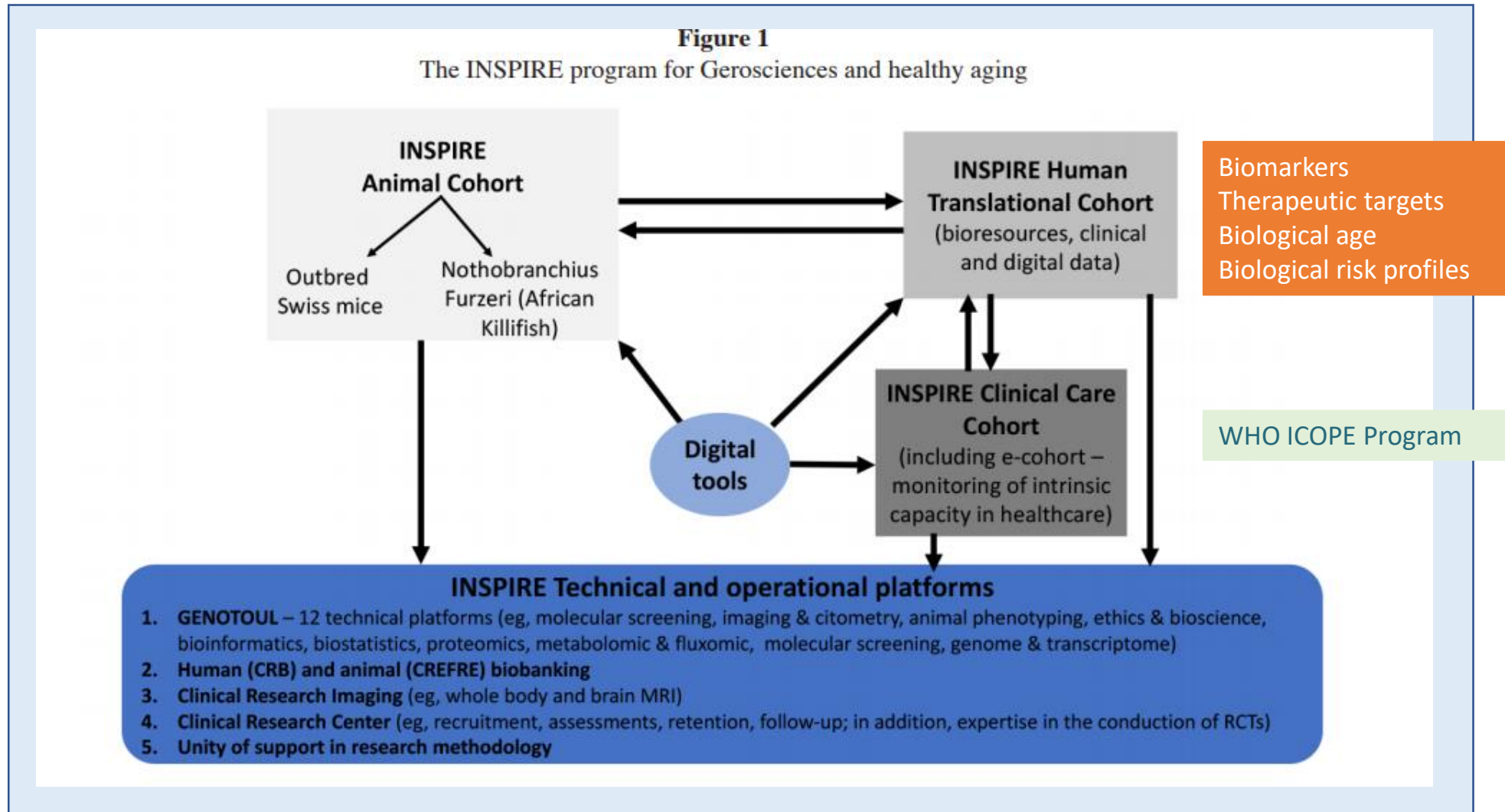# INSPIRE SAB Meeting
The Human Research Translational Cohort (INSPIRE-T)

