Leiden University
Medical Center

New concepts for research in Elderly Care and Healthy Ageing.
Game changers for prevention and treatment

P.Eline Slagboom

Leiden University Medical Centre (LUMC)

Leiden University
Medical Center

Outline Integrated Approaches in Research

Why investigate ageing

What is healthy ageing by nature

By nurture, how to monitor and influence healthy ageing

Game changers: Integrating basic, biomedical and medical research

LUMC : Medical Research Profile on Ageing

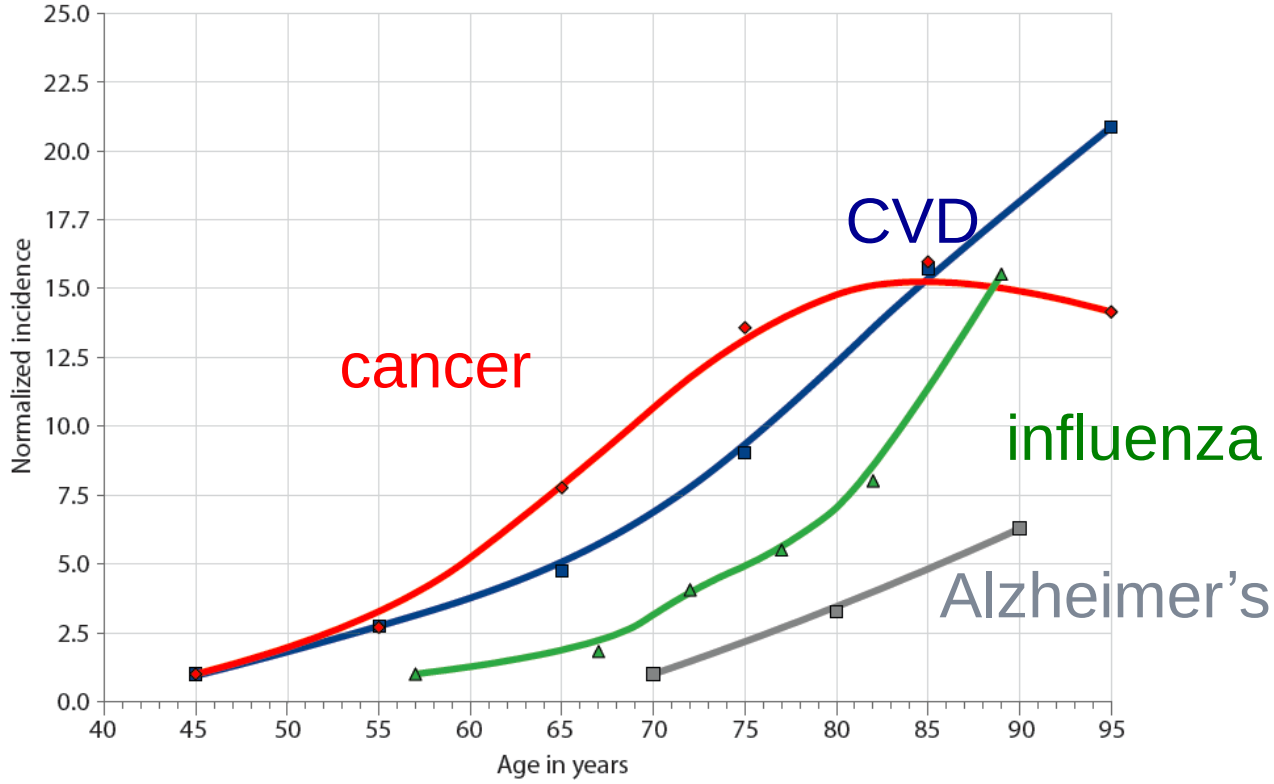
National: Dutch Society for Research on Ageing (DuSRA)

More systematic observation of elderly in the clinic

Not treating

Teaching

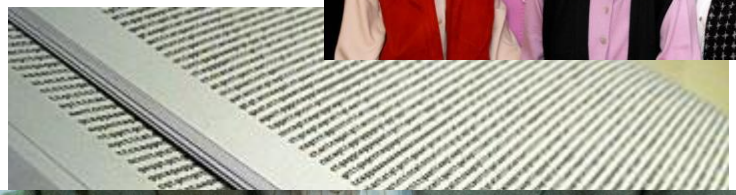
Age is the strongest risk factor for common diseases

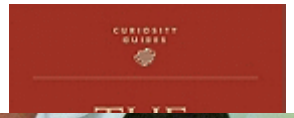


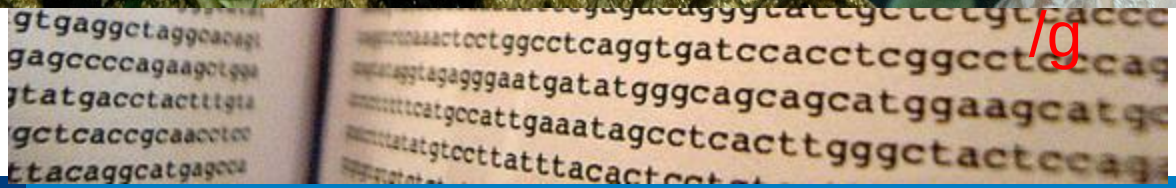
20 % of life EU citizen spend in disability

- **65 + doubles before 2060**
- **85 + triples before 2060**
- **Co-morbidity, polypharmacy, heterogeneity/biological age ---personalized medicin**

Healthy Ageing by nature.
Leiden Longevity Study (3500 individuals)







The genome of the oldest old in the EU

Joris Deelen
***Hum Mol Genet* 2014**

- EU longevity research

  APOE ; Chrome 5q3.33 ; *EBF1*

- *Worlwide longevity research (EU, US, China)*

Aging Cell (2013) 12, pp184–193 Doi: 10.1111/acel.12039

Genome-wide linkage analysis for human longevity: Genetics of Healthy Aging Study

Human Molecular Genetics, 2014, Vol. 23, No. 16 **4420–4432**
doi:10.1093/hmg/ddu139
Advance Access published on March 31, 2014

Genome-wide association meta-analysis of human longevity identifies a novel locus conferring survival beyond 90 years of age

