

DEVISING A PERSONALIZED RISK STRATIFICATION AND HOLISTIC MANAGEMENT FOR PREVENTION OF COGNITIVE IMPAIRMENT IN PATIENTS WITH DIFFERENT CARDIOVASCULAR PHENOTYPES: THE DORIAN GRAY PROJECT



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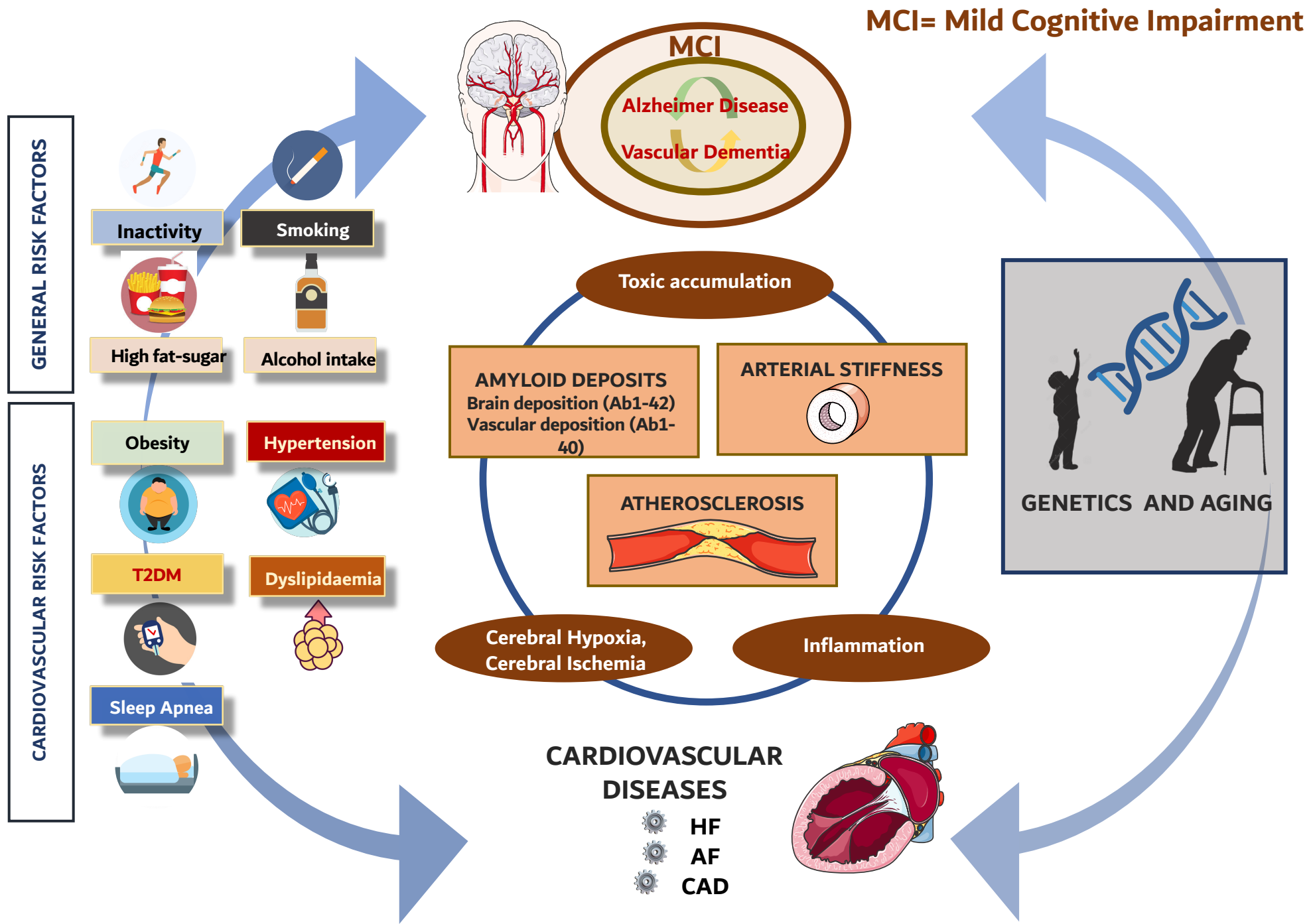
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 Regione
Lombardia
ASST Spedali Civili



