ROADMAP
Real world Outcomes across the AD spectrum for better care

EMIF

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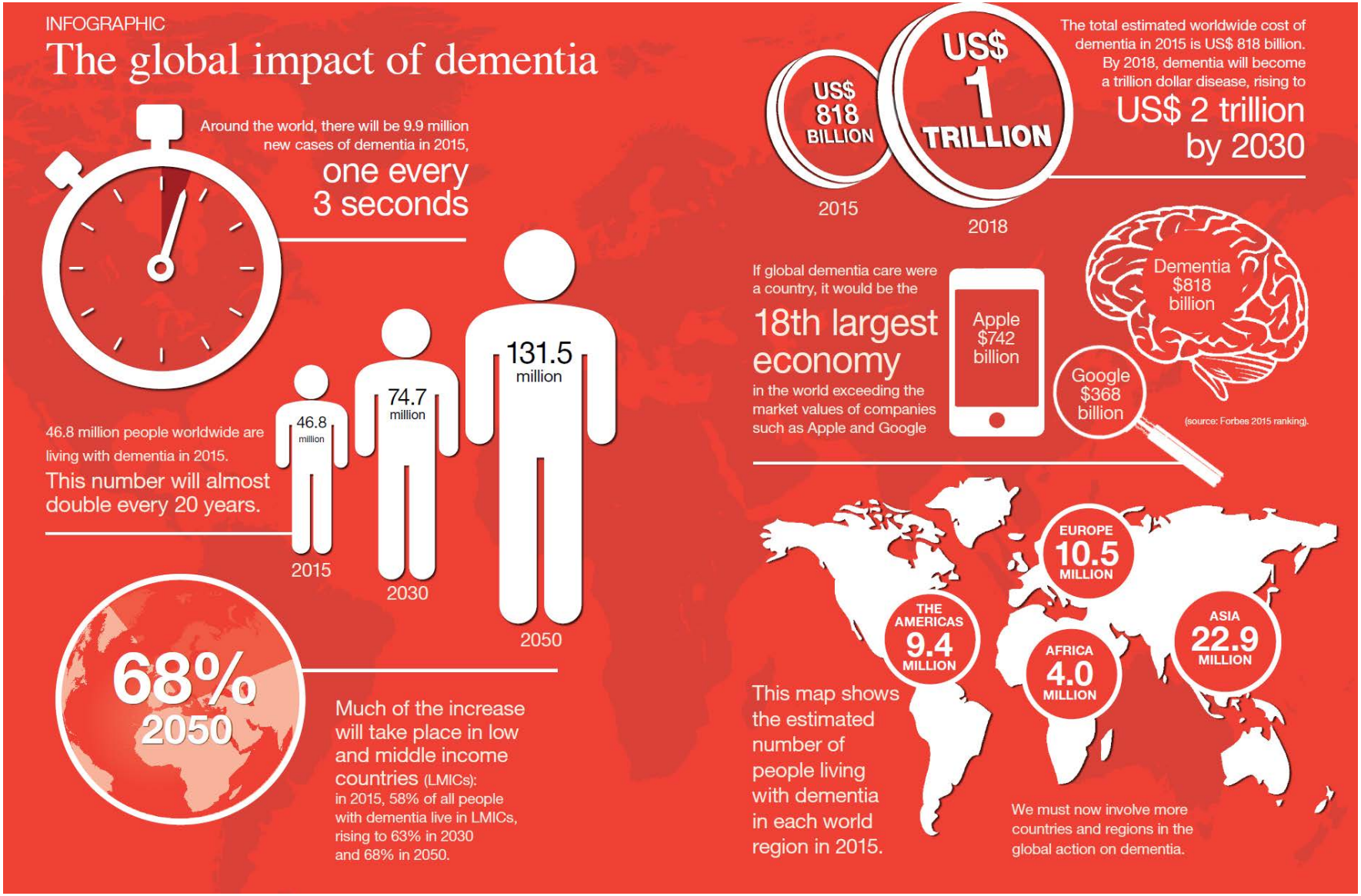
Dementia: Big Problem

Big data

Big solution?

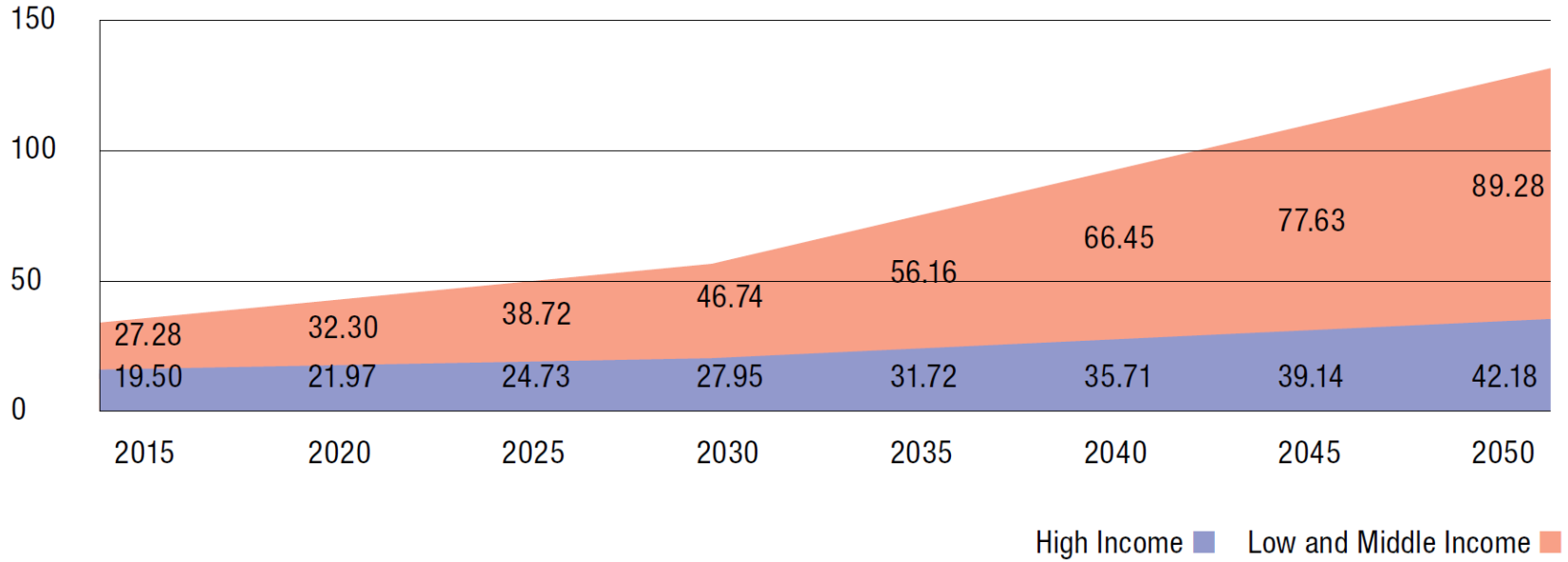
Big Problem


INFOGRAPHIC
The global impact of dementia
Around the world, there will be 9.9 million new cases of dementia in 2015,
one every 3 seconds
46.8 million people worldwide are living with dementia in 2015.
This number will almost double every 20 years.
46.8 million
74.7 million
131.5 million
2015
2030
2050
68% 2050
Much of the increase will take place in low and middle income countries (LMICs):
in 2015, 58% of all people with dementia live in LMICs, rising to 63% in 2030 and 68% in 2050.
US$ 818 BILLION
US$ 1 TRILLION
2015
2018
The total estimated worldwide cost of dementia in 2015 is US$ 818 billion. By 2018, dementia will become a trillion dollar disease, rising to
US$ 2 trillion by 2030
If global dementia care were a country, it would be the
18th largest economy
in the world exceeding the market values of companies such as Apple and Google
Apple $742 billion
Google $368 billion
Dementia $818 billion
(source: Forbes 2015 ranking).
EUROPE 10.5 MILLION
THE AMERICAS 9.4 MILLION
AFRICA 4.0 MILLION
ASIA 22.9 MILLION
This map shows the estimated number of people living with dementia in each world region in 2015.
We must now involve more countries and regions in the global action on dementia.