Leiden Longevity Study
Nature: drivers of healthy ageing

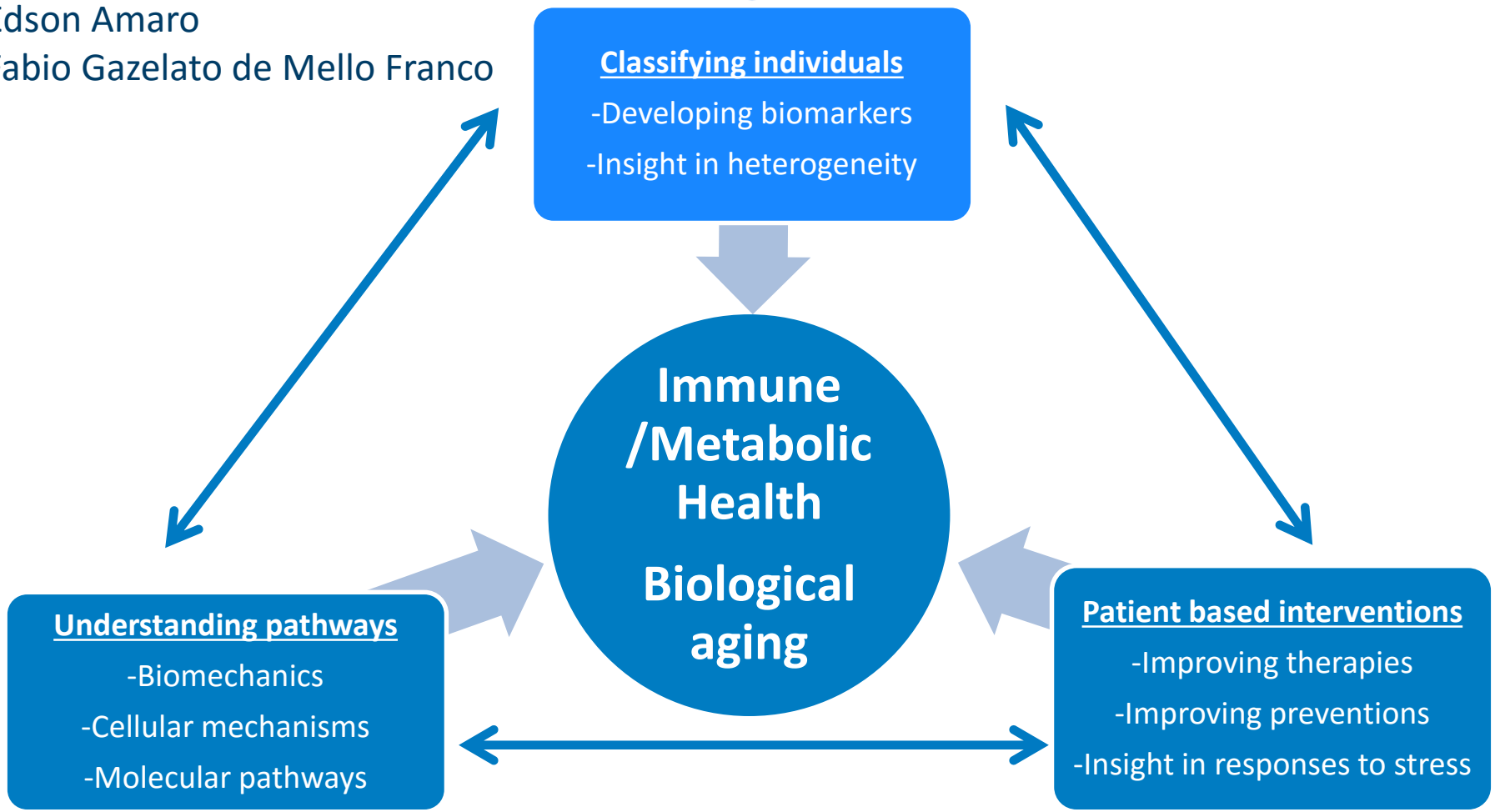
Nature : Intrinsic immune and metabolic health:
Clinical Variables, Metabolites, Imaging (brain)
Morbidity, Mortality

Energy metabolism/nutrient sensing: Lipids, Insulin, Thyroid, mTOR
Bonus

Can you influence it ?

Neuro-cardiovascular Musculoskeletal

Albert Einstein SP
Luiz Vicente Rizzo
Edson Amaro
Fabio Gazelato de Mello Franco



Growing Old Together (GOTO) Study design

13-weeks intervention

- 12.5% reduced dietary intake
- 12.5% increased physical activity

Before baseline:

- FFQ
- IPAQ
- Accelerometer
- 24 hr blood glucose
- At baseline : Blood, fat, muscle

During intervention

- 4 x 24h recalls
- Diary
- Hunger and satiety questionnaires

One week before end:

- Accelerometer
- 24 hr blood glucose
- Blood, fat, muscle

Research questions:

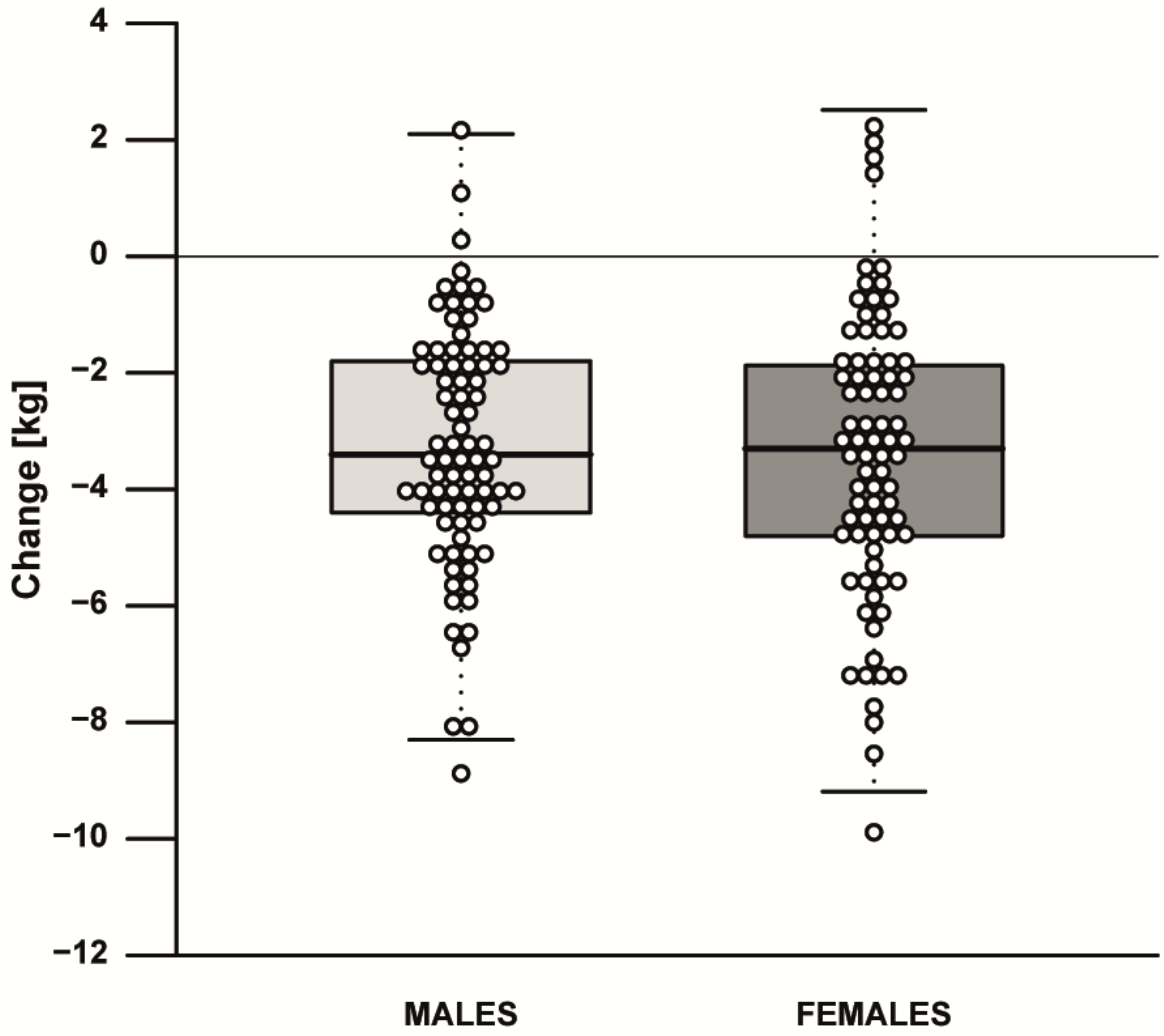
- Is this “common sense” lifestyle intervention feasible and healthy for all older adults (≈ 60 years old)?