Study	Sample size of HF patients (N)	Mean age	Prevalence of cognitive impairment	Cognitive impairment definition
Ahluwalia, 2012 (USA)	18 332	81 (75–86)	21.3%	CCW
Brunén, 2021 (ES)	3845	79 ± 9	16%	SPMSQ
Biagi, 2014 (IT)	1444	79 ± 9	35%	Pfeiffer test
Chitnis, 2015 (USA)	8062	74 ± 9	14.1%	ICD-9
Cancian, 2013 (IT)	1905	78 (65–80)	15.7%	GP data sheet
Carter, 2016 (UK)	31 760	74 ± 14	6.8%	ICD-10
Fujiki, 2022 (JPN)	1852	76 ± 8	6.9%	Previous medical reports
Yaku, 2018 (JPN)	3555	80 (70–90)	16.8%	Physician records
Lafo, 2022 (USA)	21 655	77 ± 10	36%	ICD-9
Lee, 2019 (International)	1846	61 ± 11	13.6%	≥2 MMSE points drop
Frey, 2018 (GER)	148	65 ± 10	41%	Test Battery of Attentional Performance
Sterling, 2019 (USA)	436	70 ± 9	14.9%	SIS
Sun, 2017 (CAN)	90 707	73 ± 13	3.2%	ICD-10

Abbreviations: CCW, Chronic Condition Warehouse; GP, general practitioner; ICD, International Classification of Disease; MMSE, Mini-Mental State-Examination; SIS, Six-Item Screener; SPMSQ, Short Portable Mental Status Questionnaire.

Study	Sample size (N)	HF prevalence	Mean age	Cumulative incidence (%) / hazard ratio of cognitive impairment in HF patients (follow-up duration)	Cognitive impairment definition
Aldeborg, 2017 (DK)	1 946 497	16.7%	77 (69–84)	1.21 (95% CI 1.18–1.24) (6 years)	ICD
Bressler, 2017 (USA)	9895	12.4%	59 ± 6	1.43 (95% CI 1.24–1.66)	DSST
				1.43 (95% CI 1.24–1.66)	DWRT
				1.12 (95% CI 0.98–1.28) (6 years)	WFT
Cacciatore, 1998 (IT)	1075	8%	75 ± 7	1.96 (95% CI 1.07–3.58)	MMSE
de Bruijn, 2015 (NL)	7003	3%	69 ± 9	0.87 (95% CI 0.59–1.28) (8 years)	DSM-III
Hammond, 2018 (USA)	4864	10.2%	76 ± 6	1.70 (95% CI 1.2–2.2) (5 years)	MMSE; DSST
Haring, 2013 (US)	6455	1%	73 (60–84)	1.49 (95% CI 0.73–3.04) (8.4 years)	MMSE, neurocognitive and neuropsychiatric objective exam
Legdeur, 2019 (NL)	442 428	6.8%	87 (65–115)	1.26 (95% CI 1.06–1.49) (3.6 years)	GP records
Noale, 2013 (IT)	2501	5%	71 ± 5	1.40 (95% CI 0.5724–3.4532) (7.8 years)	MMSE; ICD-10; DSM III-R
					NINCDS-ADRDA; CAMDEX;
					Pfeiffer test;
					neurological examination
Qiu, 2006 (SW)	1301	15%	83 ± 5	1.70 (95% CI 1.24–2.34) (5 years)	MMSE
Peters, 2009 (UK)	3336	0.4%	>80	0.55 (95% CI 0.08–3.91) (1.8 years)	MMSE <24 or drop ≥3 point
					DSM-IV; CERAD
Rusanen, 2014 (FI)	1510	6%	50 ± 6	1.40 (95% CI 1.01–1.93) (25 years)	DSM-IV; NINCDS-ADRDA
				0.87 (95% CI 0.35–2.16) (8 years)	
Wändell, 2018 (SW)	537 513	39%	77 ± 9	0.79 (95% CI 0.76–0.84) (4 years)	ICD-10
Witt, 2018 (USA)	6495	14.7%	76 ± 5	1.60 (95% CI 1.13–2.25) (15 years)	CDR; WMS-III, WAIS-R; DSB, BNT, MMSE

