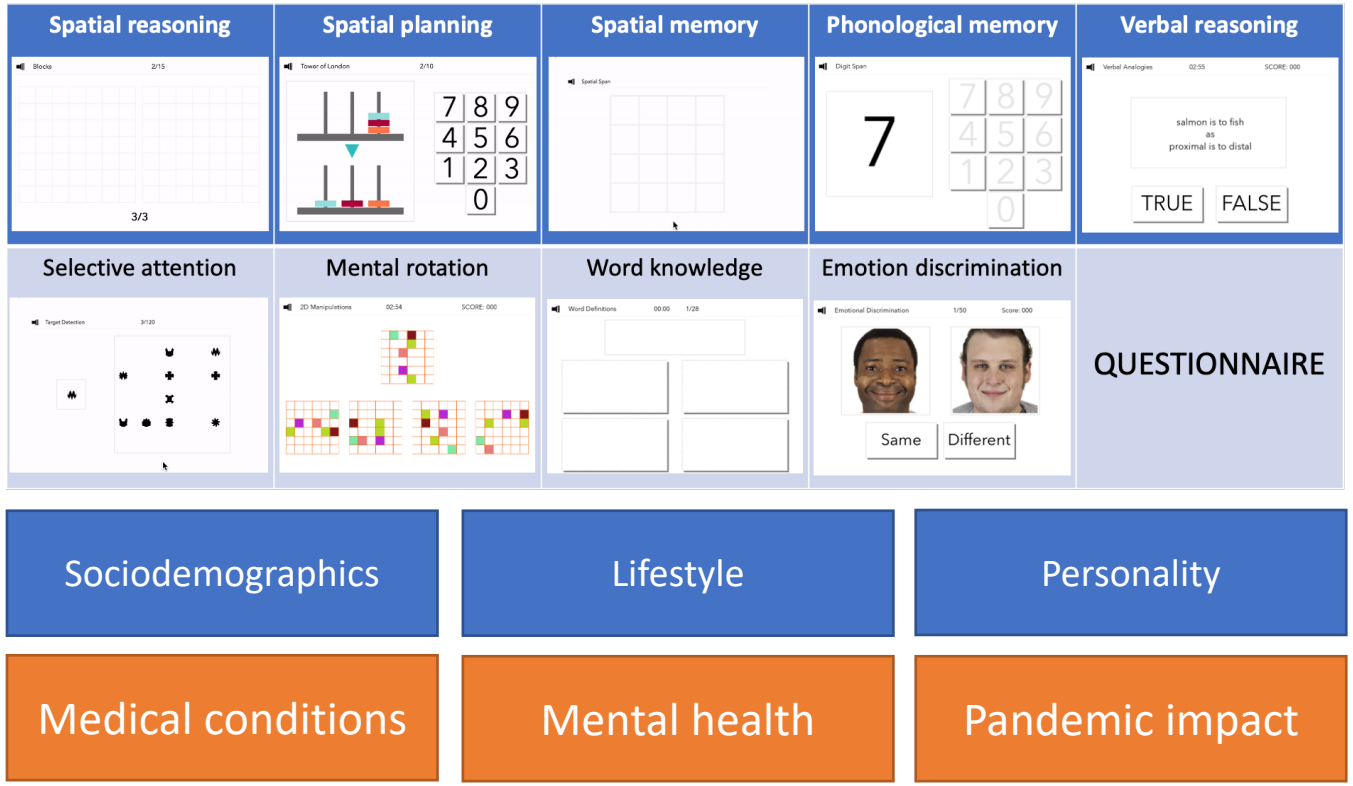
% variance
24.69
11.77
11.44
9.18
8.42
7.61
6.98
5.60
5.29
4.88
4.12

	Planning	Spatial WM	Word memory	Semantic problem solving
Word memory_delayed	0.09	0.10	**0.72**	0.05
Word memory_immediate	0.08	0.08	**0.69**	0.07
Emotion discrimiations	0.19	0.05	0.09	0.11
Digit Span	0.20	0.17	0.04	0.28
Verbal analogies	0.23	0.33	0.10	0.60
Word definitions	0.08	-0.12	0.04	0.60
Block rearrange	0.58	0.25	0.06	0.06
Tower of London	0.57	0.12	0.06	0.14
3D perspectives	0.60	0.11	0.05	0.18
2D manipualtions	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



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Covid-19 survivors – respiratory symptom severity and treatment