Healthy Ageing Result of GOTO intervention

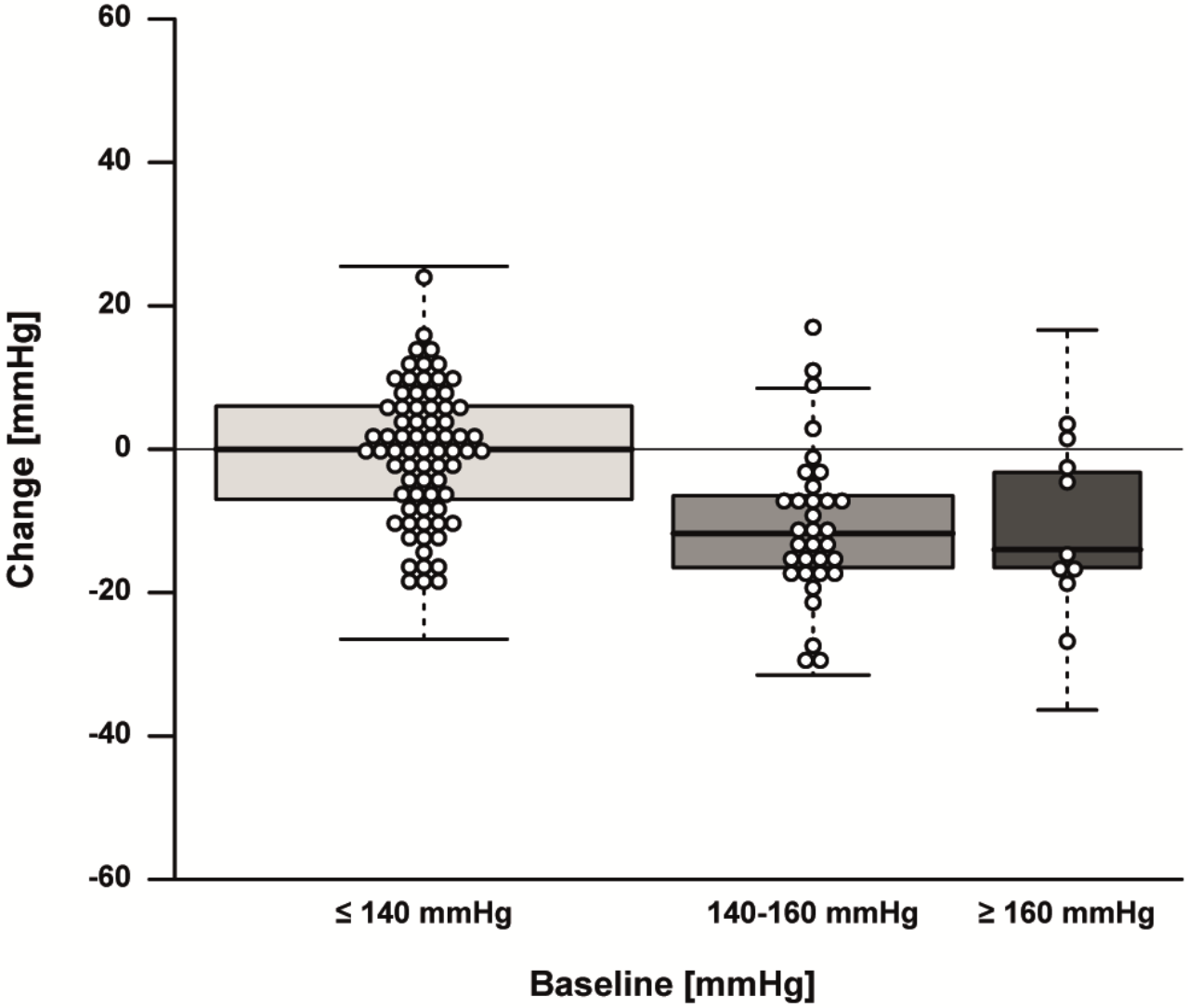
- 60-70 year old : Feasible : window of opportunity
- Buddy effect and coaching
- Well-being improved
- Sleep improved
- Metabolic health improved
- Longevity family members not different from spouse