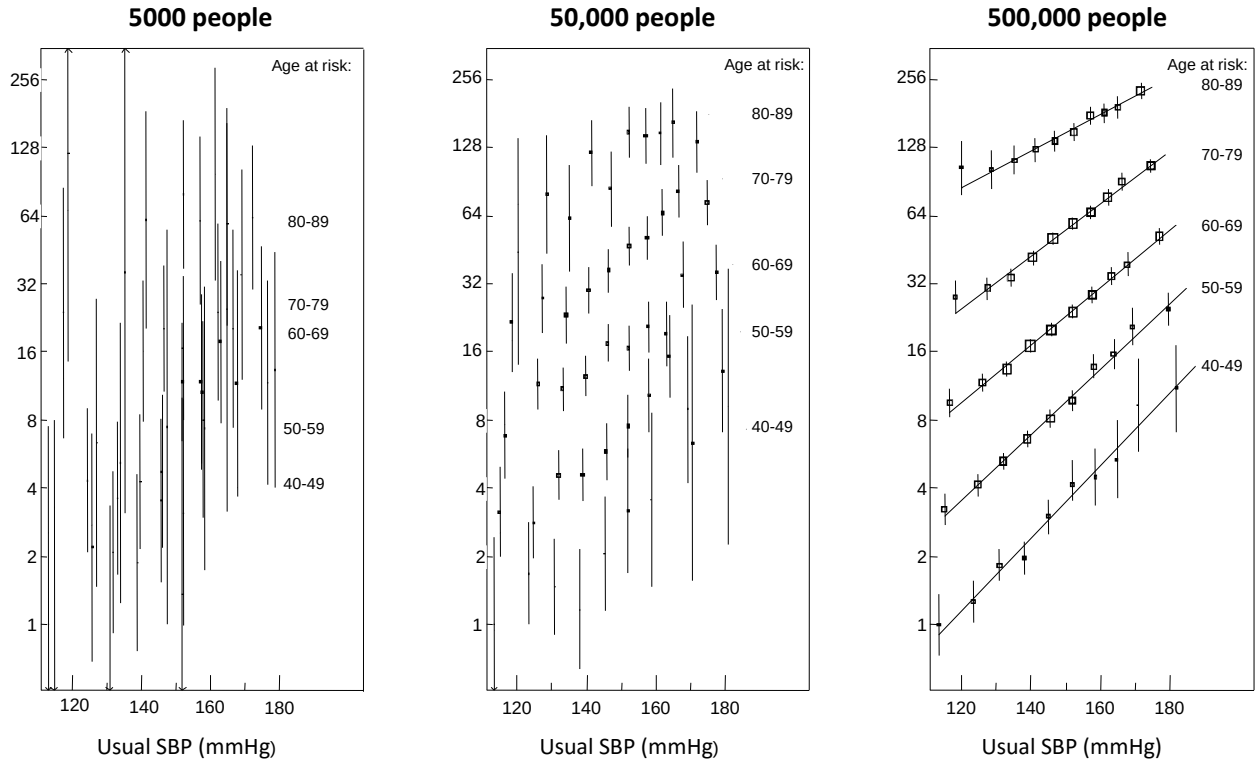
Big Problem

Figure 2.4

The growth in numbers of people with dementia (millions) in high income (HIC) and low and middle income countries (LMIC)



The precision medicine challenge



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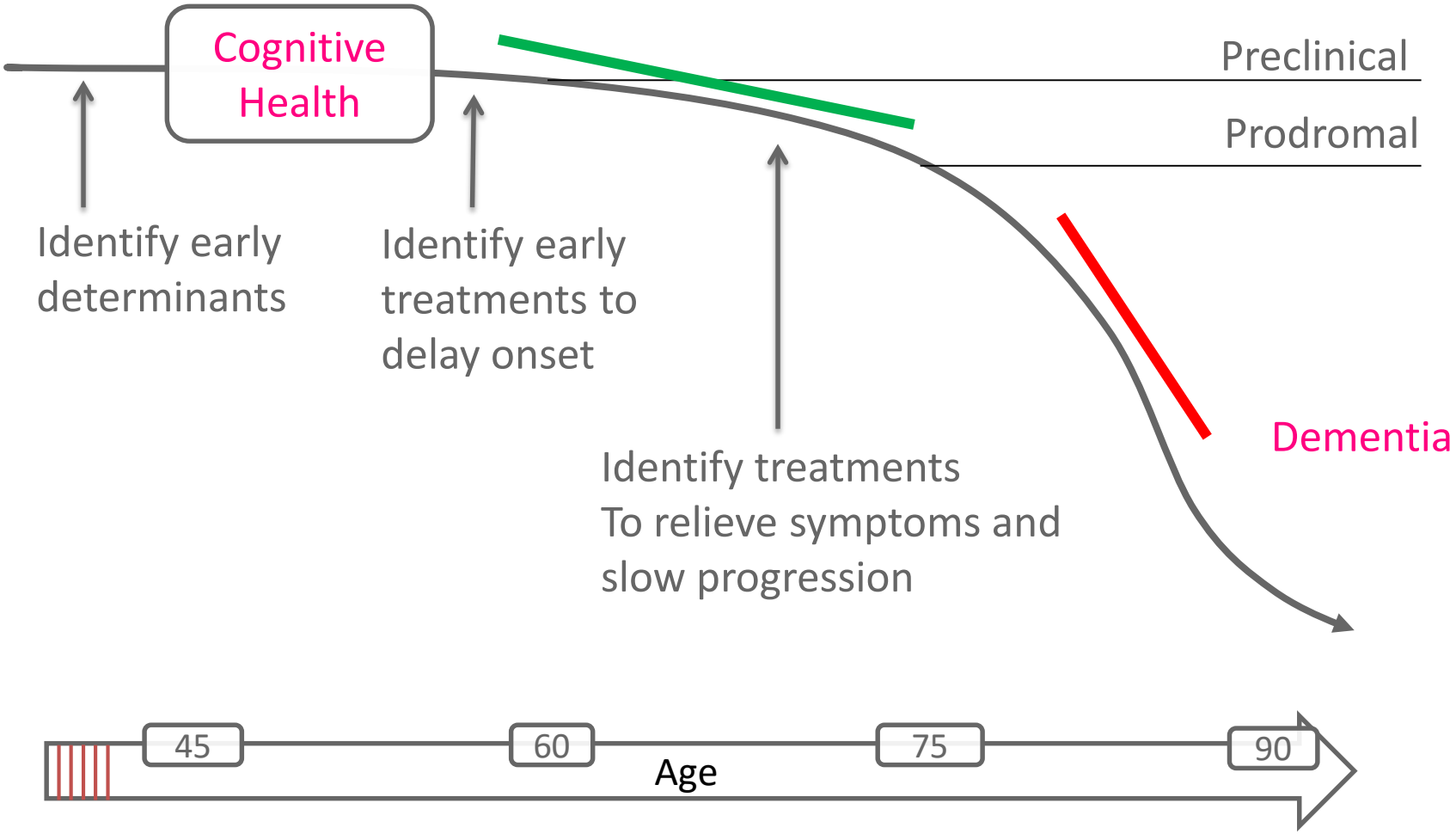
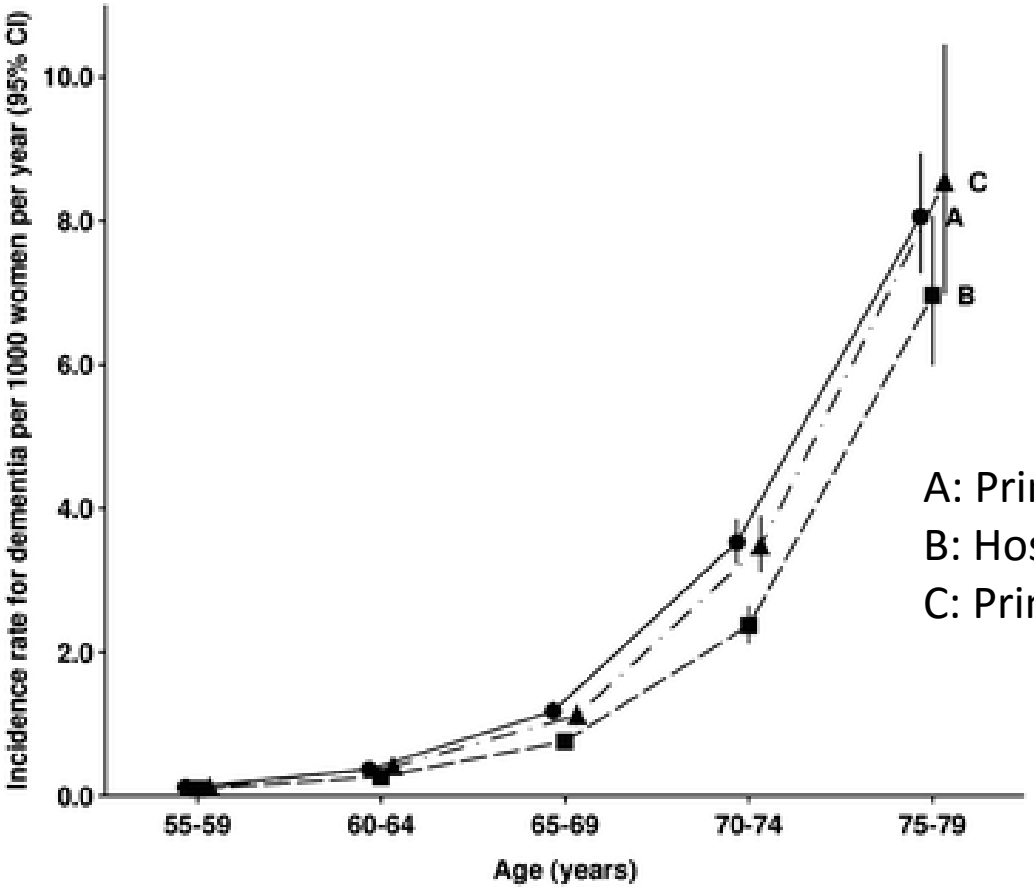
The experimental medicine challenge