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

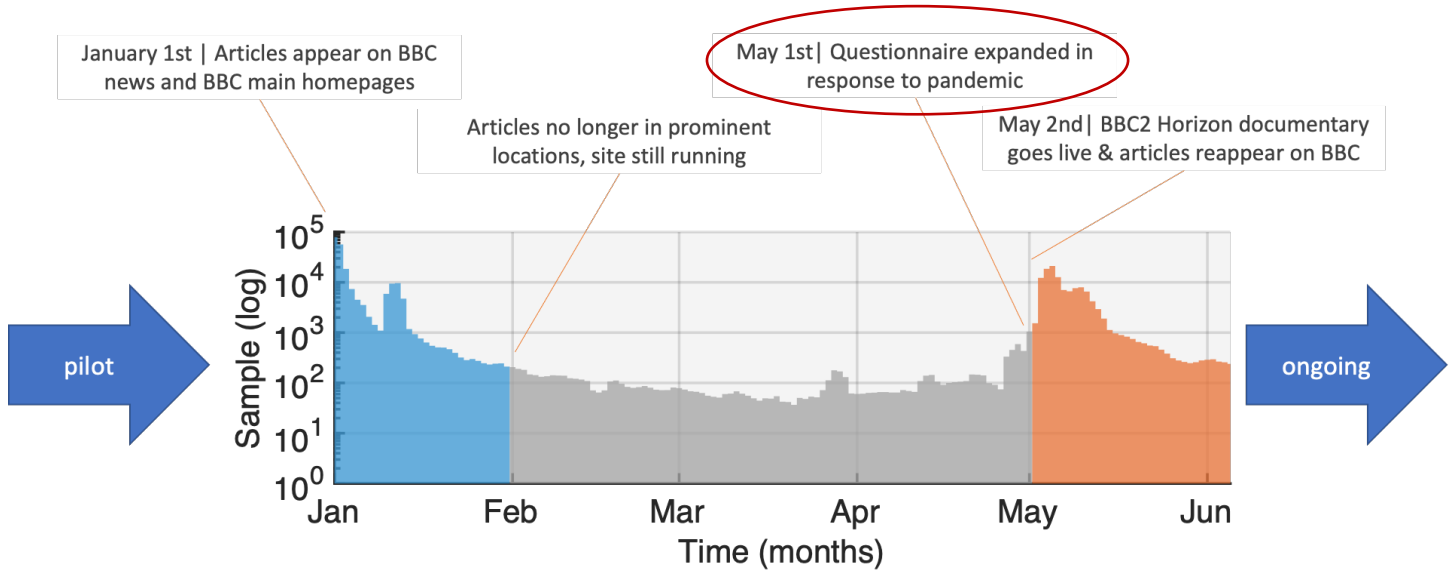
Participants organised by respiratory outcome as a proxy for severity

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	Ill 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

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)