- But: Heterogeneous responses

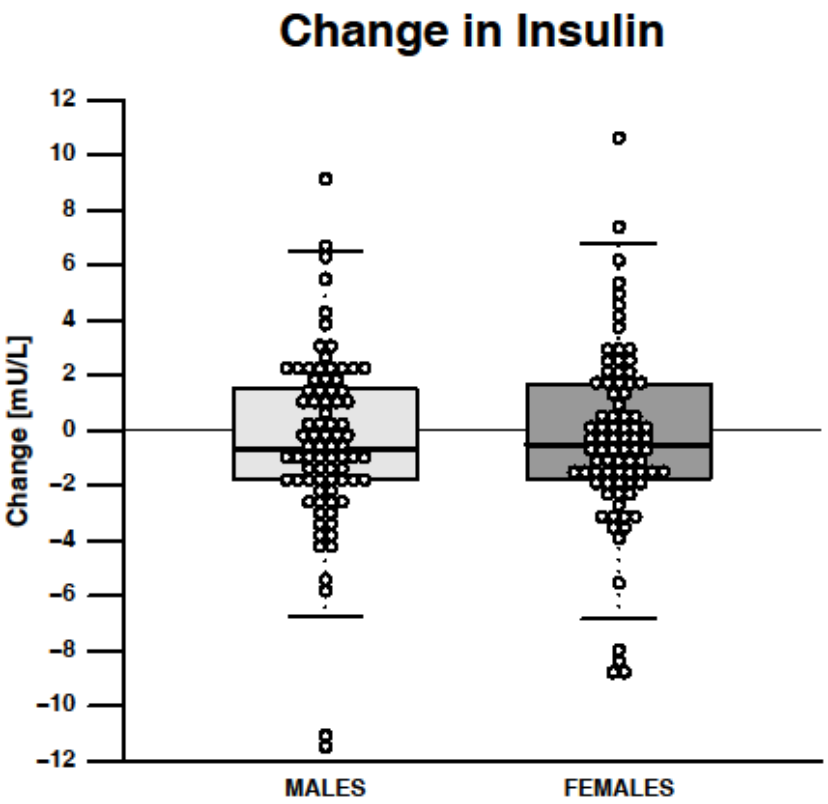
GOTO: Weight change after 13 weeks



GOTO: Change in systolic blood pressure after 13 weeks



GOTO Change in insulin after 13 weeks



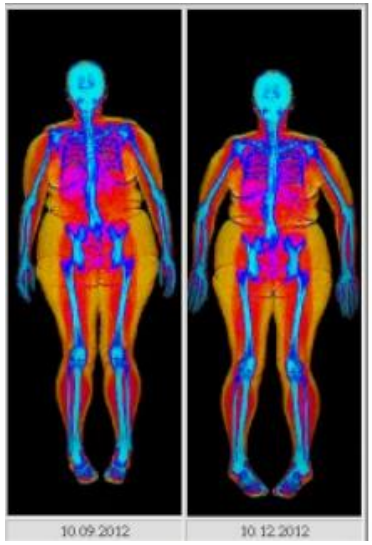
Healthy Ageing

- Heterogeneous responses

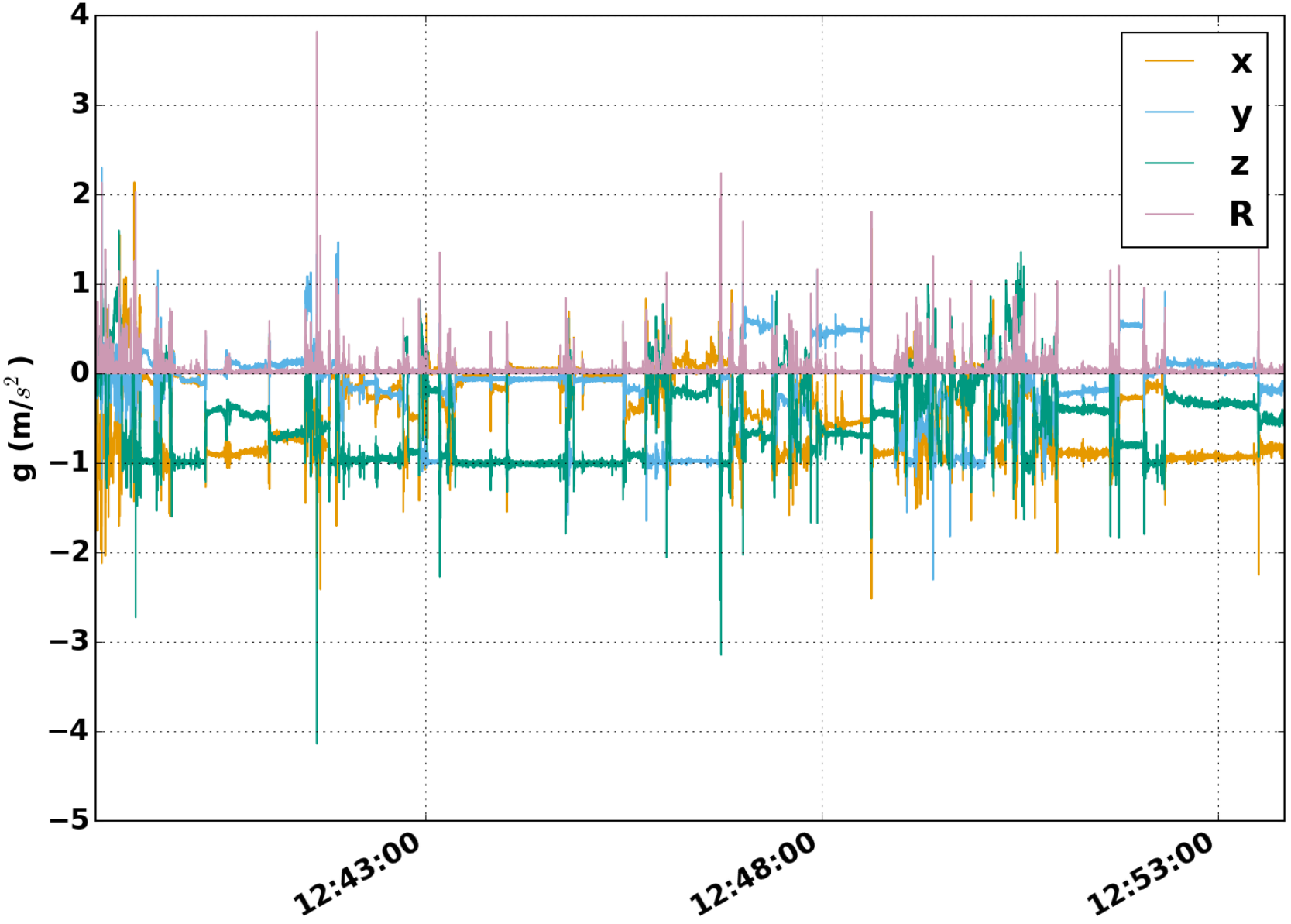
- Research in Public/Private Collaboration
- How to understand: blood, fat and muscle studies
- How to monitor: Biomarkers (Brainshake, Pfizer, Philips)
- How to motivate : AGO study in 60 +

PHILIPS

directlife



Monitoring Behavioral patterns
Sensors of heart rate variability, accelerometers etc.



Wearables not tested in elderly 'in the wild'. Investigation of 35 subjects 60-70 years

PHILIPS

directlife

Device	Location
GENEActiv	Right wrist (strap)
	Right ankle (strap)
Equivital	Chest* (belt)
Activ8	Upper leg (adhesive tape)
COSMED K4 b^2	Nose & mouth (face mask) and torso (belt)
Philips DirectLife activity monitor	Hip (belt)
	Chest (necklace)
Experimental Philips activity monitor	Left wrist (strap)
Polar Electro	Collection unit: attached to K4 b^2 belt.
	Sensor unit: chest* (belt)

Washing dishes (3 minutes)