Big Data: European EHR perspective

Country	Source (n)	Setting	Diagnosis	Cognition	Comorbidities	Medication	Care Quality	Imaging	Genetics	Health status	Lifestyle	Socio-econ
Denmark	Nat. patient registers (5.6M)	Hospital	✓		✓							
	50 linked clinical databases (5.6M)	Hospital	✓		✓							
France	Memento	Memory clinic	✓	✓	✓	✓		✓		✓		
Netherlands	IPCI (2M)	Primary care	✓		✓	✓				✓		
	Amsterdam Dementia cohort (4K)	Memory clinic	✓	✓		✓						
	Parelsnoer clinical cohort (1K)	Nat. memory clinic		✓	✓							
	ACTIFCare cohort (400)	Home living	✓	✓						✓	✓	✓
	Learn cohort (300)	Memory clinic	✓	✓	✓	✓		✓			✓	✓
Spain	SIDIAP (5.8M)	Primary care	✓		✓	✓				✓		✓
	ReDeGi register (6K)	Hospital	✓	✓	✓							
Sweden	LISA register (10M)	Insurance data										✓
	Nat. Patient registers (10M)	Hospital	✓									
	Social services register (10M)	Administrative										✓
	Tax Agency's register (10M)	Administrative										✓
	VEGA health care reg. (1.6M)	Regional reg.					✓					
	QRegPV (10M)	Primary care	✓									
	National health care regs. (10M)	Administrative			✓		✓					
	Military service register (7M)	Administrative								✓	✓	
	Gothenburg pop. studies (10K)	Population cohorts	✓	✓	✓	✓		✓	✓	✓	✓	✓
	Women's cohort (400)	Population cohort	✓	✓	✓	✓		✓	✓	✓	✓	✓
UK	CPRD (5M)	Primary care	✓		✓	✓				✓		
	SAIL (3M)	National linkage	✓		✓	✓						✓
	UK CRIS (3M)	Mental health	✓		✓	✓						
	HSCIC (56M)	Hospital	✓									
	SHIP (5.7M)	National linkage	✓		✓							✓
			✓	✓	✓	✓		✓	✓			✓

Age-specific incidence of dementia according to data source: The Million Women Study



A: Primary Care
B: Hospital Records
C: Primary Care and Hospital records

Danish National Patient Registry

22 years (1994 - 2016)
7.1 million patients

Hospital data

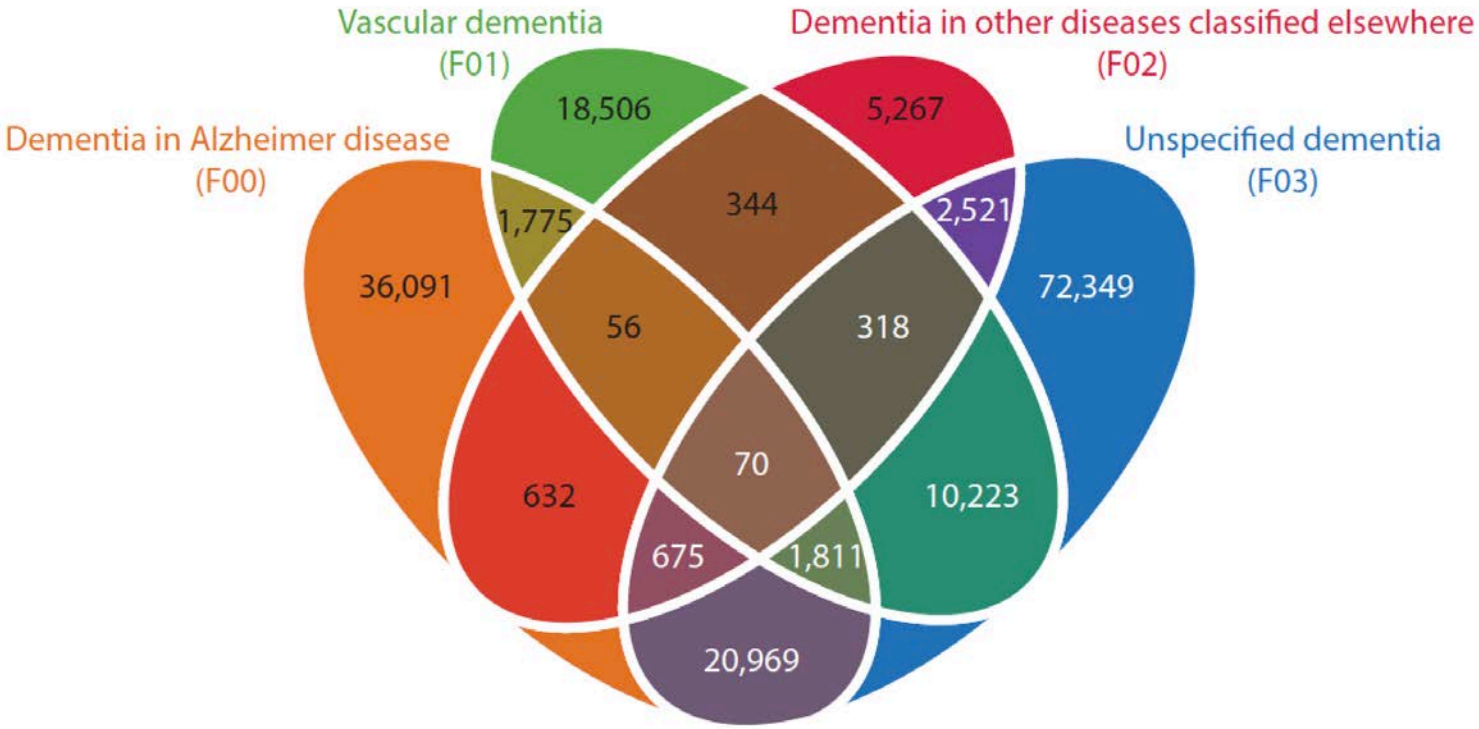
- Diagnoses (ICD-10)
- Date of diagnose
- Type of encounter
- Hospital ID
- Ward ID

Personal data

- Date of birth
- Gender
- Date of death
- Family

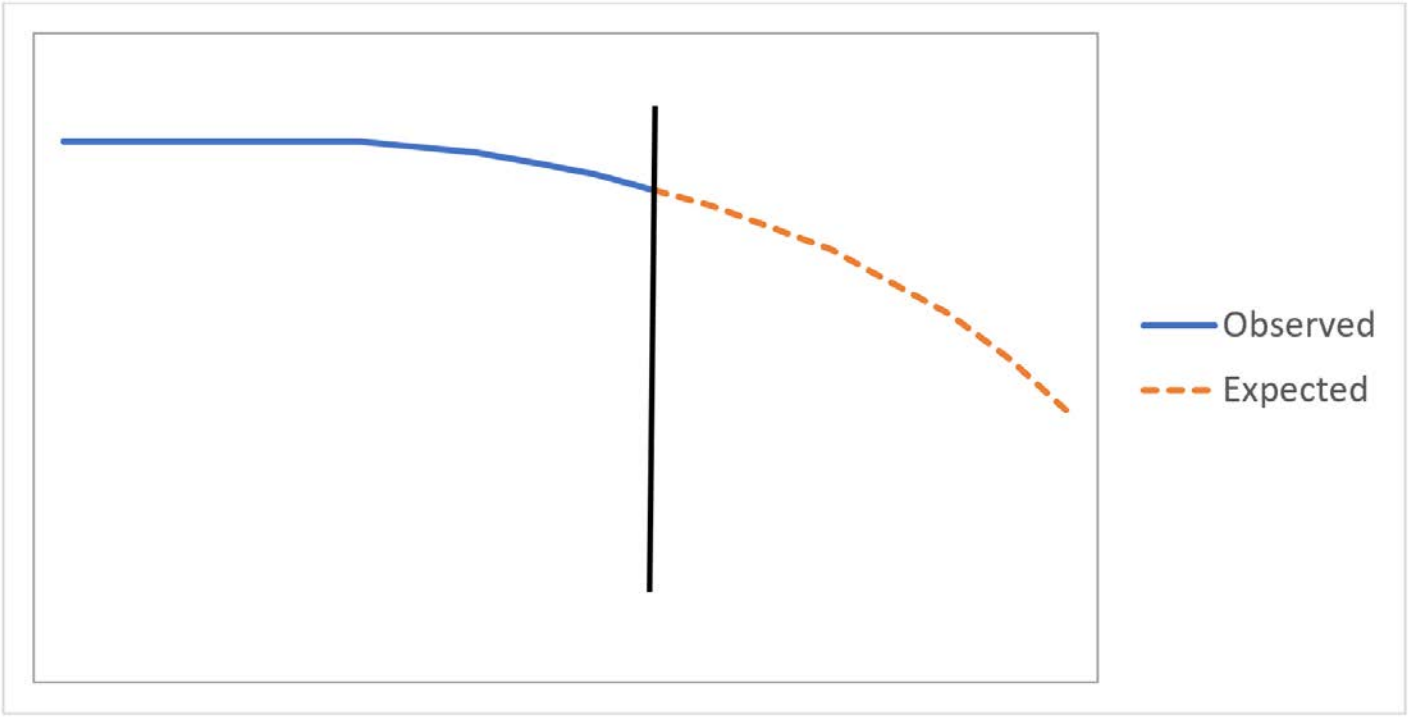
The Complexity / Diversity problem:

171,607 Dementia diagnoses



The Specificity Problem:

Limitations of disease agnostic approaches



Conclusion

Disease agnostic approaches deliver:

- Too much diversity / complexity
- Data access remains difficult
- (Sample access almost impossible)
- Increasing data security requirements
- Complicated governance
- Bespoke data models

YOU TOLD US
YOU MAKE DRILLS

YOU DON’T

YOU MAKE HOLES

Next generation cohorts (population and clincal)

Trends: Constrained funding environment
More targeted questions
Greater added value

Response: Cost-efficient technologies
Purposive designs
Consent for trials

For dementia: Dementia dedicated population and clinical cohorts
Sensitive to early detection & disease progression
Standard and efficient digital measures
- Cognition
- Function
- Mood
- Economic impact

Next generation cohorts

Purpose driven:

- Etiology vs. public health

Platform based:

- Integrated knowledge management
  - multi-modal data, standardisation, simplification
- Economies of scale
- Multiple studies from same informatics infrastructure

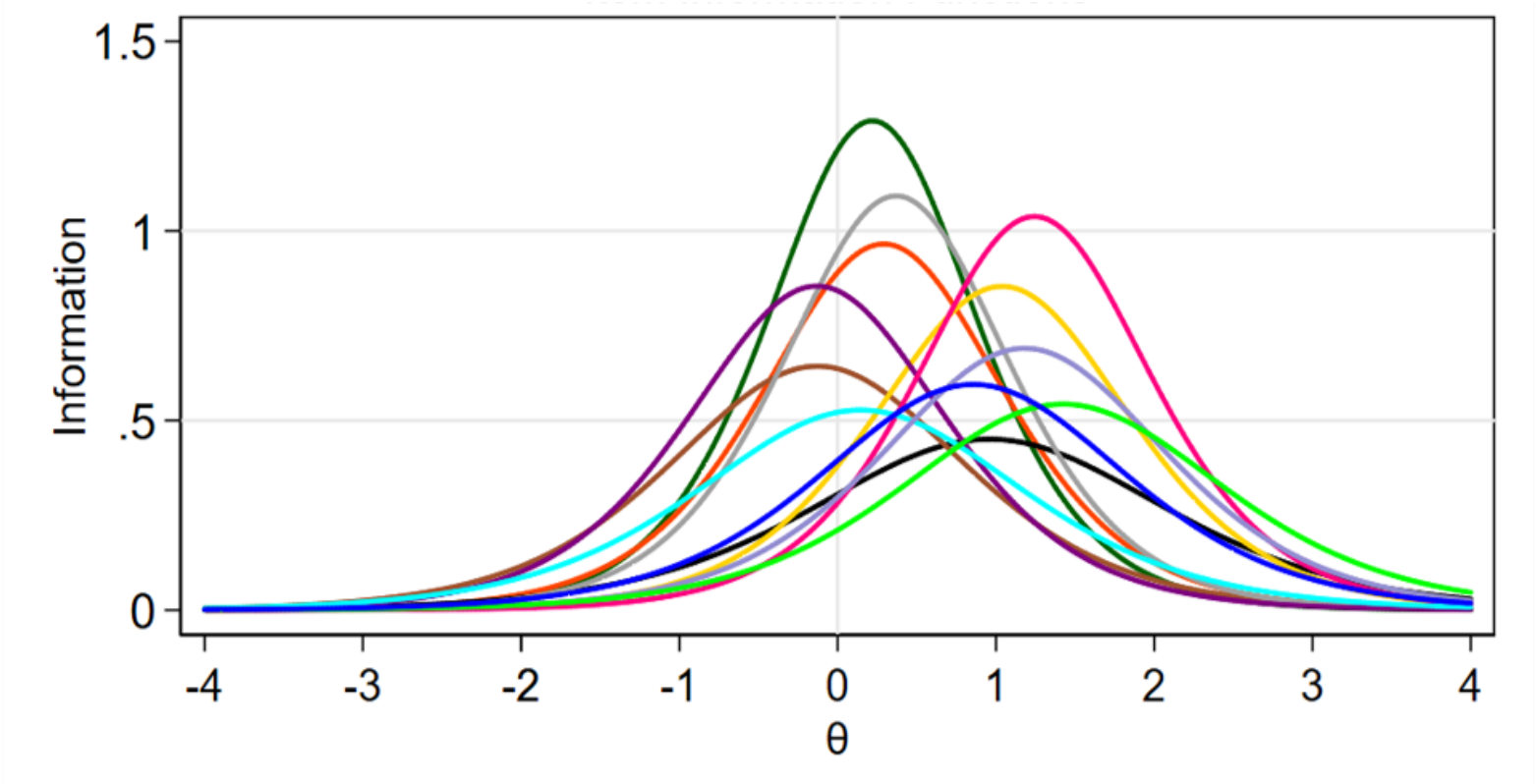
Technology led:

- Frequent, light touch digital phenotyping
- Psychometrically efficient measures
- Centralised linkage
- Dedicted biosample collection and management

Infrastructure embedded:

- Education, work, health care

Psychometric efficiency: Computer adaptive testing (EPQN –R)



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OPEN ACCESS Freely available online

PLOS | ONE

A Platform for the Remote Conduct of Gene-Environment Interaction Studies

John Gallacher[1]*, Rory Collins[2], Paul Elliott[3], Stephen Palmer[1], Paul Burton[4], Clive Mitchell[1], Gareth John[5], Ronan Lyons[6]

Age	50+ years
Invitations:	15,000 (est. 10,000 connected)
Respondents:	663 (4.5% of 15k, 6% of 10k))
Complaints:	7
Follow-up rate:	99.9% linkage

Nested biosampling trial

buccal same request	n=182	(136 samples received: 75%)
blood spot request	n=172	(19 samples received: 70%)

Population sample: Representative or heterogenious?

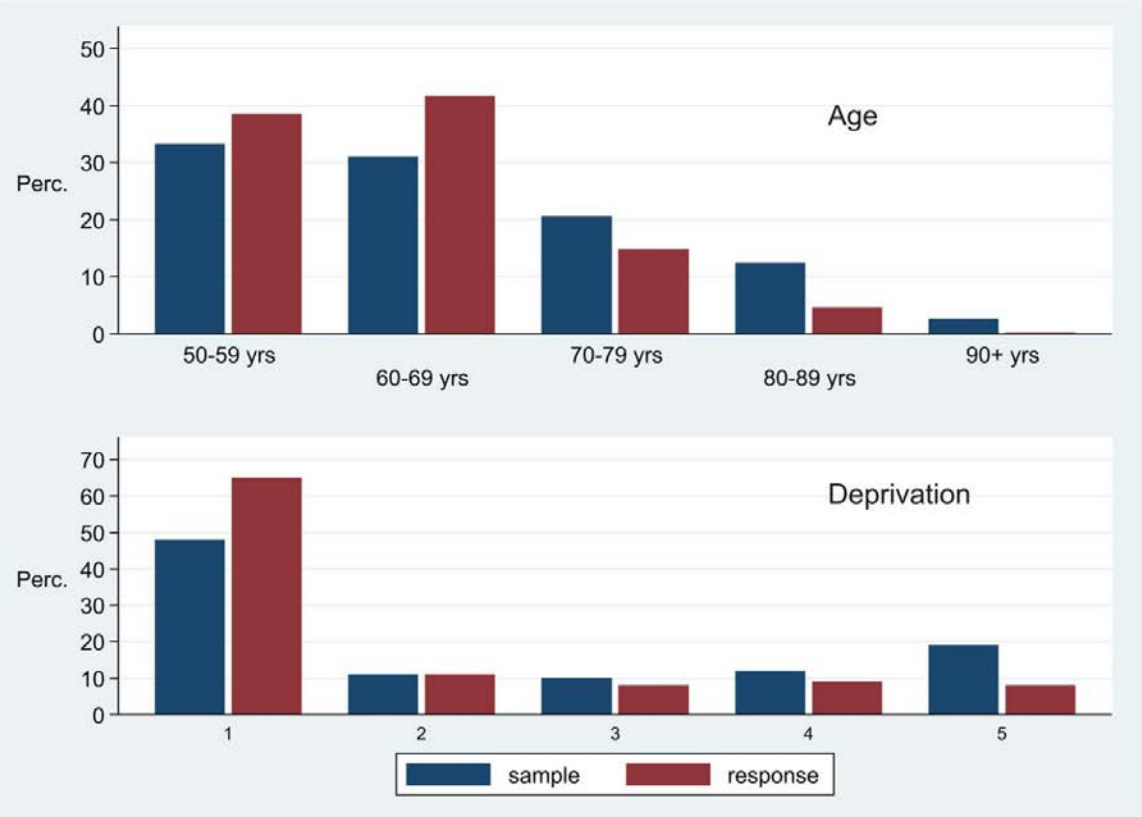

Figure 1. Distribution of age and deprivation according to invitation and response.
doi:10.1371/journal.pone.0054331.g001