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

	Not ill	Ill 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
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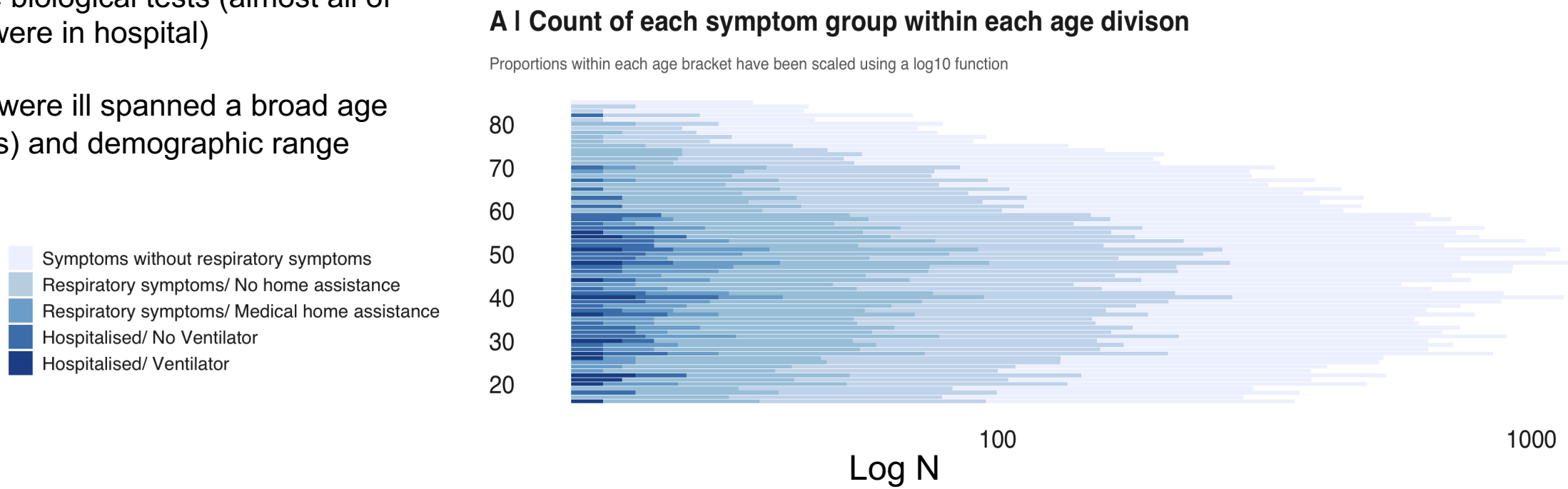
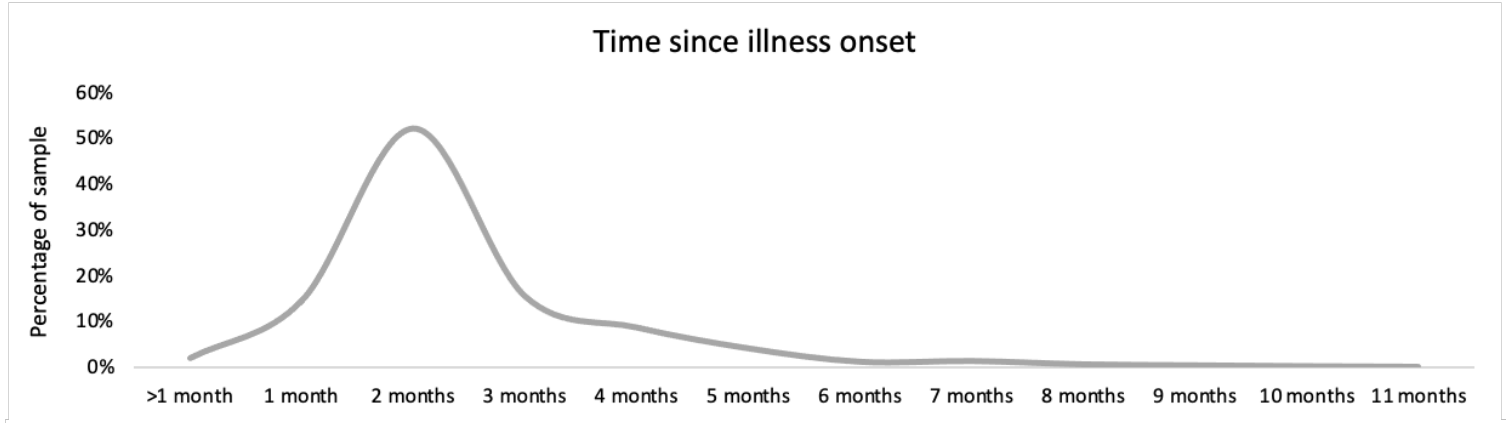
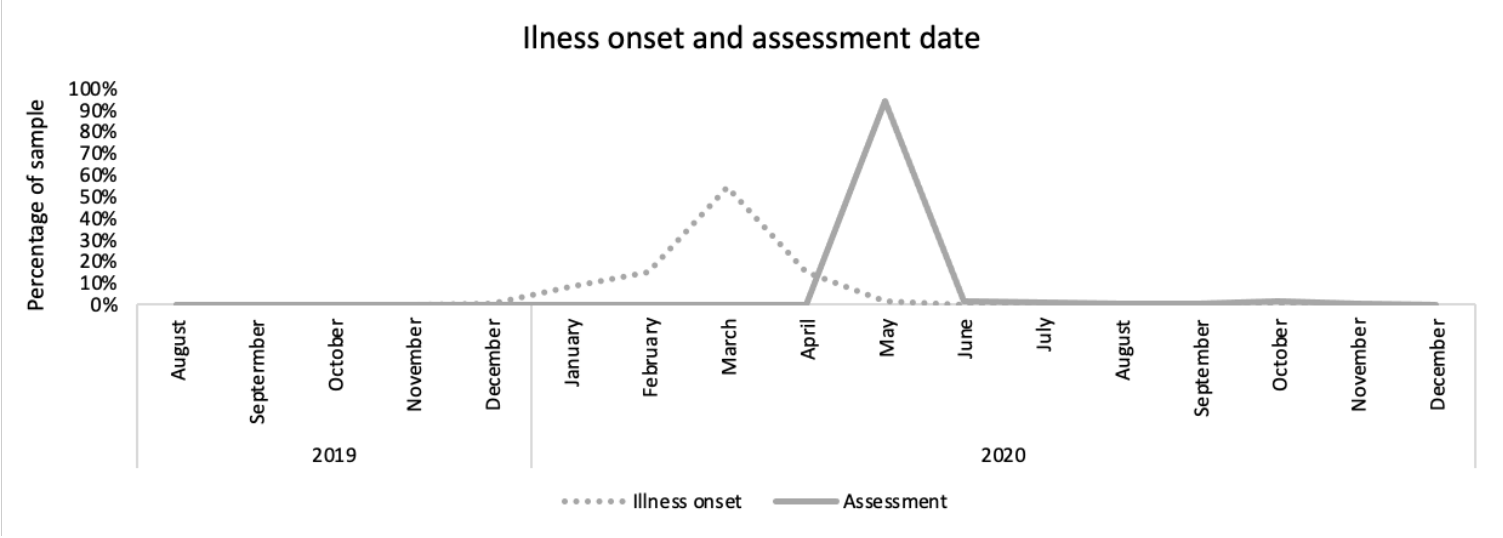