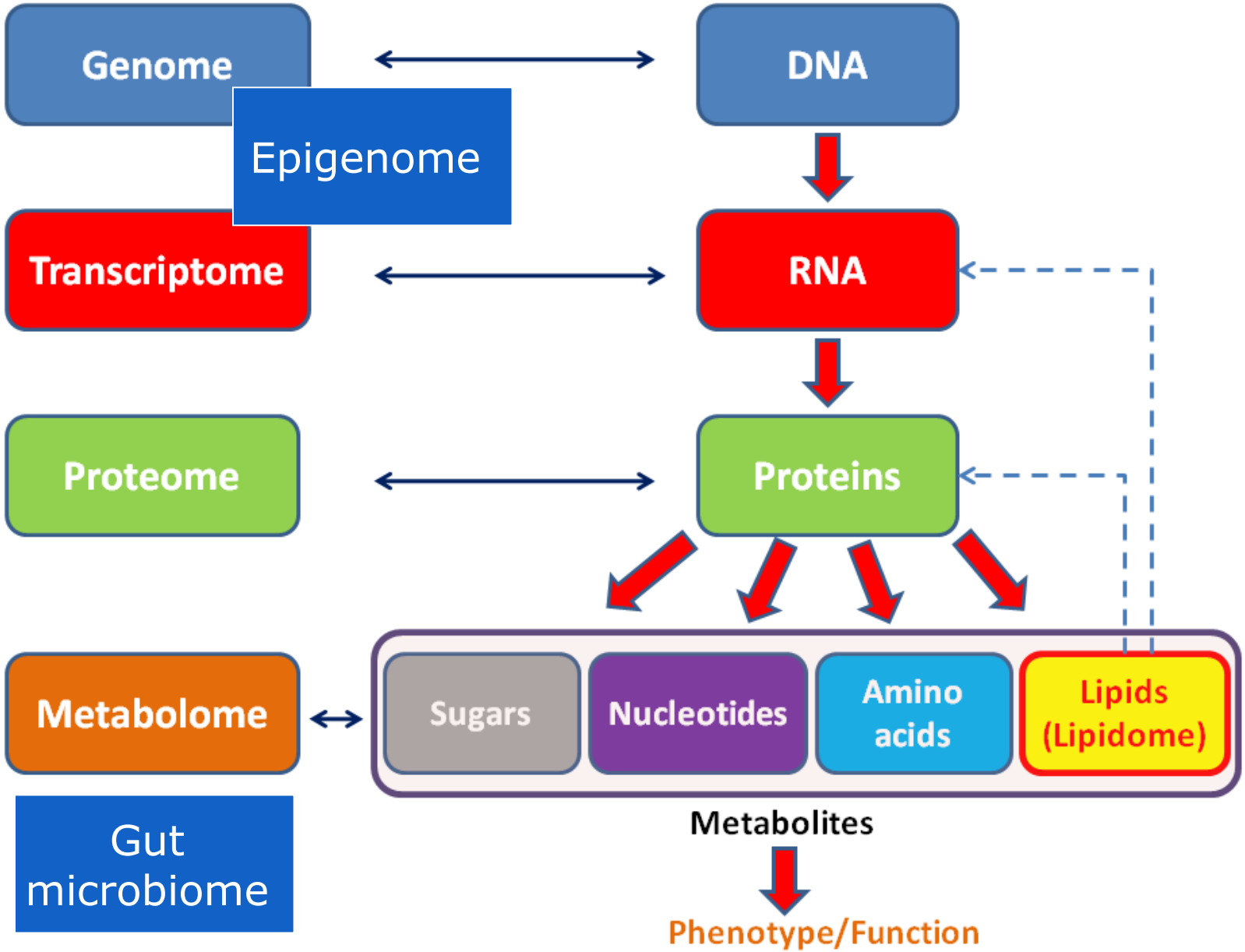
Organize bookshelf (3 minutes)

Vacuuming (3 minutes)

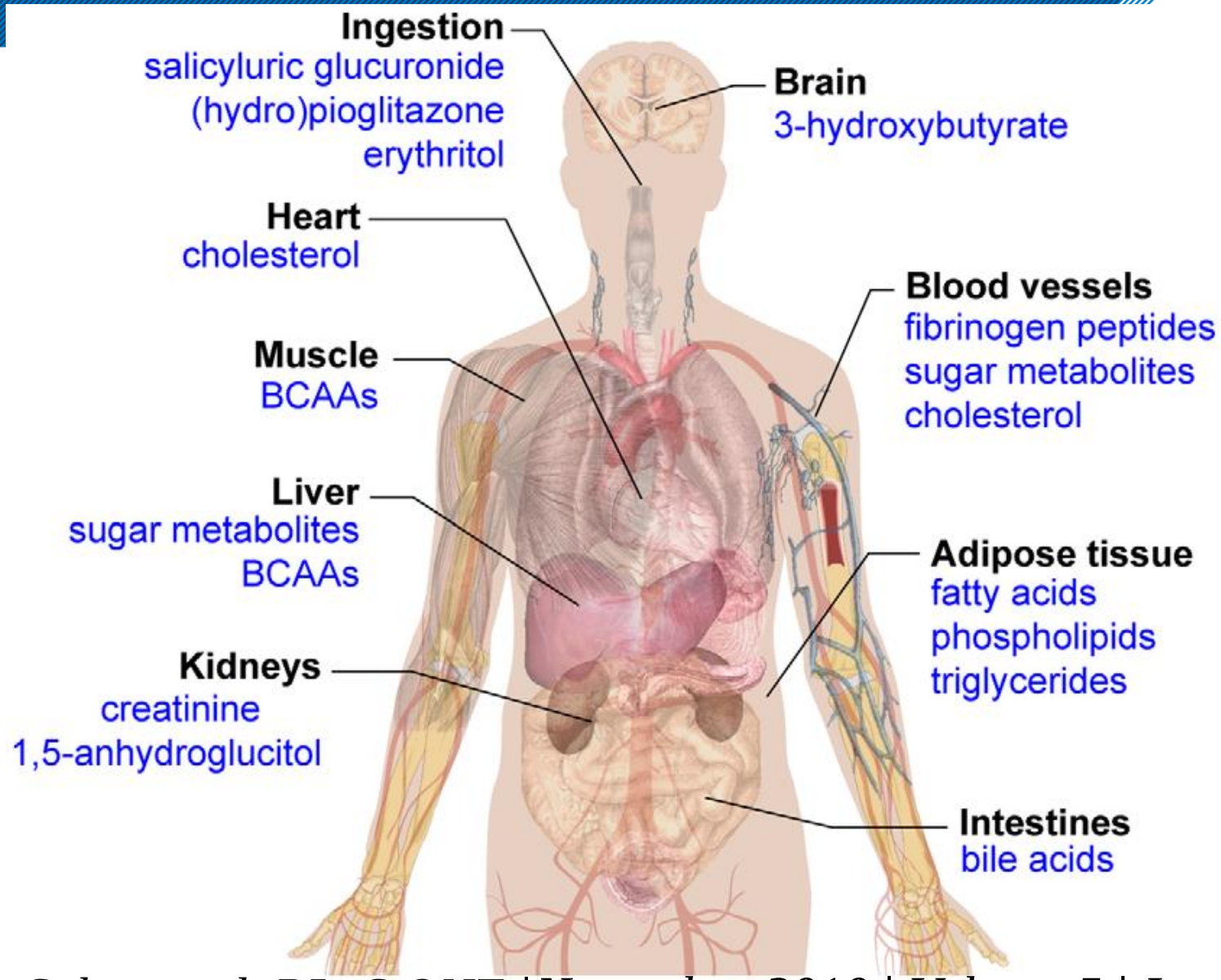
Cycling (15 minutes)

Evaluation of Interventions

Molecular Monitoring: BIOMARKERS
Big data in the right context (BBMRI)