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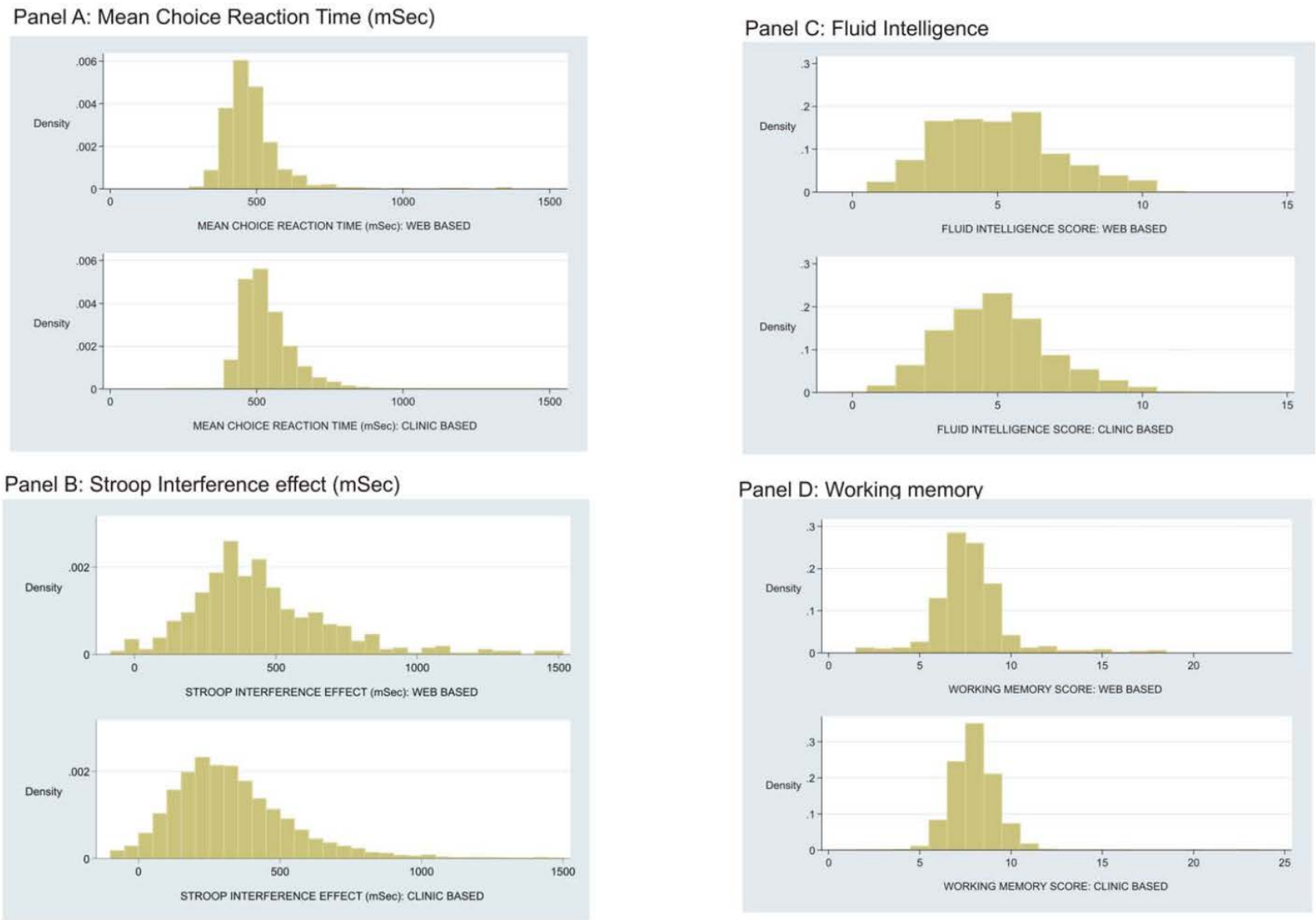


Figure 3. Distribution of cognitive performance according to web or clinic administration.
doi:10.1371/journal.pone.0054331.g003

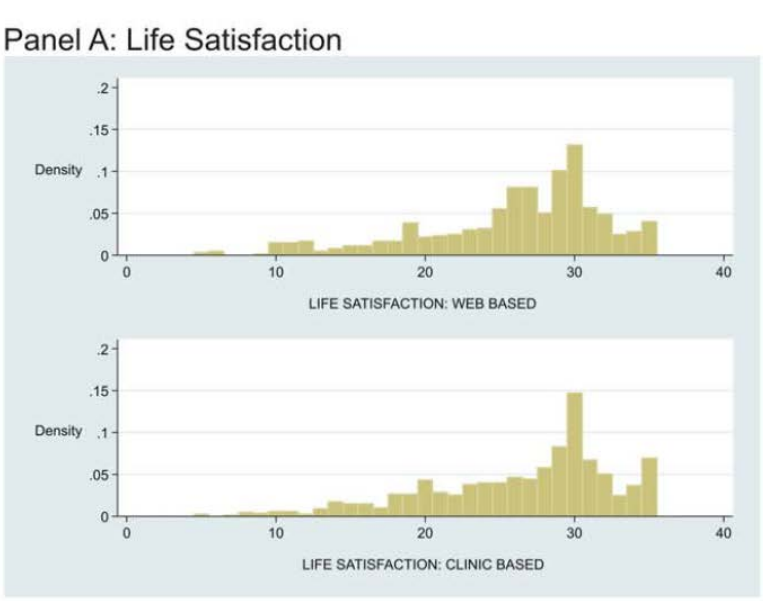
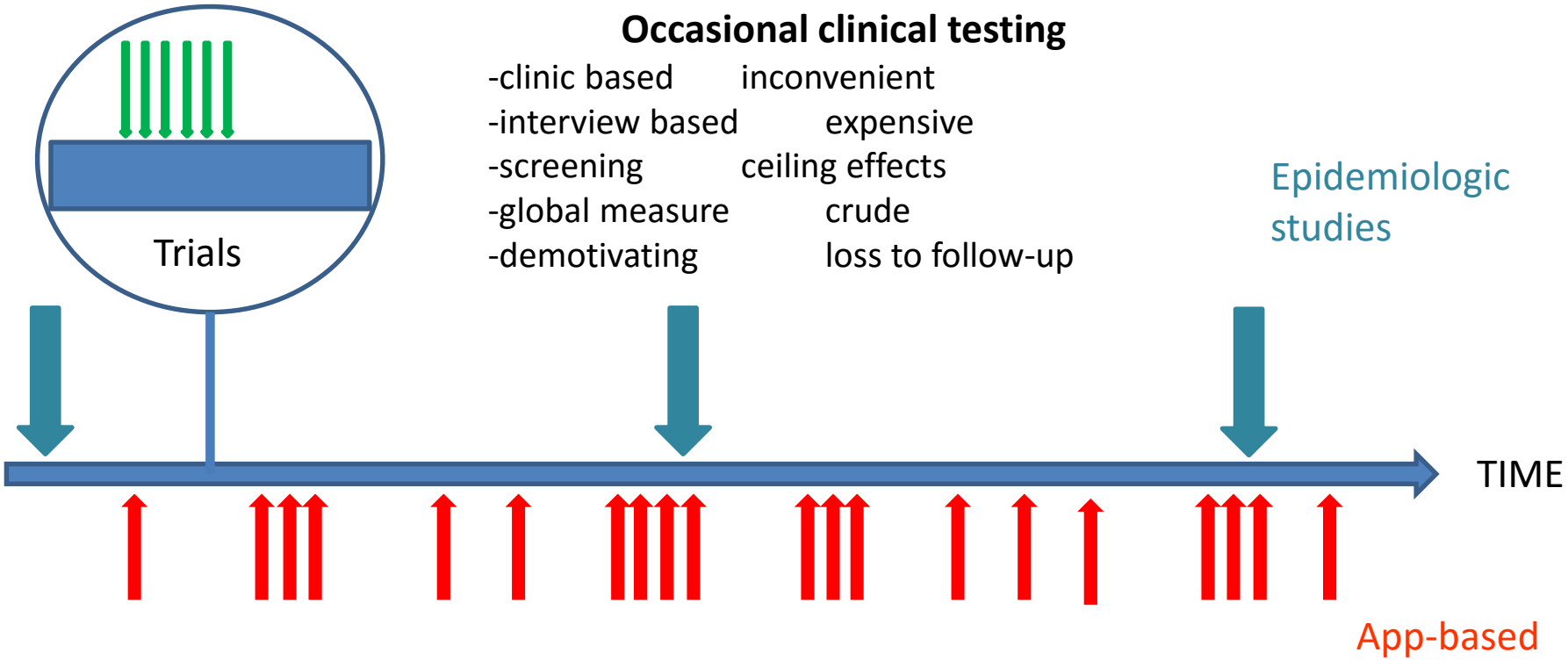