Covid-19 survivors – time from illness

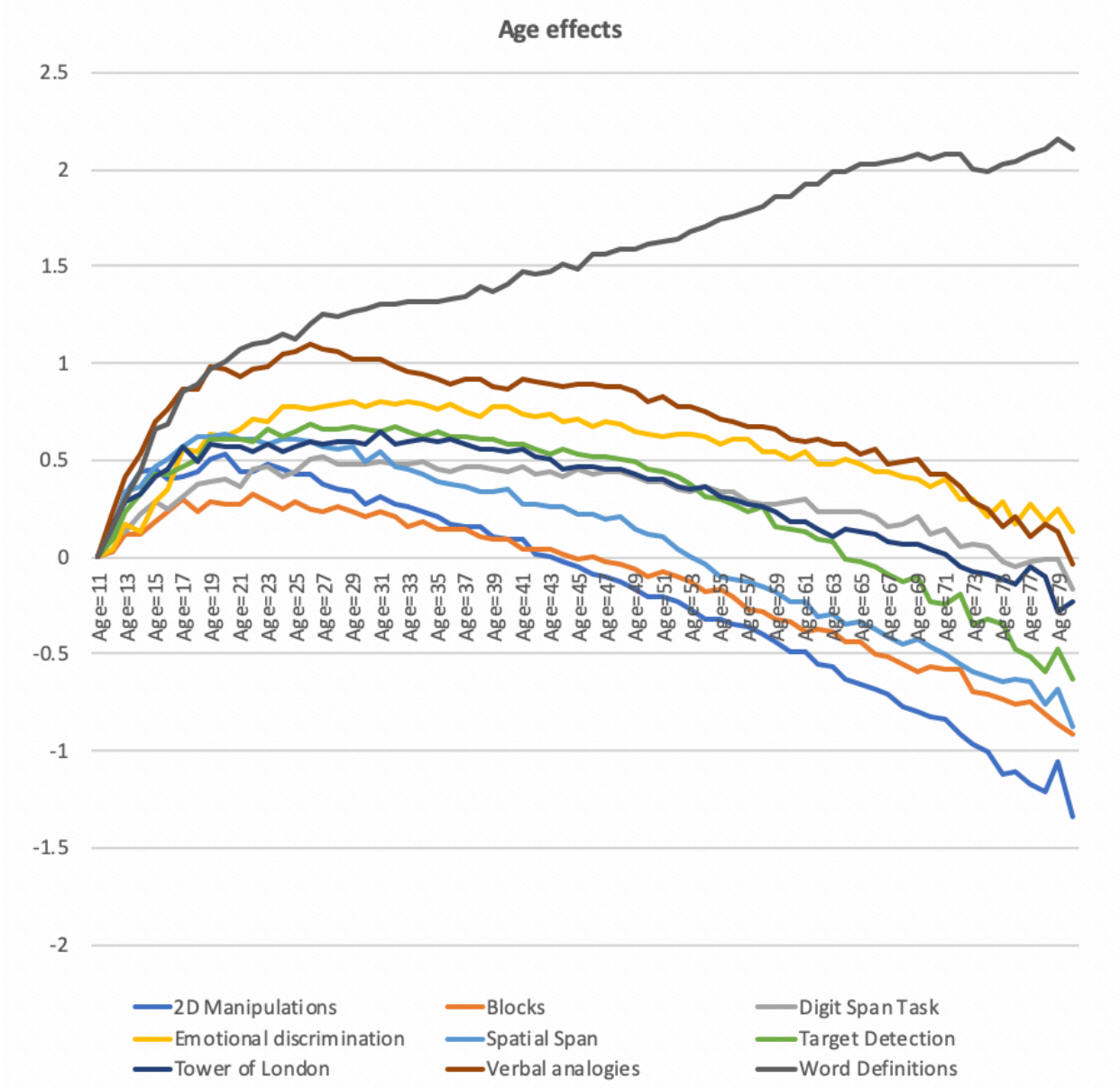
- Reported time of illness vs time of cognitive assessment in bio-confirmed cases
- Illness onset coincides with first wave peak
- Assessment offset mode ~2 months post illness