BIOMARKERS : Metabolites in blood/urine monitoring tissue conditions



Suhre et al. PLoS ONE |November 2010 | Volume 5 | Issue 11

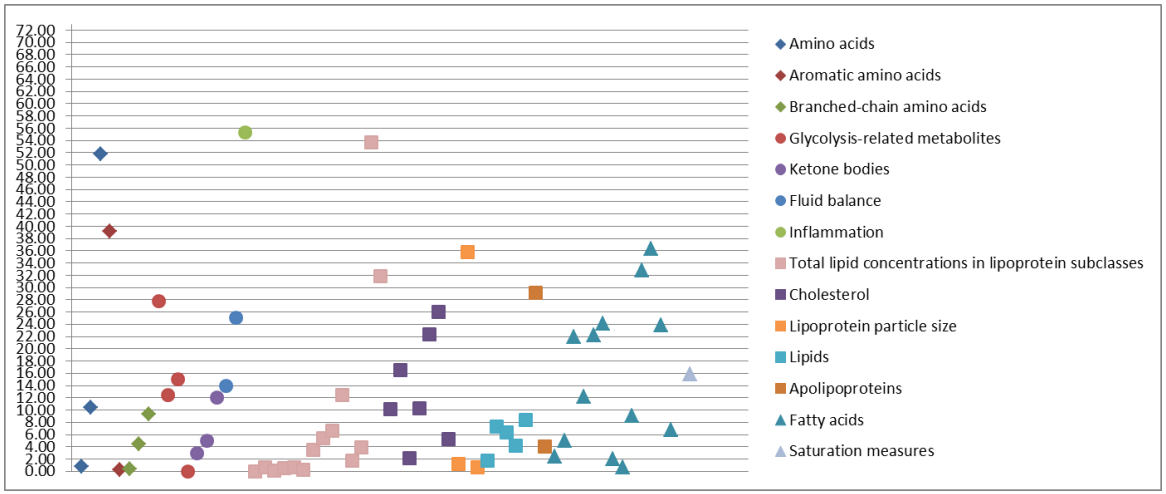
Topic	Study	Follow Up (y)	Cases	Controls
Migrain	LUMINA/CHARM/RVCL		439	125
	NTR VU	4.4	897	1000
	ERF EUMC		360	1000
Dementia	VUMC Alzheimer	3	1100	400
	EUMC dementia		1000	1000
Depression	NESDA VU	6	1200	400
	NTR VU	4.4	1000	1000
	EUMC depression		900	1000
Mortality Ageing	All cohorts			
	LLS LUMC	10	998	2313
	EUMC 85+	1-11	400	1200
	Alpha/Omega MUMC	5.5	459	476
CardioVascular Disease	BIOMArCS EUMC		900	
	STEMI UMCG		400	
	UNCORBIO UMCU	3	1200	
	PROSPER LUMC	3.2	418	579
Type 2 Diabetes	CODAM MUMC	7	145	
	Maastricht Study MUMC		854	
	DZS West-Friesland VUMC	10	1000	
	HELUIS AMC		500	
Osteoarthritis	GARP LUMC	2-6	412	2030
	RAAK-PAPRIKA LUMC		476	2030
	EUMC OA	6.6	793	1000
	CHECK	8	981	
Omics	500 FG			500
	LifeLines			1500