Sophie Guyonnet, Yves Rolland, Philipe Barreto, Sandrine Andrieu, Bruno Vellas

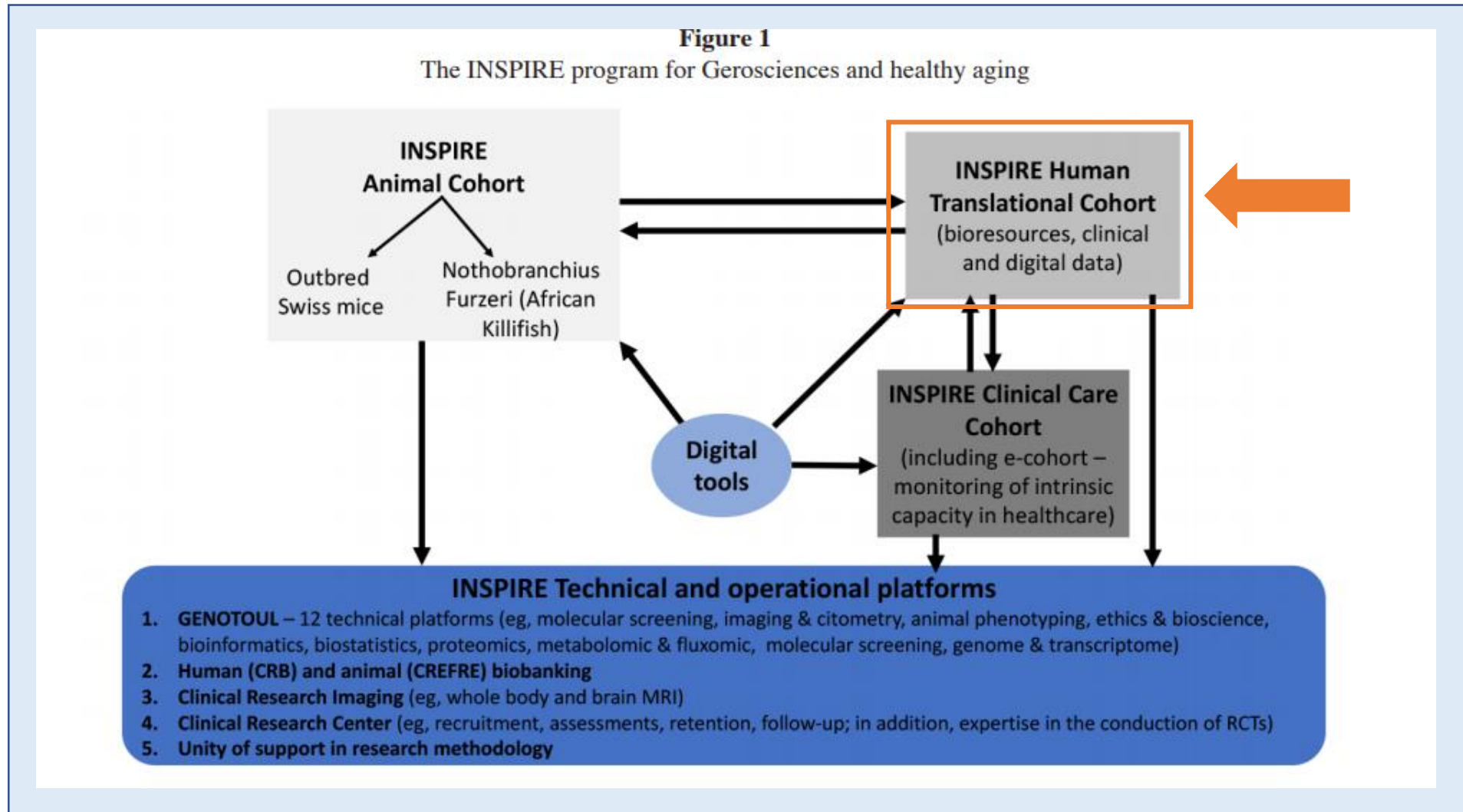Gérontopôle, CHU Toulouse – Cerpop/ UMR 1295 Axe vieillissement Maintain

The Inspire Program
Global Objective


Figure 1
The INSPIRE program for Gerosciences and healthy aging

INSPIRE Animal Cohort
- Outbred Swiss mice
- Nothobranchius Furzeri (African Killifish)

INSPIRE Human Translational Cohort (bioresources, clinical and digital data)

Biomarkers
Therapeutic targets
Biological age
Biological risk profiles

Digital tools

INSPIRE Clinical Care Cohort (including e-cohort – monitoring of intrinsic capacity in healthcare)

WHO ICOPE Program

INSPIRE Technical and operational platforms
1. **GENOTOUL** – 12 technical platforms (eg, molecular screening, imaging & citometry, animal phenotyping, ethics & bioscience, bioinformatics, biostatistics, proteomics, metabolomic & fluxomic, molecular screening, genome & transcriptome)
2. **Human (CRB) and animal (CREFRE) biobanking**
3. **Clinical Research Imaging** (eg, whole body and brain MRI)
4. **Clinical Research Center** (eg, recruitment, assessments, retention, follow-up; in addition, expertise in the conduction of RCTs)
5. **Unity of support in research methodology**

(De Souto Barreto P et al.2020)