Figure 4. Distribution of well-being scores according to web or clinic administration.
doi:10.1371/journal.pone.0054331.g004

Near continuous cognitive testing



Occasional clinical testing

-clinic based — inconvenient
-interview based — expensive
-screening — ceiling effects
-global measure — crude
-demotivating — loss to follow-up

Epidemiologic studies

App-based

Near-continuous population based testing (regulatory approved)

-app based — whenever
-fully automated — inexpensive
-population assessment — full distribution
-domain focussed — pathology specific
-engaging — incentivised return

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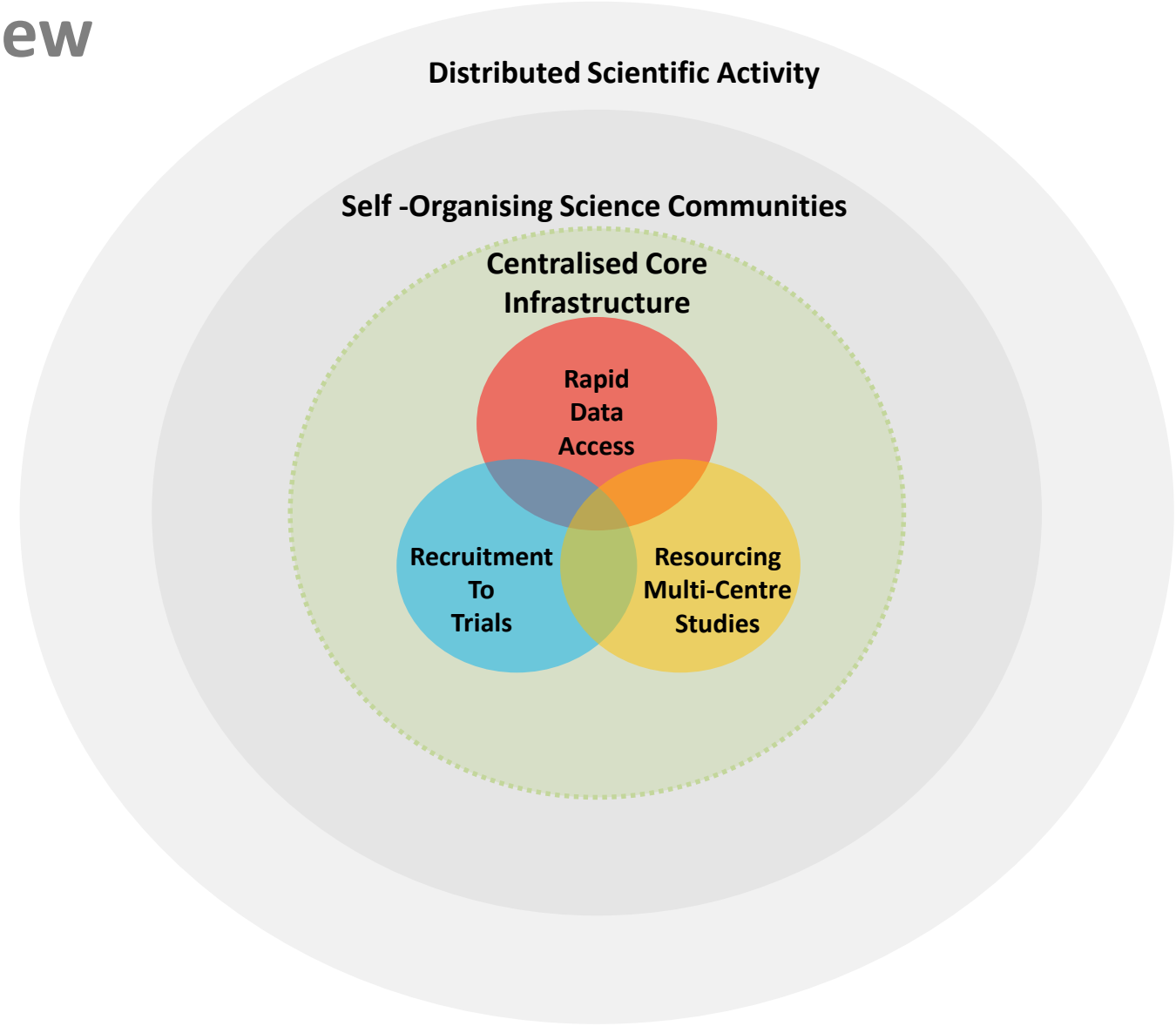
Integrating the research environment
to accelerate the discovery
of new drugs for dementia