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

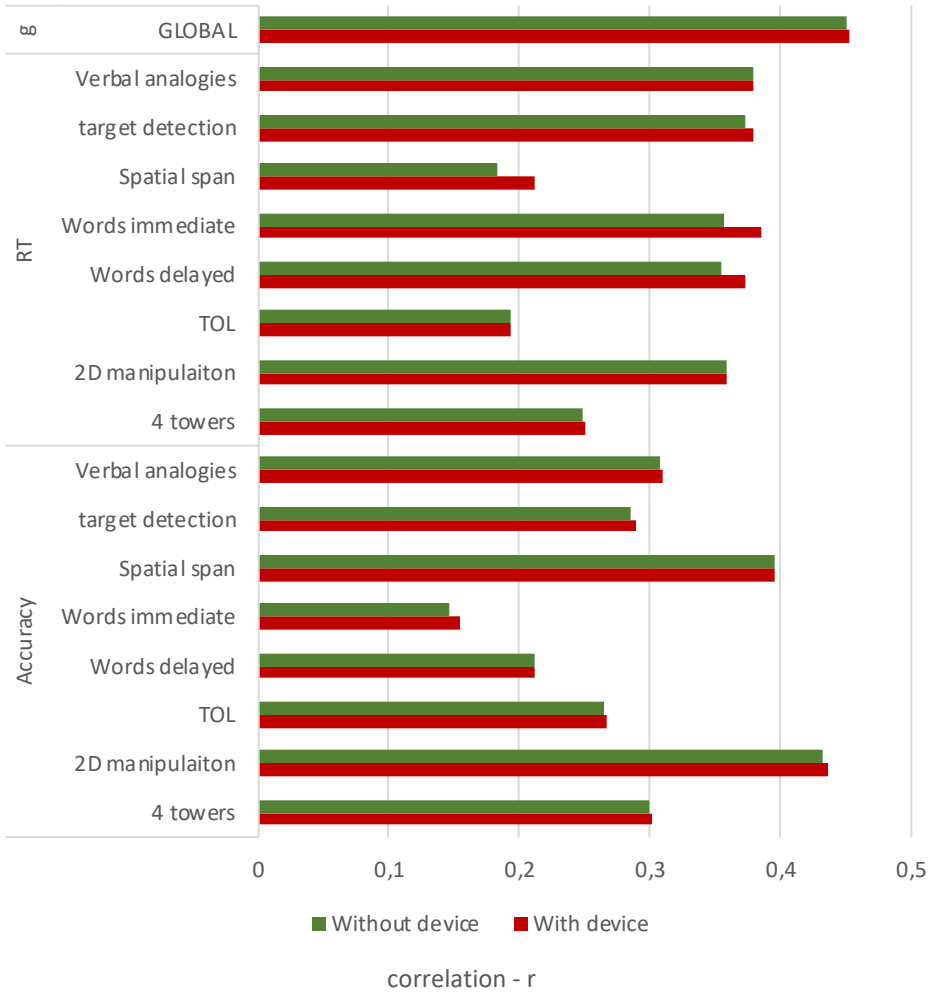
Population factor – cognitive score associations make interpretation of objective assessment results difficult

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~=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