The Inspire Program
Global Objective

Figure 1

The INSPIRE program for Gerosciences and healthy aging

(De Souto Barreto P et al.2020)
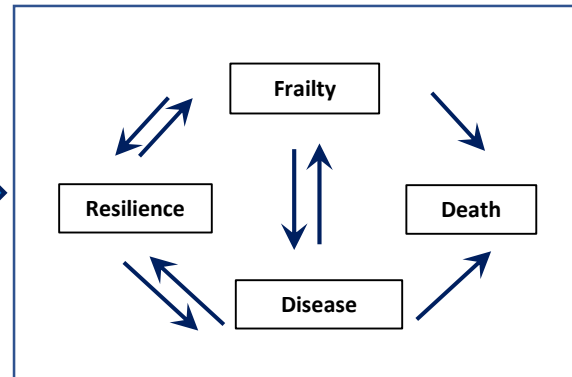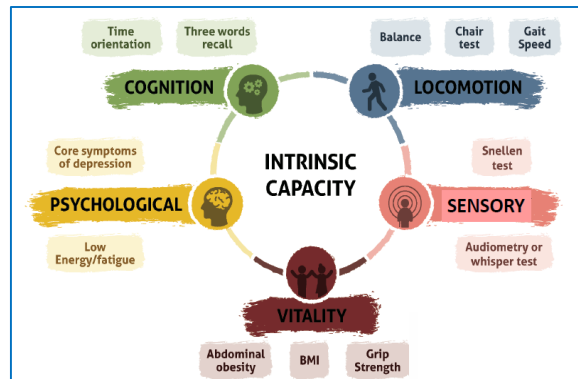
The Inspire –T cohort
Research objectives / Study population

- To recruit 1000 individuals of several chronological ages (from 20y with no upper limit of age) and functional capacity levels (from robust to frail), with baseline and follow-up biological, clinical, imaging and digital data over 10 years

- To explore and identify a set of biomarkers of aging, age-related diseases and IC evolution
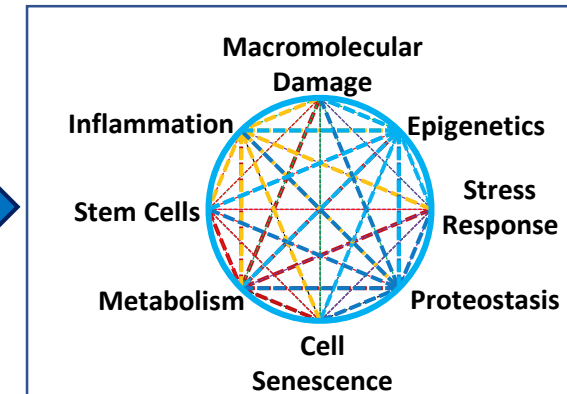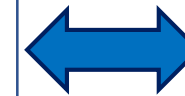
The Inspire –T cohort
Study procedures and innovative aspects

Baseline &Annual Visit
Research facilities/home
(standardized procedures)

INSPIRE-T
1000 individuals
20 – 100 and +
10 y follow-up

Clinical Data (WHO ICOPE Program)

Biospecimens (Biobanking)