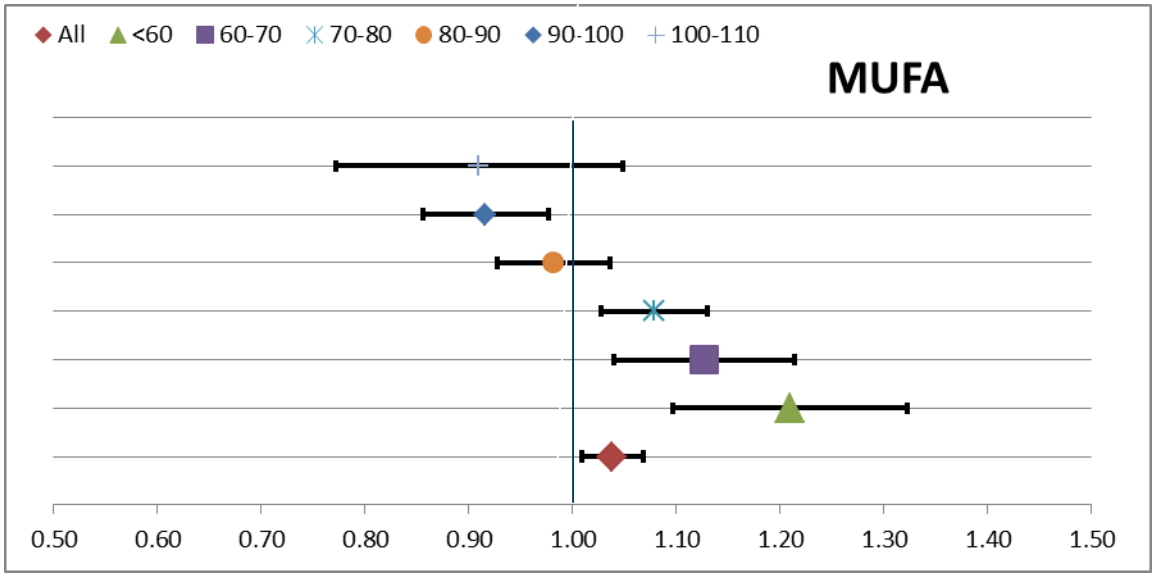
22 cohorts in BBMRI

LUMC
VU
VUMC
EUMC
UMCG
MUMC
WUR
AMC
RUMC

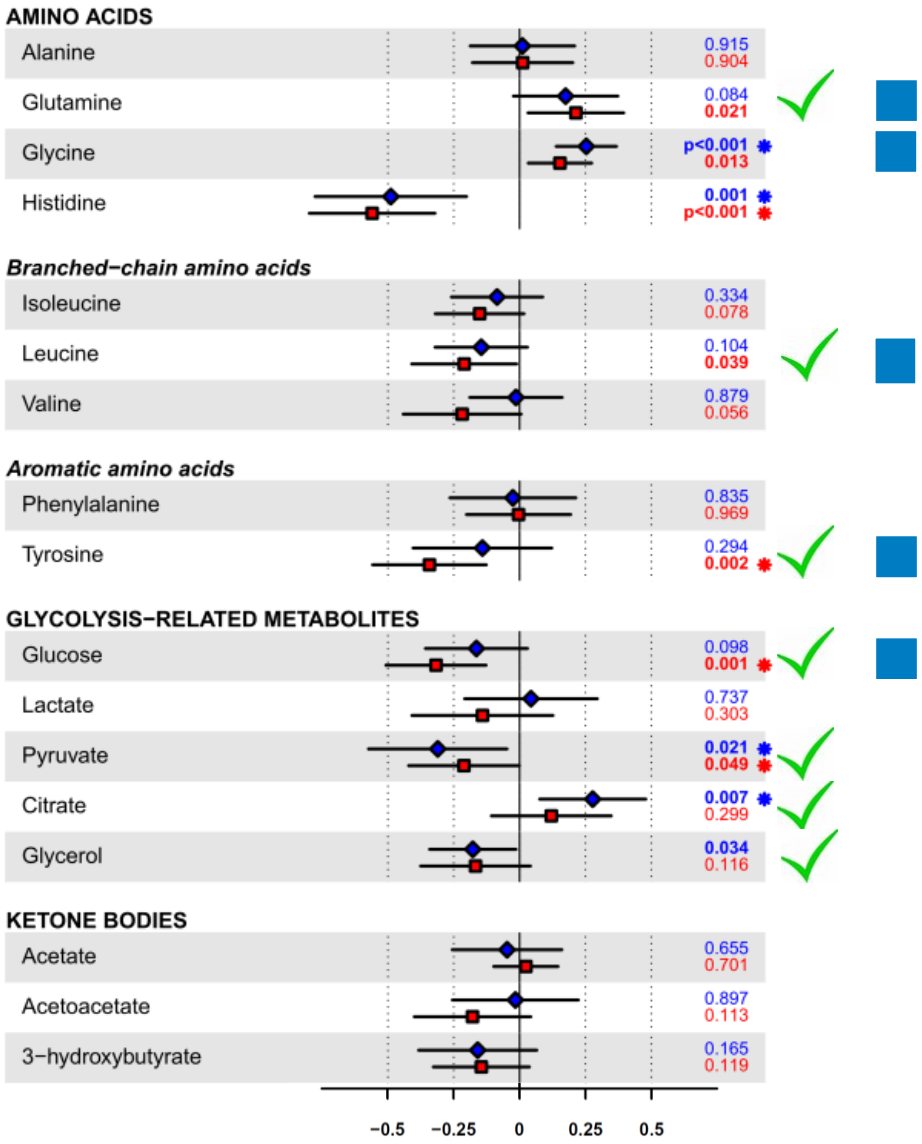
Disease-specific
Generic profiles

Metabolites and Mortality (N=40.000)
Personalised/stratified risk assessment

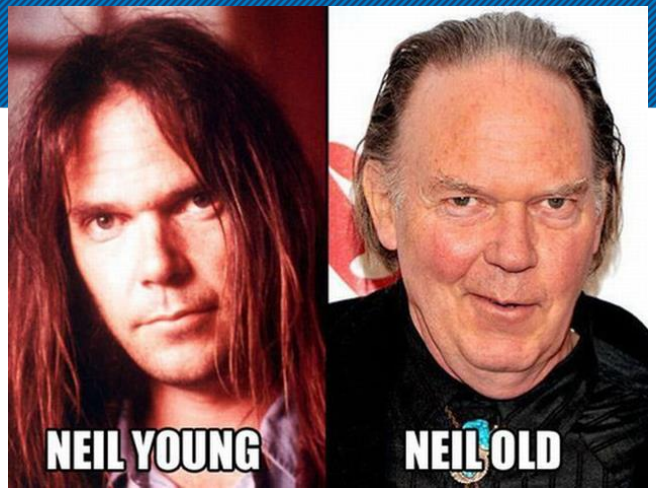




GOTO: Beneficial Profile after intervention



* Independent of weight change



Aging is Inevitable

Stay Fit, Stay Vertical

Leiden University
Medical Center

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By nurture, how to monitor and influence healthy ageing

Game changers: Integrating basic, biomedical and medical research

LUMC : Medical Research Profile on Ageing

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More systematic observation of elderly in the clinic (TENT)

Not treating

Teaching

National Biobanking : BBMRI.Nl

Triaging Elderly Needing Treatment (TENT)

Standardized vitality assessment and biobanking

Leids Universitair Medisch Centrum

HagaZiekenhuis

MCH Medisch Centrum Haaglanden

bronovo

Not Treating or Nutritional Medicin

JAMA Internal Medicine
Formerly *Archives of Internal Medicine*

Original Investigation

Effect of Discontinuation of Antihypertensive Treatment in Elderly People on Cognitive Functioning—the DANTE Study Leiden
A Randomized Clinical Trial

Justine E. F. Moonen, MD; Jessica C. Foster-Dingley, MSc; Wouter de Ruijter, MD, PhD; Jeroen van der Grond, PhD; Anne Suzanne Bertens, MD; Mark A. van Buchem, MD, PhD; Jacobijn Gussekloo, MD, PhD; Huub A. Middelkoop, PhD; Marieke J. H. Wermer, MD, PhD; Rudi G. J. Westendorp, MD, PhD; Anton J. M. de Craen, PhD; Roos C. van der Mast, MD, PhD

IMPORTANCE Observational studies indicate that lower blood pressure (BP) increases risk for cognitive decline in elderly individuals. Older persons are at risk for impaired cerebral autoregulation; lowering their BP may compromise cerebral blood flow and cognitive function.

OBJECTIVE To assess whether discontinuation of antihypertensive treatment in older persons with mild cognitive deficits improves cognitive, psychological, and general daily functioning.

DESIGN, SETTING, AND PARTICIPANTS A community-based randomized clinical trial with a blinded outcome assessment at the 16-week follow-up was performed at 128 general practices in the

Invited Commentary
page 1630

Supplemental conte
jamainternalmedicin

CME Quiz at
jamanetworkcme.co

Master Vitality and Ageing

Universiteit Leiden
The Netherlands

Leiden University Medical Center

Master Vitality and Ageing focus on

Content

- Biological mechanismes of ageing
- Older individuals
- Organisation of ageing society

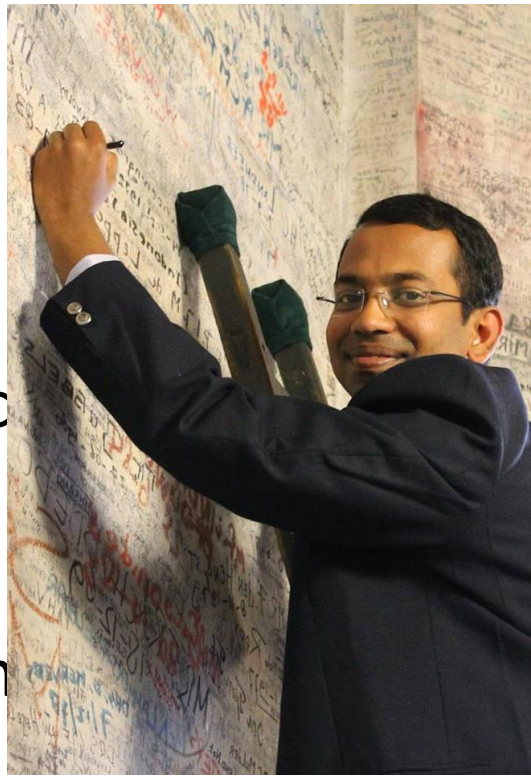
- **Skills**
- Communication in science
- Evidence – research
- Academic Skills