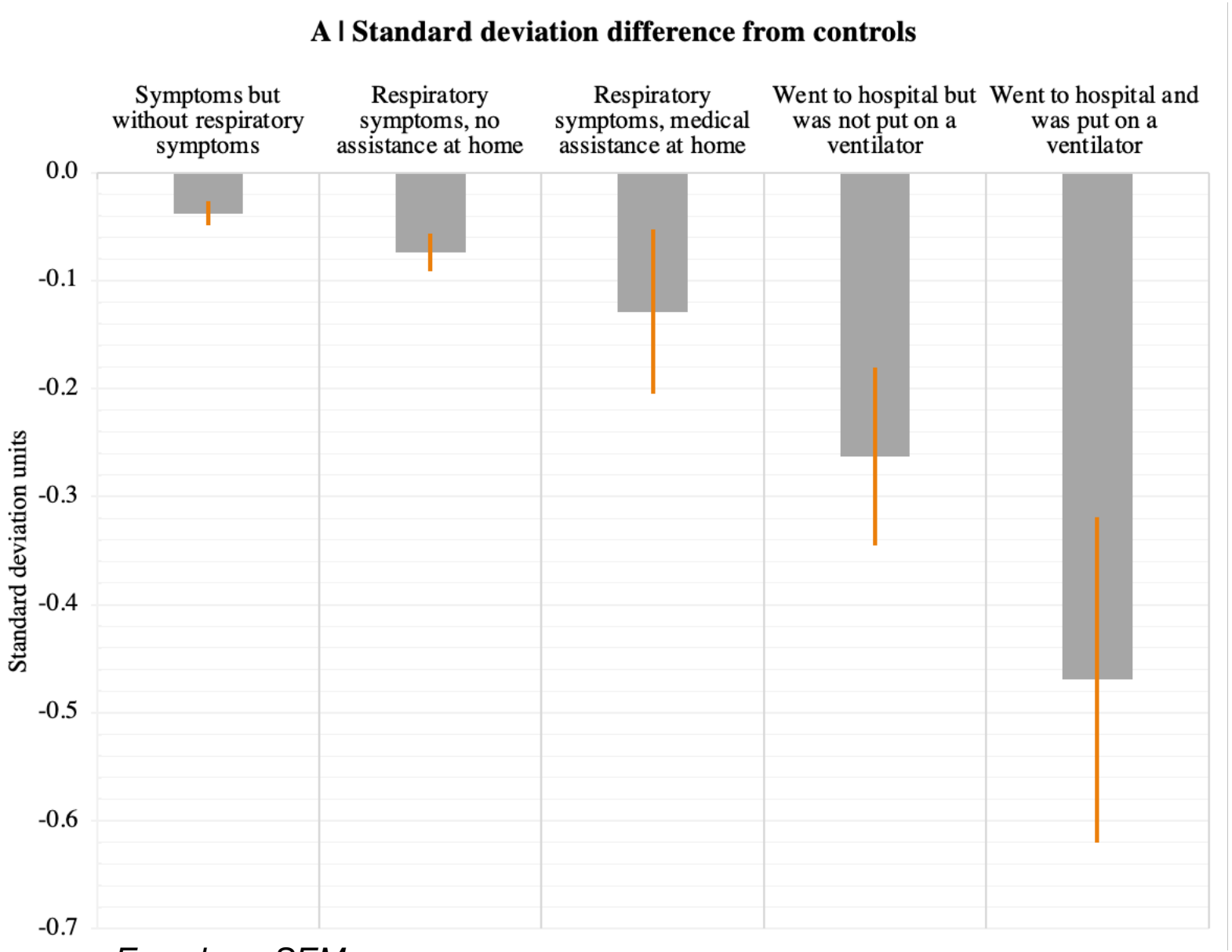


Covid-19 survivors – global cognitive deficits

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

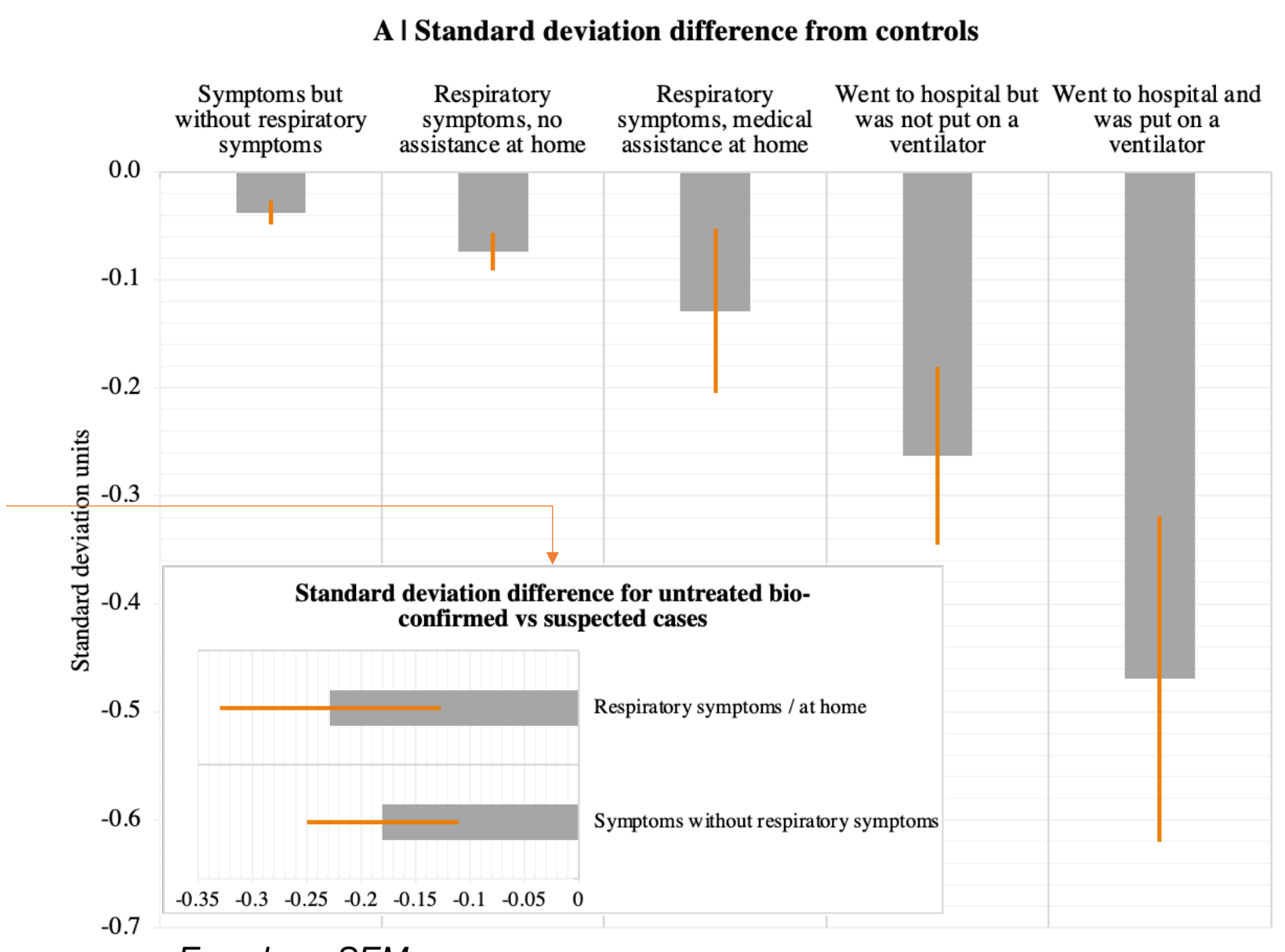


Error bars SEM

Hampshire et al., Lancet EClinicalMedicine 2021