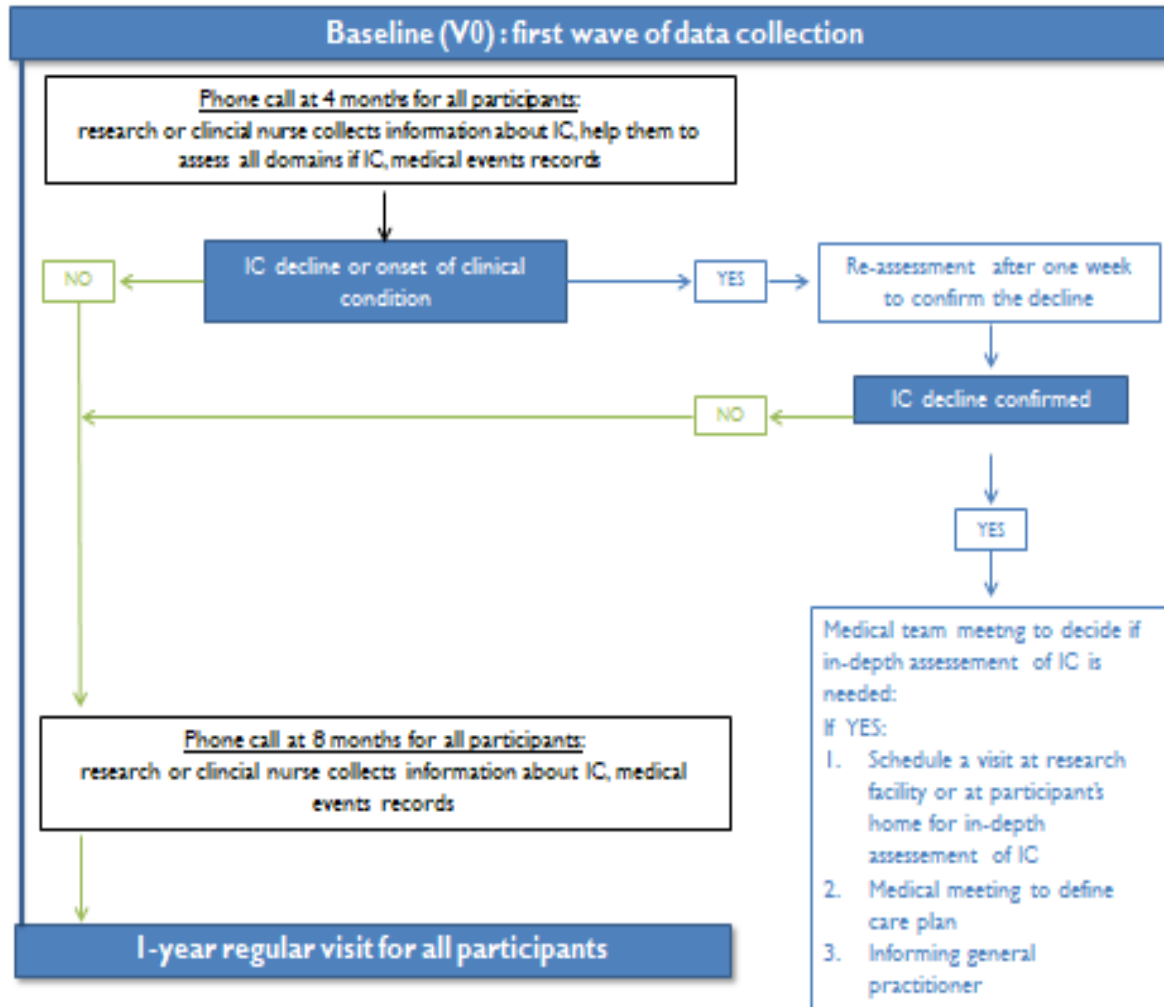**Additional investigations (sub-samples) – every 2 y**
DEXA
Whole Body/Brain MRI
Stress test (VO2 max)
Muscle strength test

The Inspire –T cohort
Study procedures and innovative aspects

Baseline (V0) : first wave of data collection

Phone call at 4 months for all participants:
research or clinical nurse collects information about IC, help them to assess all domains if IC, medical events records

IC decline or onset of clinical condition → YES → Re-assessment after one week to confirm the decline

NO

IC decline confirmed

NO ← YES

Medical team meeting to decide if in-depth assessement of IC is needed:
If YES:
1. Schedule a visit at research facility or at participant's home for in-depth assessement of IC
2. Medical meeting to define care plan
3. Informing general practitioner

Phone call at 8 months for all participants:
research or clinical nurse collects information about IC, medical events records

I-year regular visit for all participants

➢ **Close monitoring of IC** (Icope Monitor) ; each 4-month the first year and every 6-month from the second year

➢ Collection of clinical and biological data at the moment declines in IC come-up

Continuous monitoring of IC through sensors in a sub-group of 100 participants, 70 y and + (The CART France Ancillary Project)

The Inspire –T cohort
Recruitment status (September 29, 2021)

- Approval by the French Ethical Committee in October 2019

- First participant recruited on October 16 2019

- Recruitment temporarily suspended between March and the end of June 2020 (COVID-19 crisis)

- **948 volunteers** (% women : 63.5) included by September 29 2021

- **33 new inclusion visits planned** (including 26 subjects > 80 y)