HORIZON-HLTH-2024-STAYHLTH-01-05-two-stage: Personalised prevention of non-communicable diseases - addressing areas of unmet needs using multiple data sources

Specific conditions

Expected EU contribution per project

The Commission estimates that an EU contribution of between EUR 8.00 and 12.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.

Indicative budget

The total indicative budget for the topic is EUR 50.00 million.



Horizon Europe Health

Open for applications:
four new topics tackling diseases



#HaDEA #HorizonEU



**European
Commission**

 19 Sep 2023 (First Stage): 10 pages proposal (Excellence, Methodology and Impact)

Call: HORIZON-HLTH-2024-STAYHLTH-01-two-stage

(Staying Healthy (Two stage - 2024))

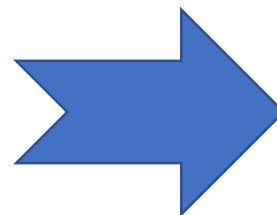
Topic: HORIZON-HLTH-2024-STAYHLTH-01-05-two-stage

Type of action: HORIZON-RIA
(HORIZON Research and Innovation Actions)

Type of Model Grant Agreement: HORIZON Lump Sum Grant

Proposal number: 101156266-1

Proposal acronym: DORIAN GRAY



Excellence 5/5

Impact 5/5

Total score 10/10

5° out of 208 proposals
12 proposals admitted to stage 2

 11 Apr 2024 (Second Stage): 50 pages proposal

Call: HORIZON-HLTH-2024-STAYHLTH-01-two-stage

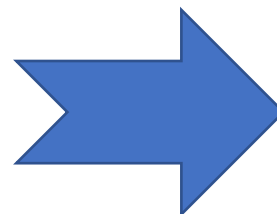
(Staying Healthy (Two stage - 2024))

Topic: HORIZON-HLTH-2024-STAYHLTH-01-05-two-stage

Type of Action: HORIZON-RIA
(HORIZON Research and Innovation Actions)