Rapid data access

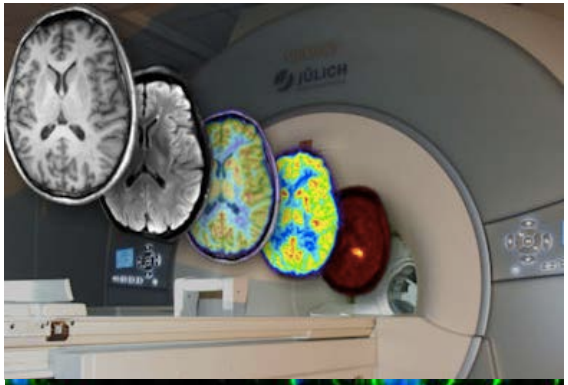
Recruitment to trials

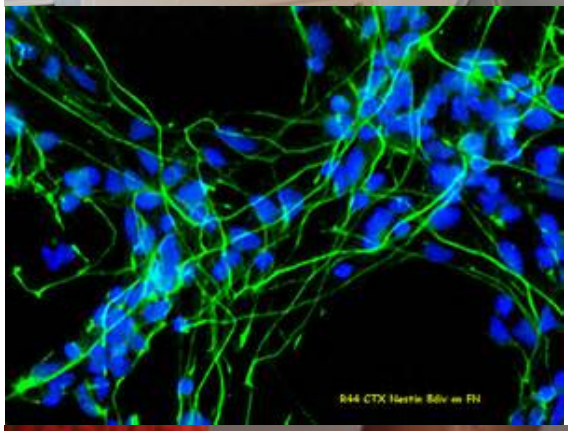
Resourcing multi-centres studies

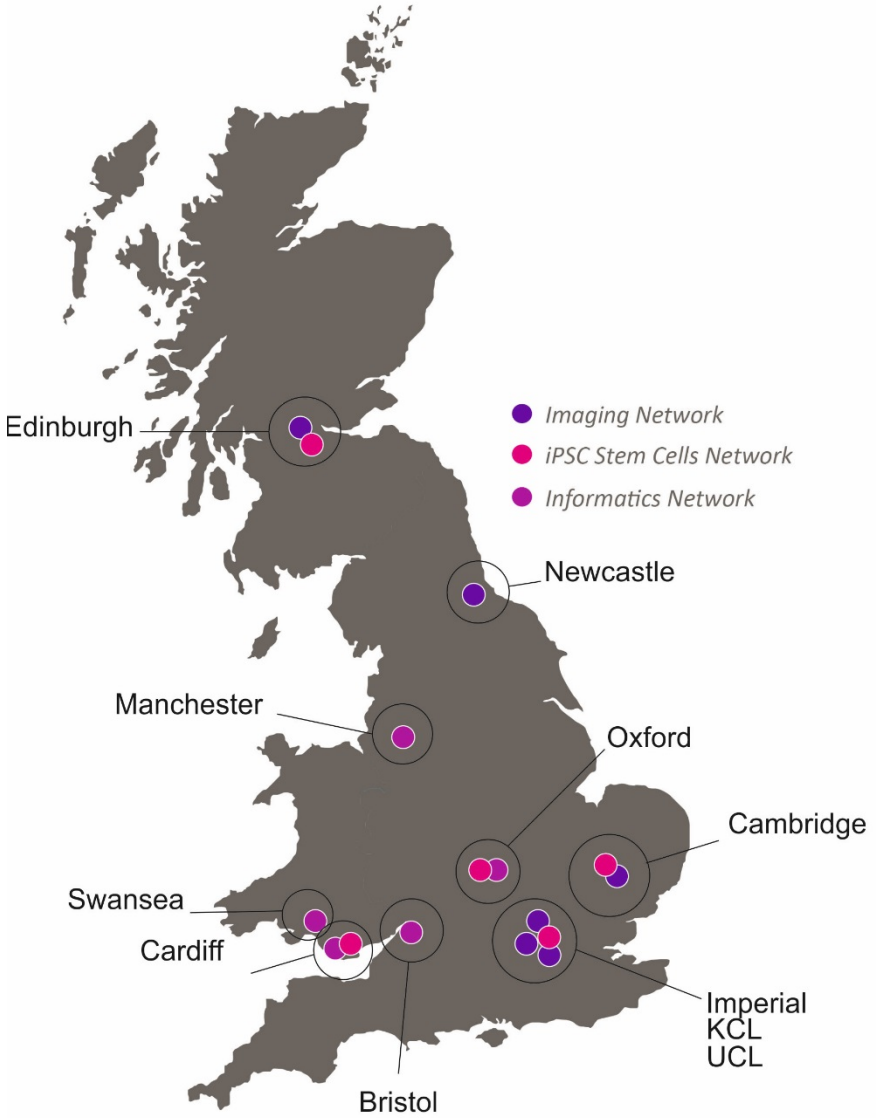
DPUK Overview



Technology Networks







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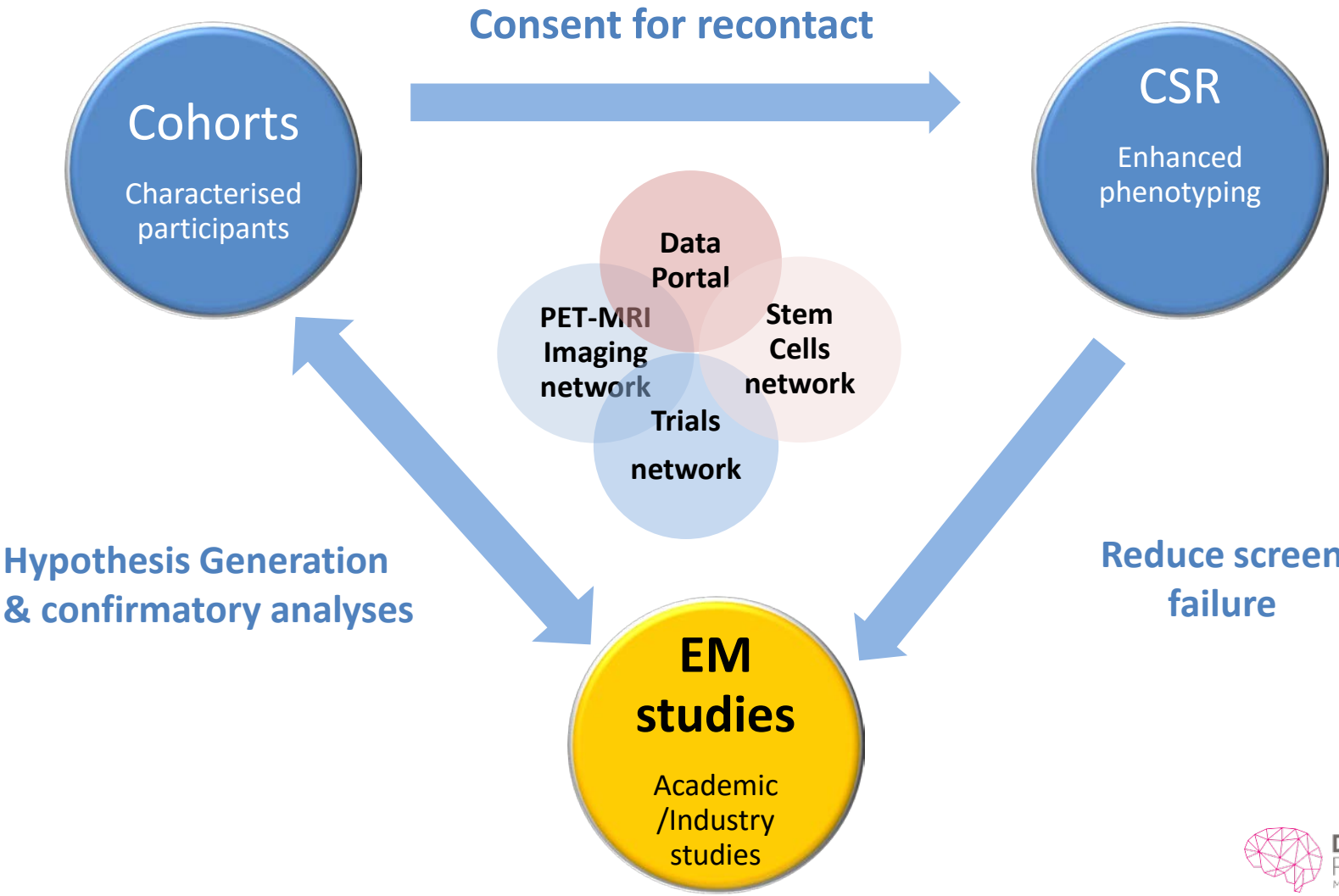
Integrating the environment



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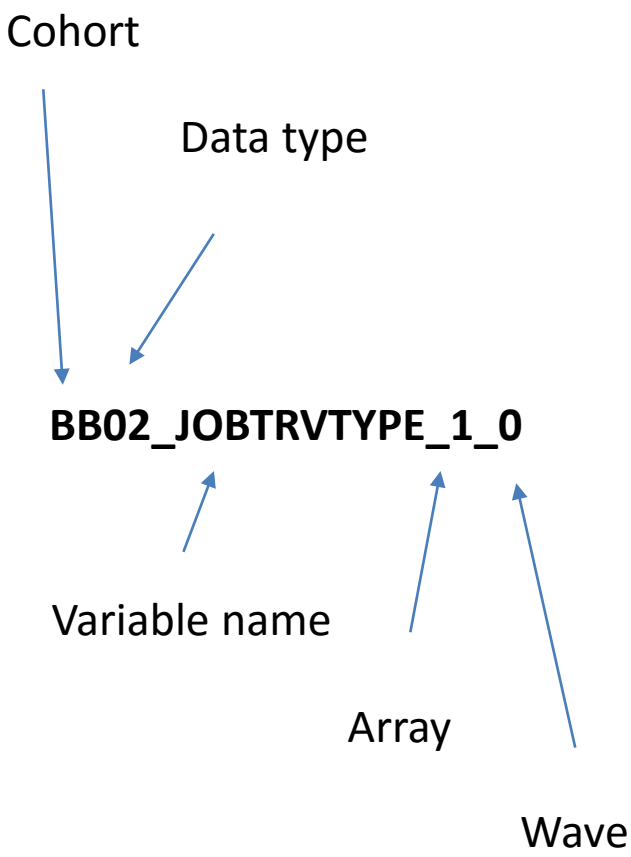
	Data status	Cohort	Institution	Access process	n	Total
1	Full data upload to portal	Airwave [10]	Imperial	Portal + Cohort	53,280	
2		BRACE [11]	Bristol	Portal	2,000	
3		Cam-CAN [12]	Cambridge	Portal + Cohort	3,000	
4		CamPaiGN [13]	Cambridge	Portal	142	
5		CaPS [14]	Bristol	Portal + Cohort	2,512	
6		CFAS I [15]	Cambridge	Portal	18,005	
7		CFAS II [16]	Cambridge	Portal	7,524	
8		Cygnus [17]	Manchester	Portal	200	
9		DFP pilot [18]	Oxford	Portal	15	
10		ELSA [19]	UCL	Portal	11,391	
11		EPINEF [20]	Yonsei (RoK)	Portal	2,008	
12		Generation Scotland [21]	Edinburgh	Portal	23,960	
13		GERAD LOAD [22]	Cardiff	Portal	10,454	
14		GERAD EOAD [23]	Cardiff	Portal	4,397	
15		ICICLE-PD [24]	Newcastle	Portal	318	
16		NIMROD [25]	Newcastle	Portal	276	
17		OPDC Discovery [26]	Oxford	Portal	1,589	
18		SMC Amyloid [27]	SMC Seoul (RoK)	Portal	120	
19		TRACK-HD [28]	UCL	Portal	366	
20		Whitehall II [29]	UCL	Portal + Cohort	10,308	151,865
21	Data upload per project	ALSPAC [30]	Bristol	Cohort	15,656	
22		BDR [31]	Bristol	Portal	3,200	
23		DIAN [32]	UCL	Portal + Cohort	437	
24		EPIC Norfolk [33]	Cambridge	Portal	25,639	
25		GENFI [34]	UCL	Portal + Cohort	515	
26		Healthwise Wales [35]	Cardiff	Portal + Cohort	6,000	
27		LBC1936 [36]	Edinburgh	Portal + Cohort	1,091	
28		Million Women [37]	Oxford	Cohort	1,300,000	
29		NSHD [38]	UCL	Portal + Cohort	5,362	
30		PICNICS [39]	Cambridge	Portal	290	
31		Protect [40]	Exeter	Cohort	14,000	
32		SABRE [41]	UCL	Portal + Cohort	4,858	
33		UK Biobank [42]	Oxford	Cohort	502,000	1,879,048
34	Meta-data only available	AMPLE [43]	Newcastle	Portal	80	
35		CHARIOT [44]	Imperial	Portal + Cohort	24,509	
36		CMERC [45]	Yonsei (RoK)	Portal	3,000	
37		Delphic [46]	UCL	Cohort	2,000	
38		EXTEND [47]	Exeter	Portal + Cohort	10,000	
39		HKU-NCDC [48]	Hong Kong University	Portal	500	
40		KOGES [49]	Yonsei (RoK)	Portal	200,000	
41		LEWY-PRO [50]	Newcastle	Portal	100	
42		Memento [51]	Bordeaux (Fra)	Portal + Cohort	2,323	
43		NAMGARM-2 [52]	Gyeongsang (RoK)	Portal	1,000	
44		NICOLA [53]	Queen's Belfast	Portal	8,500	
45		PaMIR [54]	Nottingham	Cohort	400	
46		PREVENT [55]	Edinburgh	Portal + Cohort	750	
47		PRIME [56]	Queen's Belfast	Portal	2,745	255,907