- **402 visits at 1 year**

- **34 dropped out**

RETENTION STRATEGIES

MAINTAIN A POOL OF 1000 SUBJECTS

INSPIRE-T
N=948 (20-103)
% women: 63.5
> 70 y : n= 357 (37.6%)
> 80 y: n=157 (16.6%)
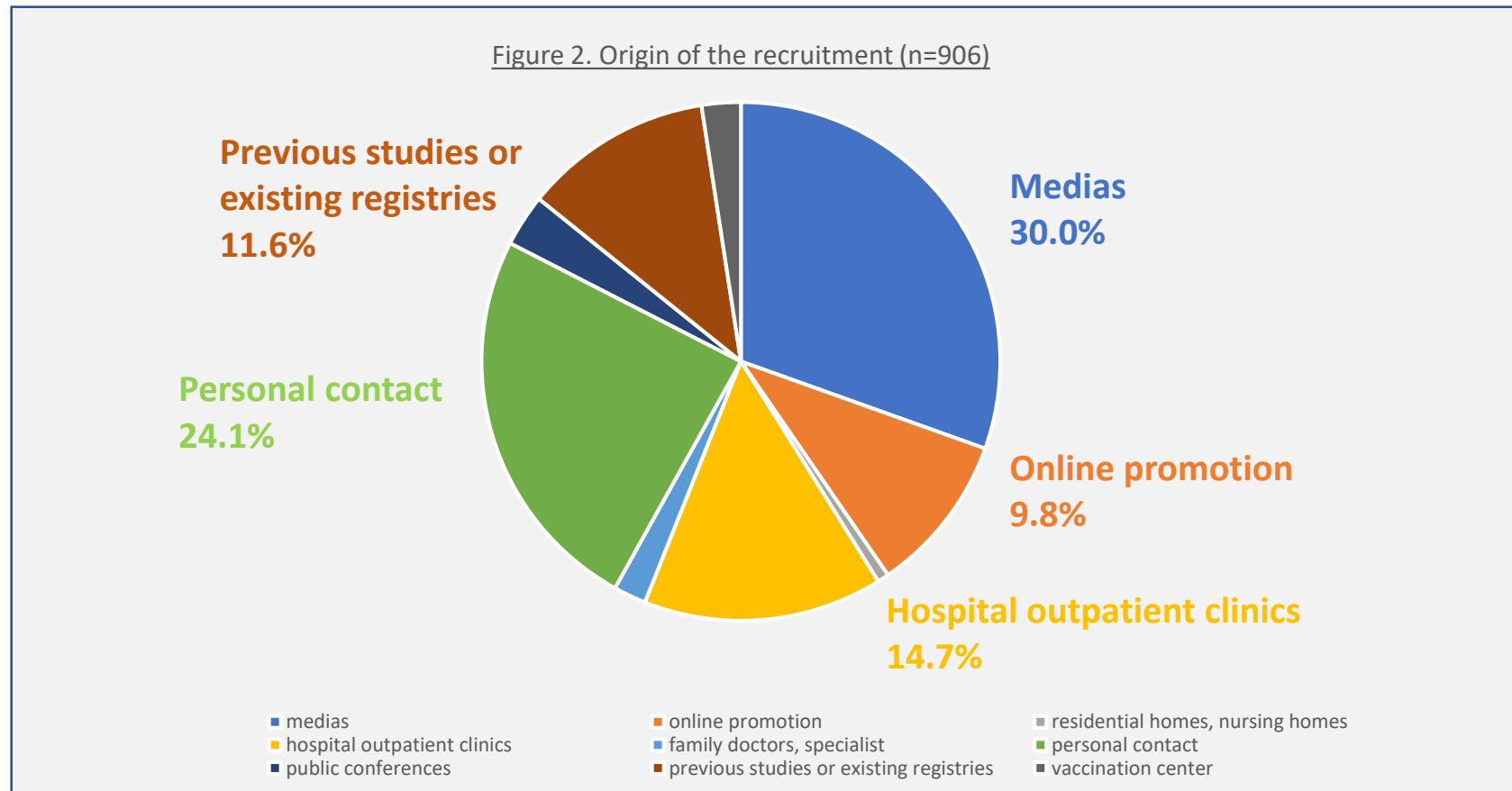
Figure 1. Population Size Per Decade (September, 29 2021)
Expected, n=1000; Recruited, n=948

Legend: Expected, Recruited

98.8% | 108.8% | 103% | 115.8% | 97.8% | 117.6% | 81.8% | 18.0%

20-29 y | 30-39 y | 40-49 y | 50-59 y | 60-69 y | 70-79 y | 80-89 y | 90 and +
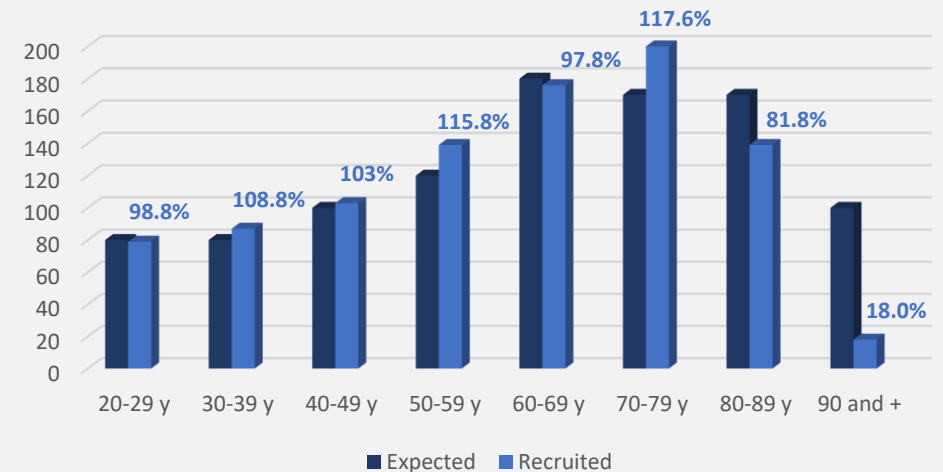
The Inspire –T cohort
Origin of the recruitment