Proposal number: 101156266-2

Proposal acronym: DORIAN GRAY



Excellence 5/5

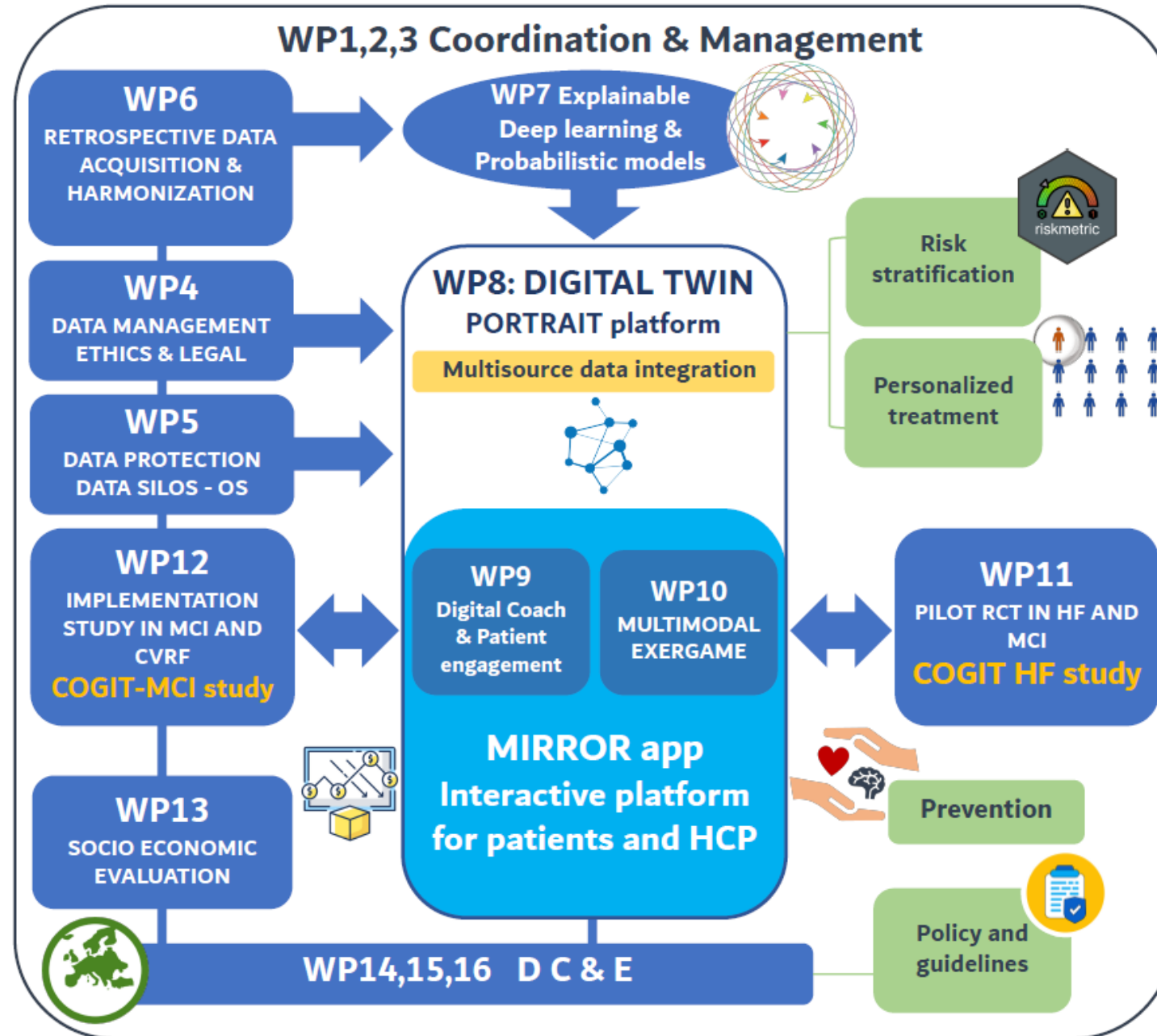
Impact 5/5

**Quality and Efficiency of the
implementation 5/5**

Total score 15/15

1° out of 12 proposals
4 proposals funded

Type of Model Grant Agreement: HORIZON Lump Sum Grant



RETROSPECTIVE DATASETS



Training Datasets

Validation Datasets

Cognition Measurements
Omics Data: Genomic, metabolomic, proteomic
MRI Neuroimaging
Cardiovascular Phenotype

Data harmonization integration and sharing
GDPR Compliant, built in safeguarding and privacy

Omic and Imaging Biomarkers Identification

AI & CAUSAL MODELING

Static Probabilistic Model

Dynamic Probabilistic Model

Causal Models

Digital Biomarkers Extended Models

Digital Twin PORTRAIT PLATFORM



Risk Stratification
Risk Progression
Disease Trajectories
Causal Graphs



Explainability
Per domain analyses
LLM Integration



User behaviour and engagement metrics
Personalized Coaching Plans
Exergame progressions
Personalised guidance
Feedback



RWD Prospective Multi-Source Data Integration
User self-monitoring data
System usage data
User data
Smartwatch data
Performance data
Clinical Data



Pilot RCT – COGIT-HF
HF and MCI **150 patients** (IT, GE, CZ, RO, UK)



Clinical Dashboard
HCP patient interaction & Clinical Supervision



Implementation Study – COGIT-MCI Study
MCI and CVRF **150 patient** (IT, GE, CZ)