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



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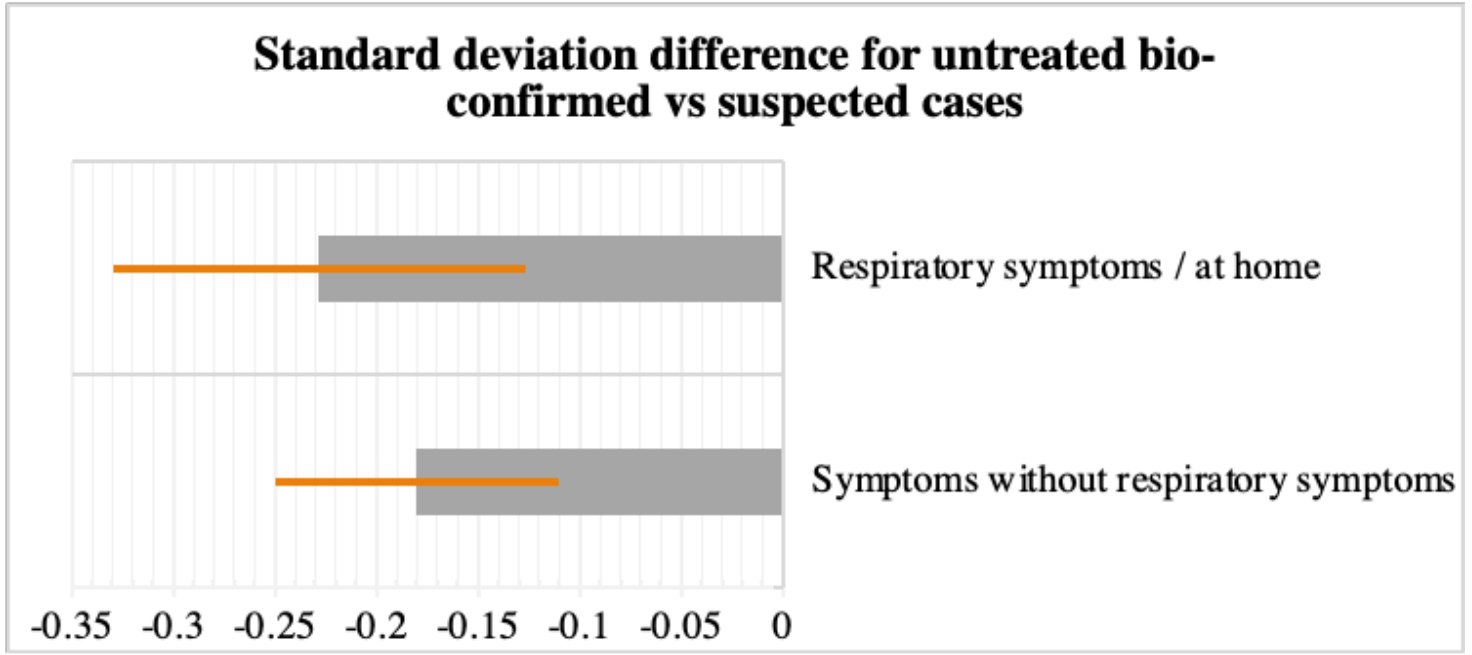
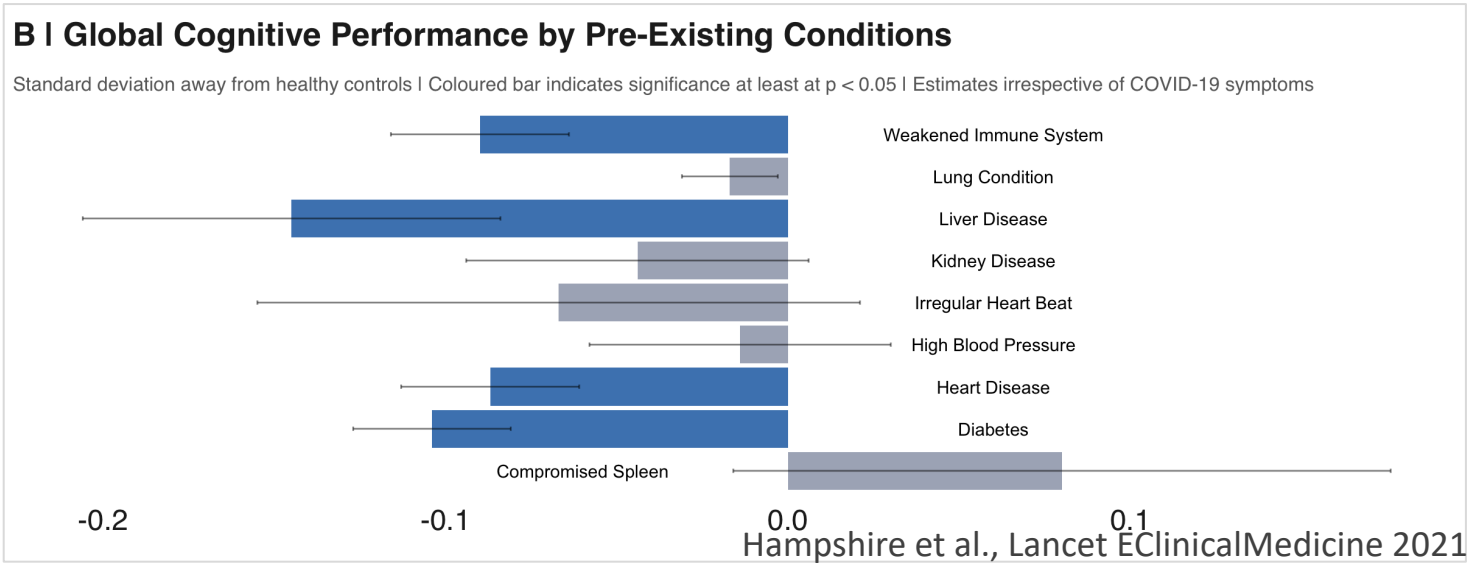
Covid-19 survivors – global cognitive deficits