Figure 2. Origin of the recruitment (n=906)

Previous studies or existing registries 11.6%

Personal contact 24.1%

Medias 30.0%

Online promotion 9.8%

Hospital outpatient clinics 14.7%

Legend:
- medias
- hospital outpatient clinics
- public conferences
- online promotion
- family doctors, specialist
- previous studies or existing registries
- residential homes, nursing homes
- personal contact
- vaccination center

The Inspire –T cohort
Phenotype of frailty

Mean age, n=904: 59.7 ± 18.6

Figure 3. Five items of phenotype of frailty (n=908)

- Sedentarity: 24.5%
- Slow walking speed: 2.4%
- Low grip strength: 11.7%
- Fatigue: 8.4%
- Involuntary weight loss: 2.9%
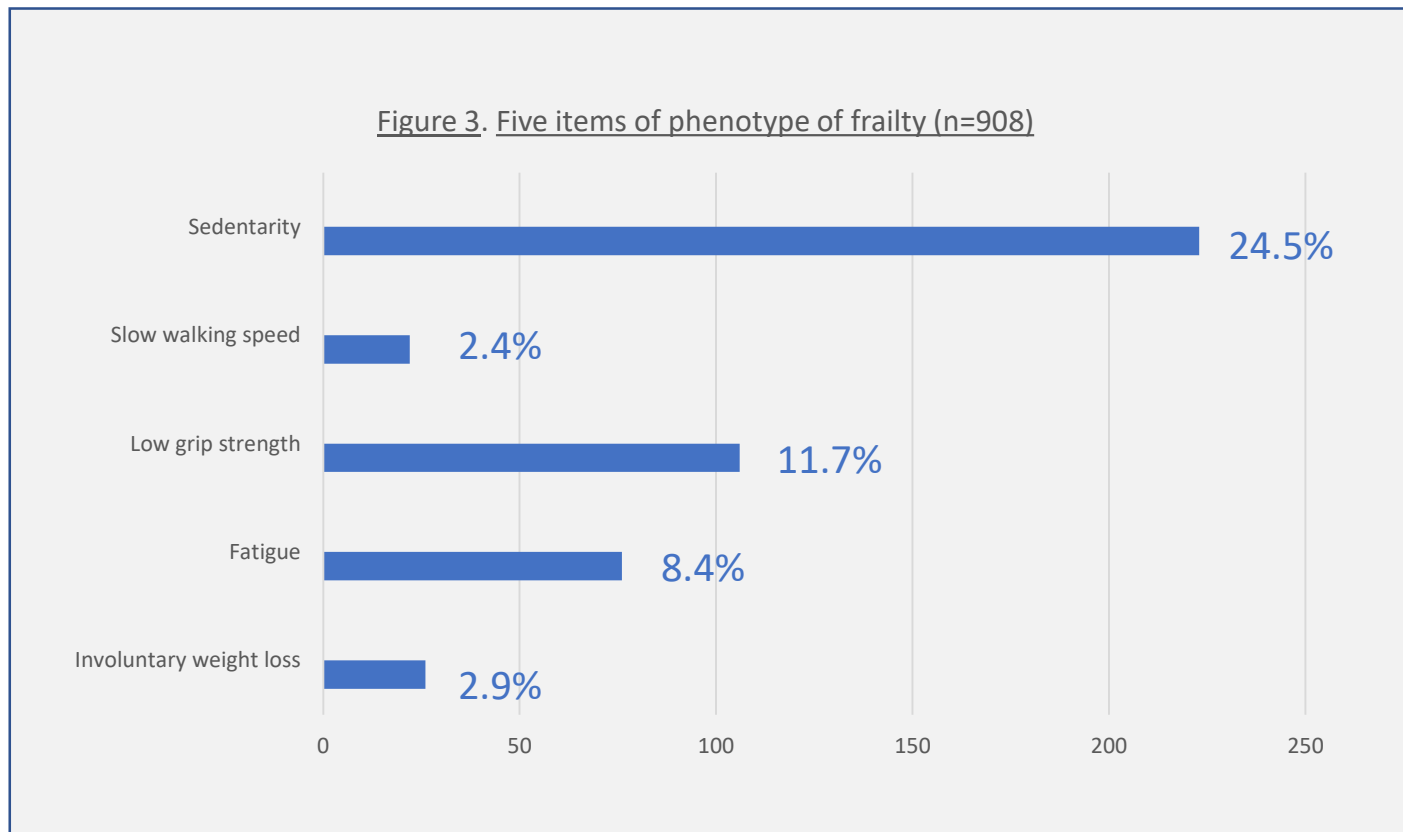
PHENOTYPE OF FRAILTY (FRIED)