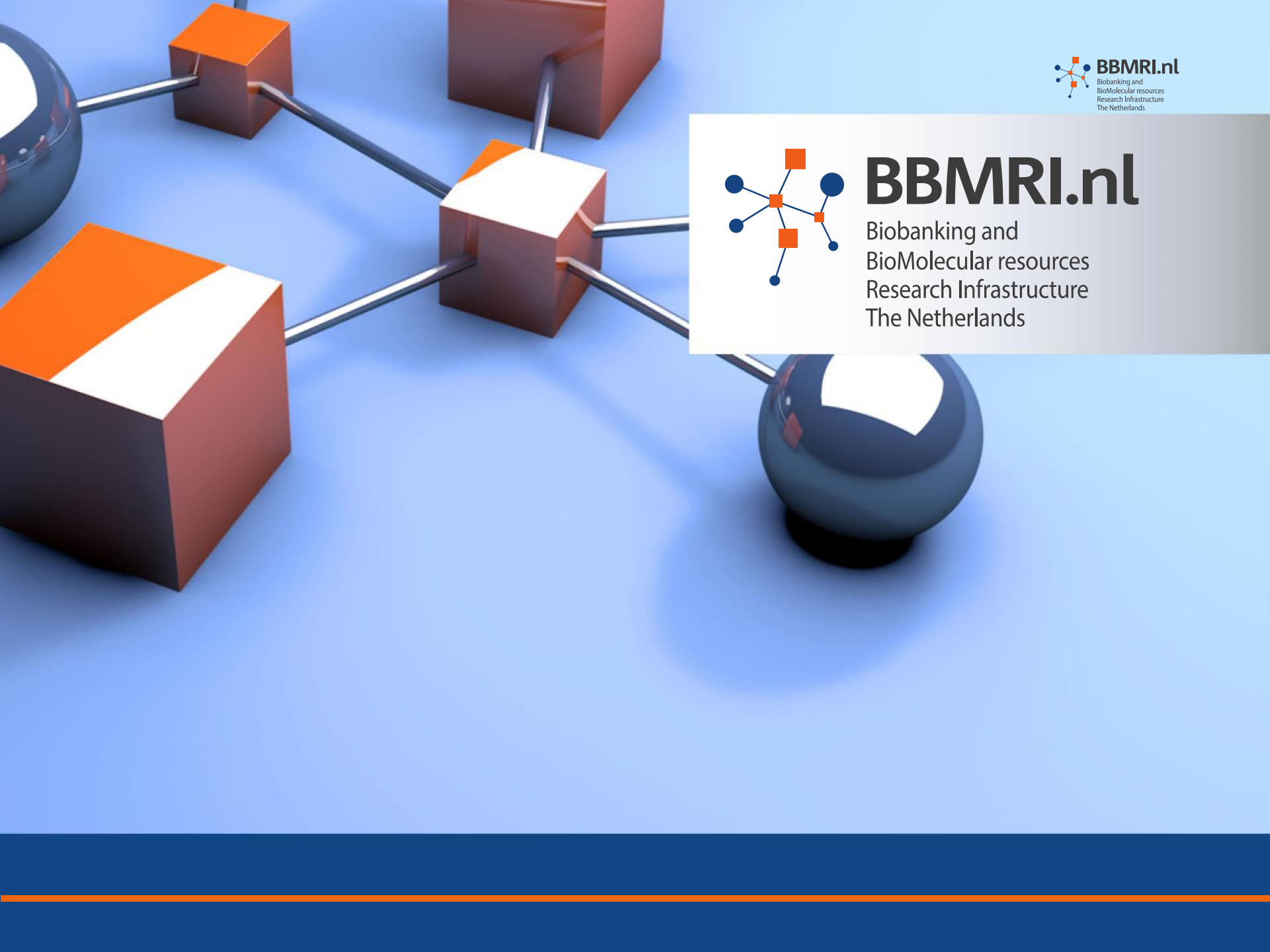
After graduation

Scientific career
Further education in science
(leading to a PhD degree)

Medical career
Further medical education
(geriatrics, internal medicine, general prac

Management career
Management position in care organisation
governmental organisations




BBMRI.nl
Biobanking and
BioMolecular resources
Research Infrastructure
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BioMolecular resources
Research Infrastructure
The Netherlands

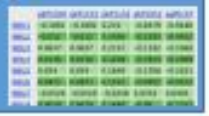
BBMRI-NL : Biobanking and BioMolecular resources Research Infrastructure in The Netherlands

- Nation wide biobanking infrastructure
- Founded in 2009: Dutch node of EU BBMRI-ERIC
- > 200 Dutch biobanks
- Sharing of Molecular, Clinical, Imaging Data. Accessible for scientific community.
- Big data combined to stimulate personalized /stratified medicine
- Dutch National Tissue Bank Portal

Ambition BBMRI-NL

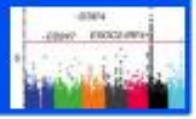
Catalogue
Find data item and sample collections

Data
Filter and download for further analysis



Workflows
Data entry and management workflows

GWAS
Explore summary level GWAS data



Harmonisation
Ontologies, standards, tools

Analyse
Multi-omics association & visualization tools

Pipelines
Next-Generation Sequencing

Integration
Personalized and stratified medicine markers

Share
Friends, Groups and Permission management

Mutation
Explore genetic mutations and patho-genicity effects

Organization
Institutes, Departments, People, Locations & Containers

Imaging
File storage and analysis for images and data

Website BBMRI.nl

Catalogue with > 200 biobanks

ELSI center of expertise

BBMRI.nl
Biobanking and BioMolecular resources Research Infrastructure The Netherlands

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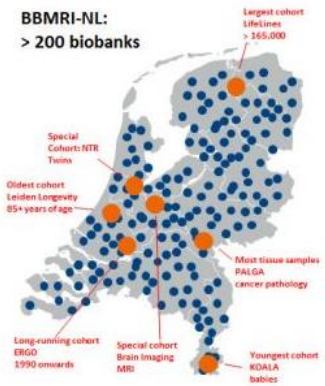
Tools & Applications

WELCOME TO THE BBMRI-NL WEBSITE

For over six years, BBMRI-NL has been actively promoting collaboration and standardization between biobanks in the Netherlands. We represent the main body of biobanks in this country, including the PALGA pathology collections, large population cohorts such as LifeLines, ERGO, NTR, and LLLS, and clinical collections (Parelsnoer Institute, HEBON, KOALA, to name but a few).

Now, we have set our aims at uniting all relevant biomedical research infrastructures into one streamlined, efficient body of research infrastructure.

Towards a National Biobanking Infrastructure



SEARCH

Search ... GO

RECENT NEWS

Vidi grant for Morris Swertz

FAQs on the General Data Protection Regulation for biobanking

BBMRI-NL at Open Science Conference 4-5 april

One national research infrastructure for prevention, personalized treatment, and health

De maatschappelijke adviesraad zoekt deelnemers

BBMRI.nl Ethical, Legal, Social issues the site for the public, donors, politics and press

http://www.bbmri.nl/wp-

Music, Science and Humor
Collaborations with Brasil