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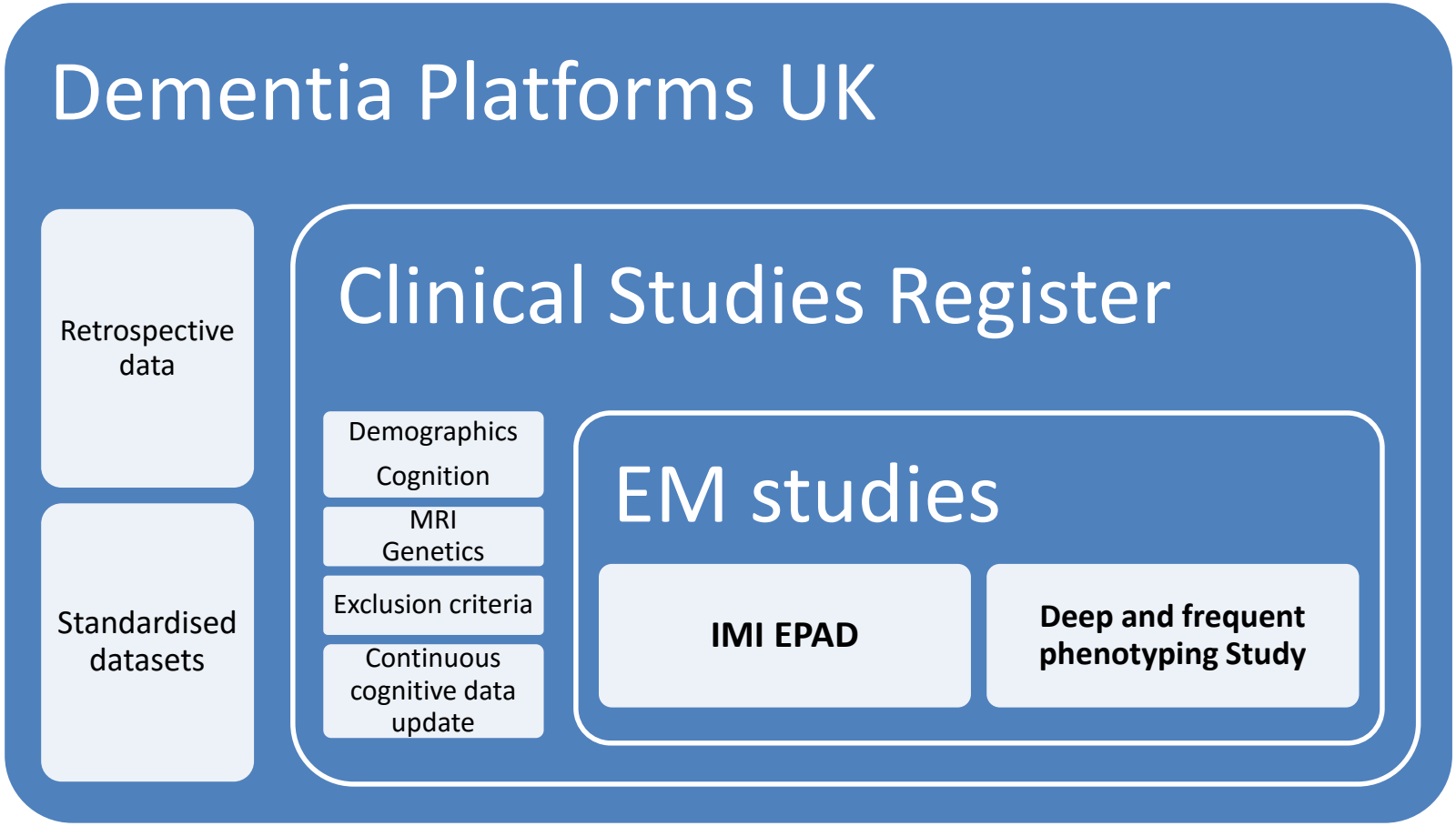
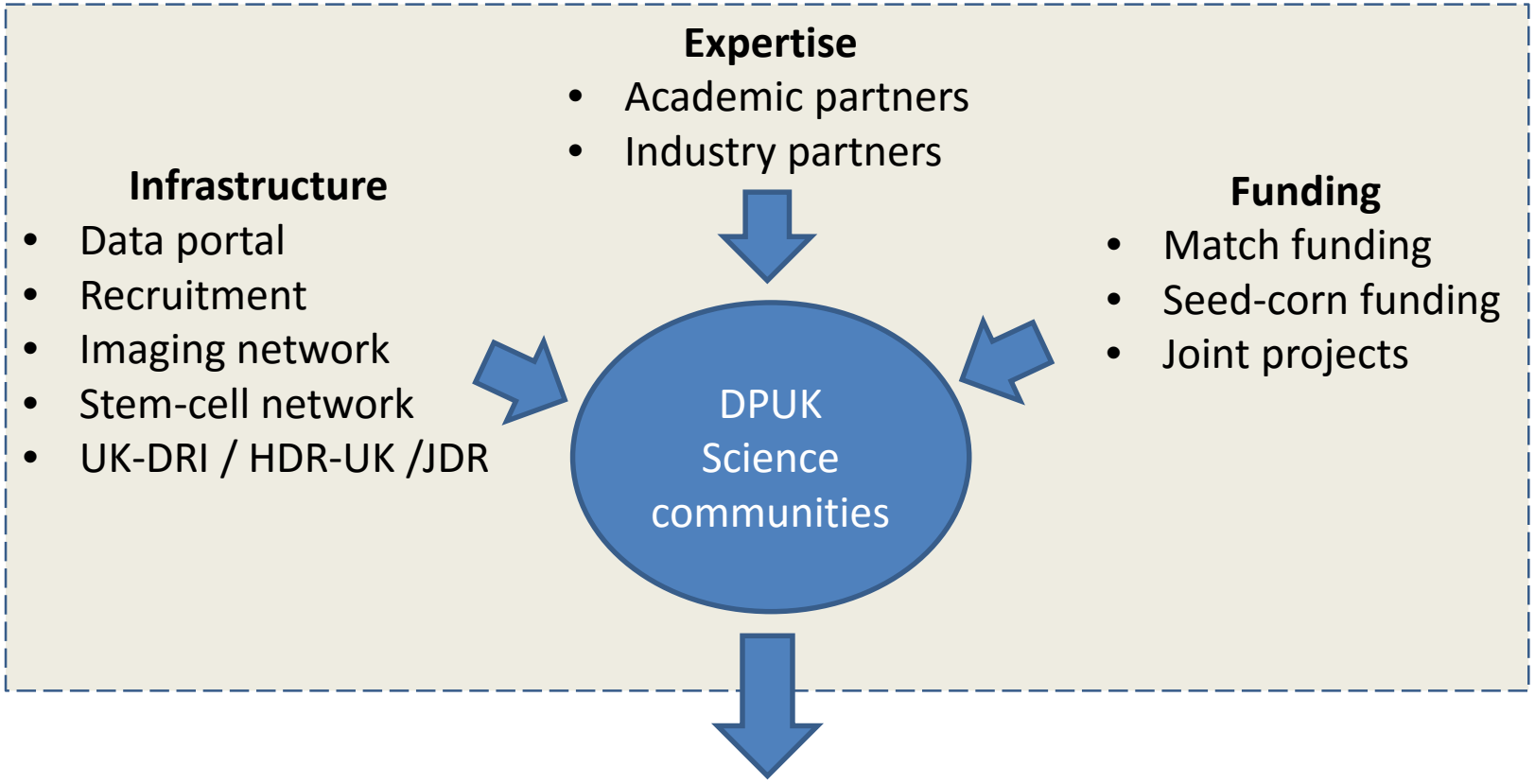
Clinical Studies Register Structure



By end of the DPUK1 project - expect to have enlisted 3 cohorts, recruited 2,000-5,000 volunteers, and have started recruiting from the register for EM studies.

Multicentre experimental studies: EM Incubator

Pre-competitive knowledge brokerage



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Swansea University

Prifysgol Abertawe

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UCL

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