ROBUST (0 Item)
n=627, 66.1%

PRE-FRAIL (1-2 items)
n=266, 28.1%

FRAIL (3 and + items)
n=48, 5.1%

The Inspire –T cohort
Baseline characteristics

BASELINE AND EVERY YEAR

Physical examination (including medication, prurit and visceral pain), **Autonomy** (ADL, IADL) & **Frailty phenotype** (Fried)

Sociodemographics & **Lifestyle** (physical activity and sleep parameters with ActivPal accelerometer, sedentarity time, smoking, alcohol consumption, alimentation, participant-reported outcomes for cognition (CFI), mobility, fatigue and social isolation (PROMIS)

ICOPE (Step 1 to 3) – IC ASSESSMENT
Nutrition : MNA, OHAT
Depression: PHQ 9
Mobility : SPPB, Chair rise test (30 sec)
Cognition: MMSE
Vision: WHO simple eye chart, Amsler grid
Audtion : Audiometry (from 1y visit)

ADL (/6), n=910 : 5.90 ± 0.31 (2.5 – 6)
IADL 8 items (/31), n=839: 8.35 ± 1.83 (8 – 27)

MNA (/30), n=906 : 27.39 ± 2.07 (17.5 – 29)
at risk of manutrition : 6.51%
PHQ 9 (/27), n=900: 3.04 ± 3.5 (0 – 27)
moderate to severe depression (score > 9): 5.55%
SPPB (/12), n=899: 11.54 ± 1.40 (1-12)
score <10: 5.34%
MMSE (/30), n=906 : 28,66 ± 1,75 (15 – 30)
score <26: 5.4%

The Inspire –T cohort
Abnormalities in domains of IC

WHO ICOPE SCREENING TOOL

MONITORING OF IC (STEP1 ICOPE)

Priority conditions associated with declines in intrinsic capacity	Tests	Assess fully if any answer in each domain triggers this	
COGNITIVE DECLINE (Chapter 4)	1. Remember three words: flower, door, rice (for example)		
	2. Orientation in time and space: What is the full date today? Where are you now (home, clinic, etc)?	Wrong to either question or does not know	
	3. Recalls the three words?	Cannot recall all three words	**2.0%**
LIMITED MOBILITY (Chapter 5)	Chair rise test: Rise from chair five times without using arms. Did the person complete five chair rises within 14 seconds?	No	**3.7 %**
MALNUTRITION (Chapter 6)	1. Weight loss: Have you unintentionally lost more than 3 kg over the last three months?	Yes	**6.1 %**
	2. Appetite loss: Have you experienced loss of appetite?	Yes	
VISUAL IMPAIRMENT (Chapter 7)	Do you have any problems with your eyes: difficulties in seeing far, reading, eye diseases or currently under medical treatment (e.g. diabetes, high blood pressure)?	Yes	**88.1%**
HEARING LOSS (Chapter 8)	Hears whispers (whisper test) *or* Screening audiometry result is 35 dB or less *or* Passes automated app-based digits-in-noise test	Fail	**37.7%**
DEPRESSIVE SYMPTOMS (Chapter 9)	Over the past two weeks, have you been bothered by – feeling down, depressed or hopeless?	Yes	**23.1 %**
	– little interest or pleasure in doing things?	Yes	

The Inspire –T cohort

Samplings proposed to participants for the creation of the biobank for omics analysis, analysis of microbiome and cell cultures

BASELINE AND EVERY YEAR

From all subjects
- Blood/PBMC (60 ml each visit)
- Urine (20 ml at each visit)
- Saliva (10 ml at each visit)
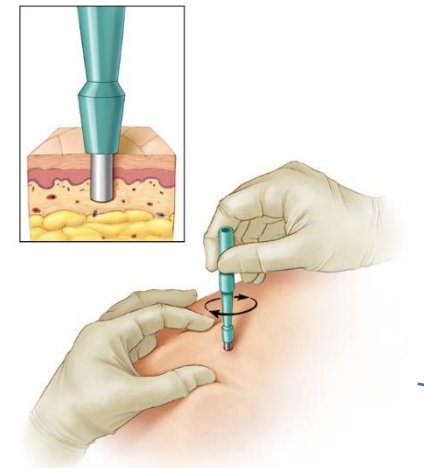- Dental plaque (4 samples)

BASELINE AND EVERY 2 YEARS

- Nasopharyngeal swabs
- Skin swab and stripping

From all subjects

BIOPSIES FROM SURGERIES

BASELINE AND AT 2 YEARS

Optional
- Skin biopsy
- Hair bulb
- Feces (every 2 years)

SKIN BIOPSY

Amplification and biobanking of human fibroblasts

Omics analysis

The Inspire –T cohort
Status of clinical samples for experimental research (September 29, 2021)