- 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*





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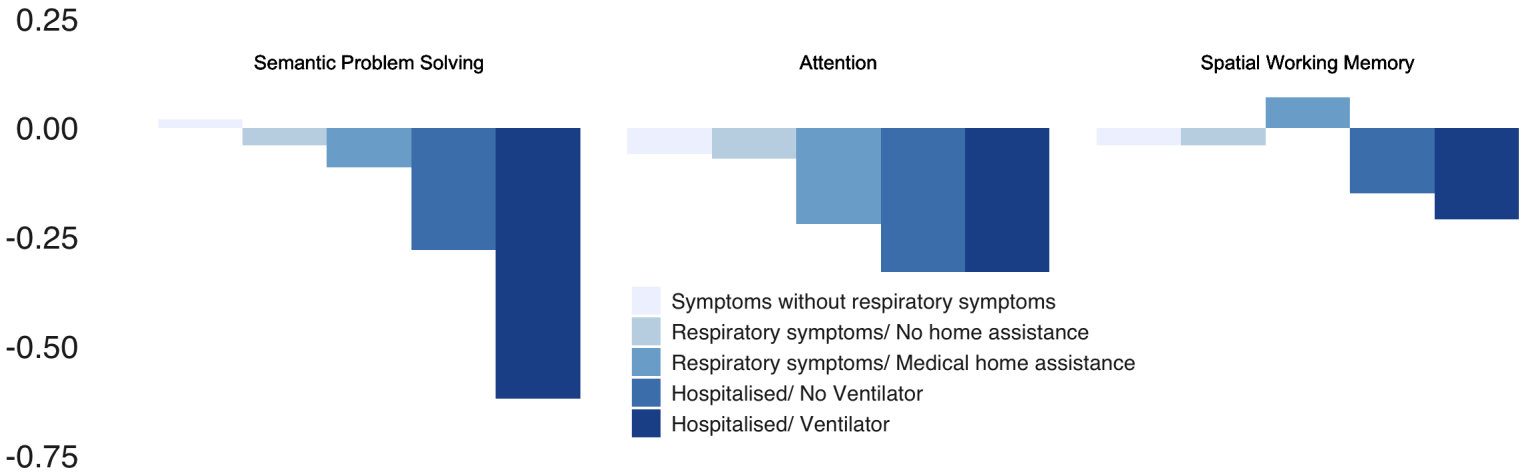
Covid-19 survivors – domain specificity of cognitive deficits

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

A I Principal Component Analysis Estimates

Estimates are standard deviations away from healthy controls



B I Individual Test Performance by Symptom Severity

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

	1	2	3	4	5
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 Discrimiation	0.04	-0.02	-0.07	-0.18	-0.01
Digit Span	0.01	-0.04	-0.02	0	0.32

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

Hampshire et al., Lancet EClinicalMedicine 2021

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