Inform Guidelines
Recommendation
& Policies

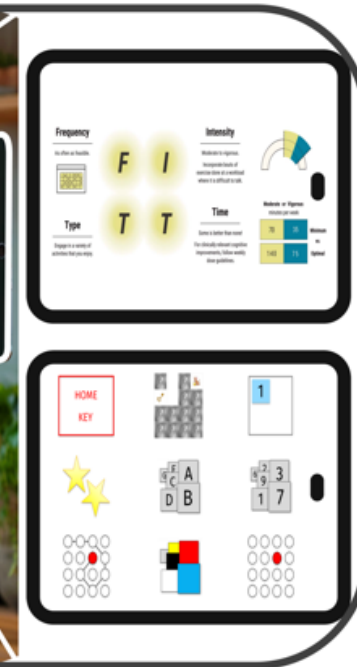
Interaction with
HCP users &
stakeholders



End User
Involvement



Avatar-based Coaching Exergame Mirror App



PATHWAYS TO IMPACT => Socio Economic Analysis, Cost-effectiveness, Digital Accessibility, Patient Acceptability, Lifestyle Changes and Empowerment | HEALTHY AGEING

Result

Outcome

Impact

	UK				Netherlands	Czech Republic	Italy	GERMANY		USA	
	UK Biobank	Whitehall II	ELSA Study	EPIC-Norfolk Study	Maastricht Study	Kardiovize Study	LIFE-Bio cohort	LIFE Study	BeLOVE	Mark VCID	Mount Sinai Data
Patients (n)	25900	6629	10109	8000	3000	2123	360	1800	365	660	236905
Follow-up	7 years	20 years	15 years	13 years	8 years	7 years	1 year	7 years	2 years	2 years	23 years
Age range (y)	40-69	35-55	50-90	40-75	40-75	25-64	50-90	18-79	18-90	26-90	50-90
Sex	M & F	M & F	M & F	M & F	M & F	M & F	M & F	M & F	M & F	M & F	M & F
Cognition measurement	Multidom Composite	Multidom Composite	Multidom Composite	Multidom Composite	Multidom Composite	MOCA	MOCA	Multidom Composite	MOCA	MOCA	MOCA
Genetics	N=20000	N=5666	N=6185	N=6000	N=3000	-	N=360	N=7669	N=200	-	N=5000
Metabolomics single	Nightingale Health N=251 biomarkers. N=15365	Nightingale Health n=251 biomarkers n=5374	-	DiscoveryHD4® platform, Metabolon, Inc.N=940 metabolites N=1503	Nightingale Health N=226 biomarkers. N=3441	-	-	LC–MS/MS N=9622	Biocrates Quant 500	-	-
multiple	N=3289	-	-	-	N=1850	-	-	N=1,000	-	-	-
Proteomics: single	Olink 3072 PEA N=2982	Olink panel (n=543) & SOMAscan version 4 assay N=2274	NA	Olink 1536 panel (N=1180), 368 proteins from the CVII,CVIII, Cardiometabolic, inflammation panels (N=822)	NA	NA	SIMOA (7 selected proteins)	Olink CVIII, n=96 proteins (N=2016)	OLINK-3368 panel (N=70)	NA	NA
MRI: single	N=14195	N=800	-	-	N=3000	-	360	N=1200	N=50	N=660	-
multiple	N=248	-	-	-	N=2500	-	50	N=1000	N=25	-	-
ECG: single	N=14341	n=5200	-	-	n=3000 (2200 24h ECG) N=3000	n=737	360	N=9000	N=365	-	N=200000
multiple	N=250	N=4000	-	-	(2000 24h ECG)	-	-	N=1000	N=25	-	150000

Abbreviations: LC–MS/MS: Liquid chromatography—mass spectrometry and liquid chromatography—tandem mass spectrometry; MR, magnetic resonance imaging. *≥2cognition measurements and ≥2 CVRF measurements

RETROSPECTIVE DATA – learning from BIOBANKS