Biospecimens	At inclusion	At 1y
Blood/PBMC (60 ml each visit)	944	402
Nasopharyngeal sample	214	-
Urine (20 ml at each visit)	944	402
Saliva (10 ml at each visit)	572	402
Dental plaque (4 samples)	549	402
Skin samples : -swabbing, delamination	528	-
-skin biopsy (optional) for omics	117	-
-skin biopsy (optional) for fibroblasts	130	-
Hair bulb (optional)	655	-
Feces (optional)	366	-

Optional

- 944 participants (99.6%) gave their consent for the basic biobanking (blood, urine, saliva, dental plaque)

- **62 360 biospecimens** collected at this time

- Collection of saliva, dental plaque and nasopharyngeal swabs have been temporarily suspended during COVID crisis (hospital policy)

Existing Gerontopole Biobanks

- **COG-FRAIL**
- 317 frail subjects (CDR=0.5 or 1), 70 y and +, 2 y follow-up
- Observational study
- Plasma (EDTA, LitHep), Serum, PMBC

	INSPIRE		COG-FRAIL		TOTAL		TOTAL
	H	F	H	F	H	F	
70-79 ans							
Non-évalué							
Robuste	60	80	0	0	60	80	140
Préfragile	23	30	11	30	34	60	94
Fragile	3	4	12	17	15	21	36
Total	86	114	23	47	109	161	270
80-89 ans							
Non-évalué							
Robuste	26	27	0	0	26	27	53
Préfragile	29	32	46	62	75	94	169
Fragile	2	23	25	46	27	69	96
Total	57	82	71	108	128	190	318
90 et +							
Non-évalué							
Robuste	2	2	0	0	2	2	4
Prefragile	1	3	4	6	5	9	14
Fragile	4	6	2	14	6	20	26
Total	7	11	6	20	13	31	44

+ 71

+ 16

The Inspire –T cohort

- VO$_2$max has been accepted by **334 volunteers** (221 realized)

- Isocinetic muscle strength by **339** (221 realized)

- DEXA by **835**

- and Brain/whole body MRI by **111** (33 realized)
  - Visceral adipose tissue
  - Abdominal and sub-cutaneous adipose tissue
  - Liver fat infiltration by proton density
  - Total adipose tissue
  - Intra-muscular adipose tissue
  - Volumes of specific muscles groups
  - Volumes of individuals muscles
  - Total lean mass

The Inspire –T cohort
Status of paraclinical examinations (September 29, 2021)

- **111** subjects will have both culture cells and VO$_2$max examination

- Plus blood samples before and between 3 to 5 minutes after the "challenge"
  - EDTA samples (CRB) $\Rightarrow$ PBMC (1 aliquot, 5x10^6 cells)
  - Heparin blood sample + perchloric acid (IFB) $\Rightarrow$ pyruvates, lactate, ketone bodies

$\Rightarrow$ To challenge the redox metabolism homeostasis (the return to redox homeostasis can be delayed in pre-frail individuals) / to correlate results from isolated cells and human (Restore team)

The Inspire –T cohort

NEXT STEP ⇒ Inspire 2 « Simultaneous measurement of hallmarks of ageing over the entire cohort » -same approach as ADNI
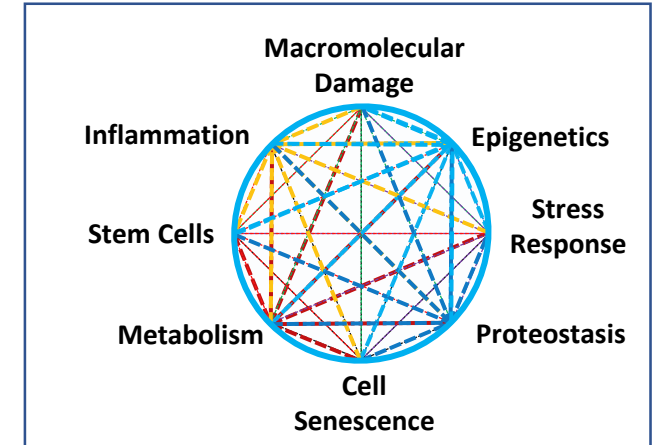
Sept 2019 – Sept 2022

| INSPIRE 1 |

Recrutment of volunteers,
Data acquisition and data-base,
Data-sharing

Oct 2022 – Oct 202X

| INSPIRE 2 |

Investigate the hallmarks of ageing (gerosciences); Identify outcome measures for future geroscience RCT; Design the new generation of RCT (geroprotector trial); Data-sharing

Geroscience

Sierra & Kohanski
J Gerontol (2014)

Kennedy et al. Cell Nov 2014

The Inspire Platform
Acknowledgments