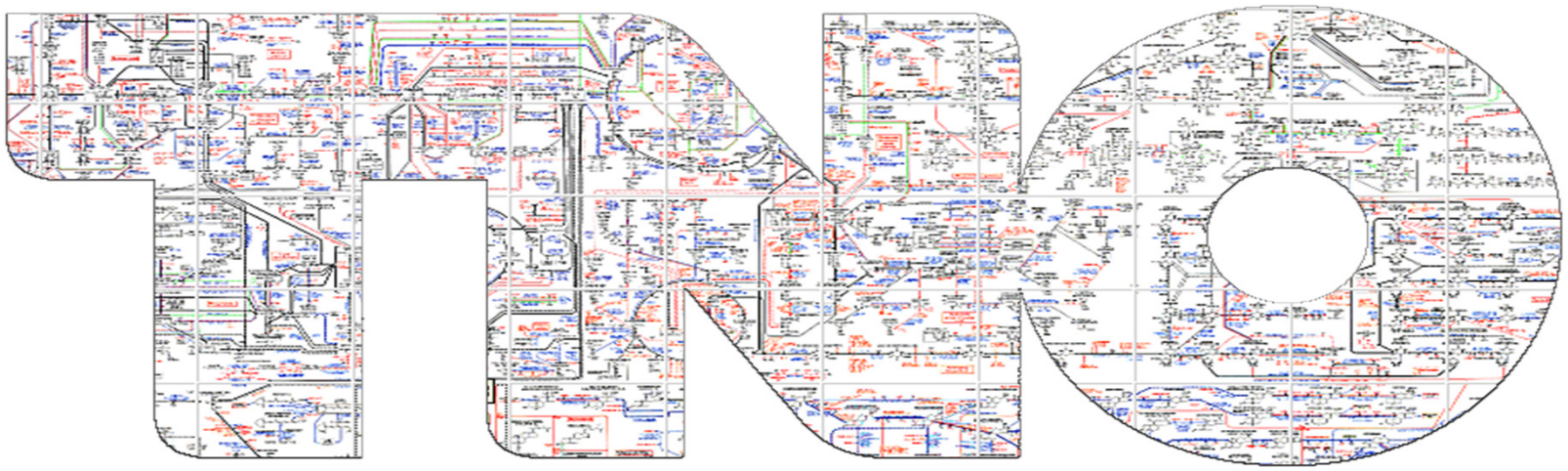
TNO innovation for life

State of the Science and Technology in Personalized Nutrition

Ben van Ommen



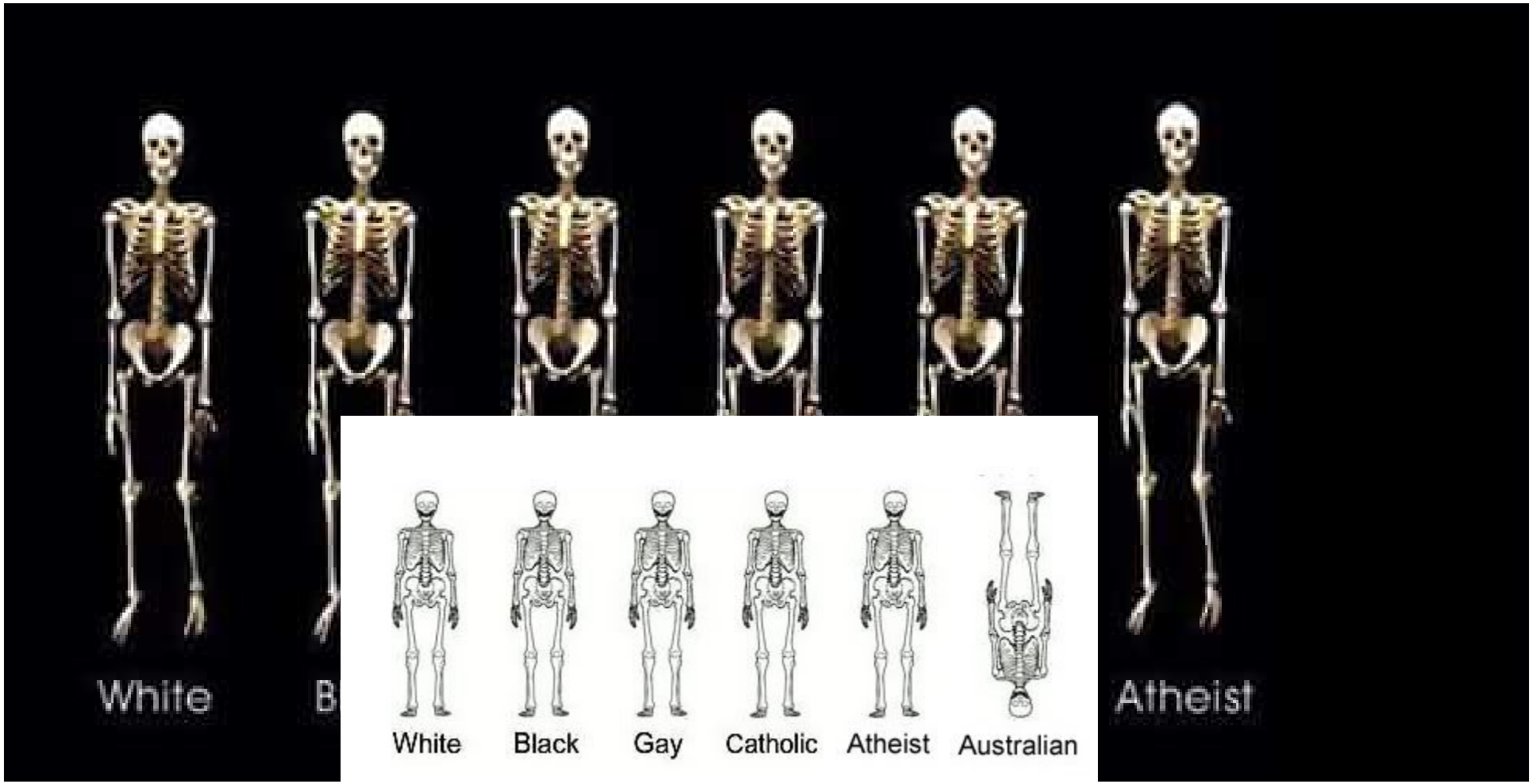
Personalized nutrition – the questions

- Are we different in our nutritional needs?

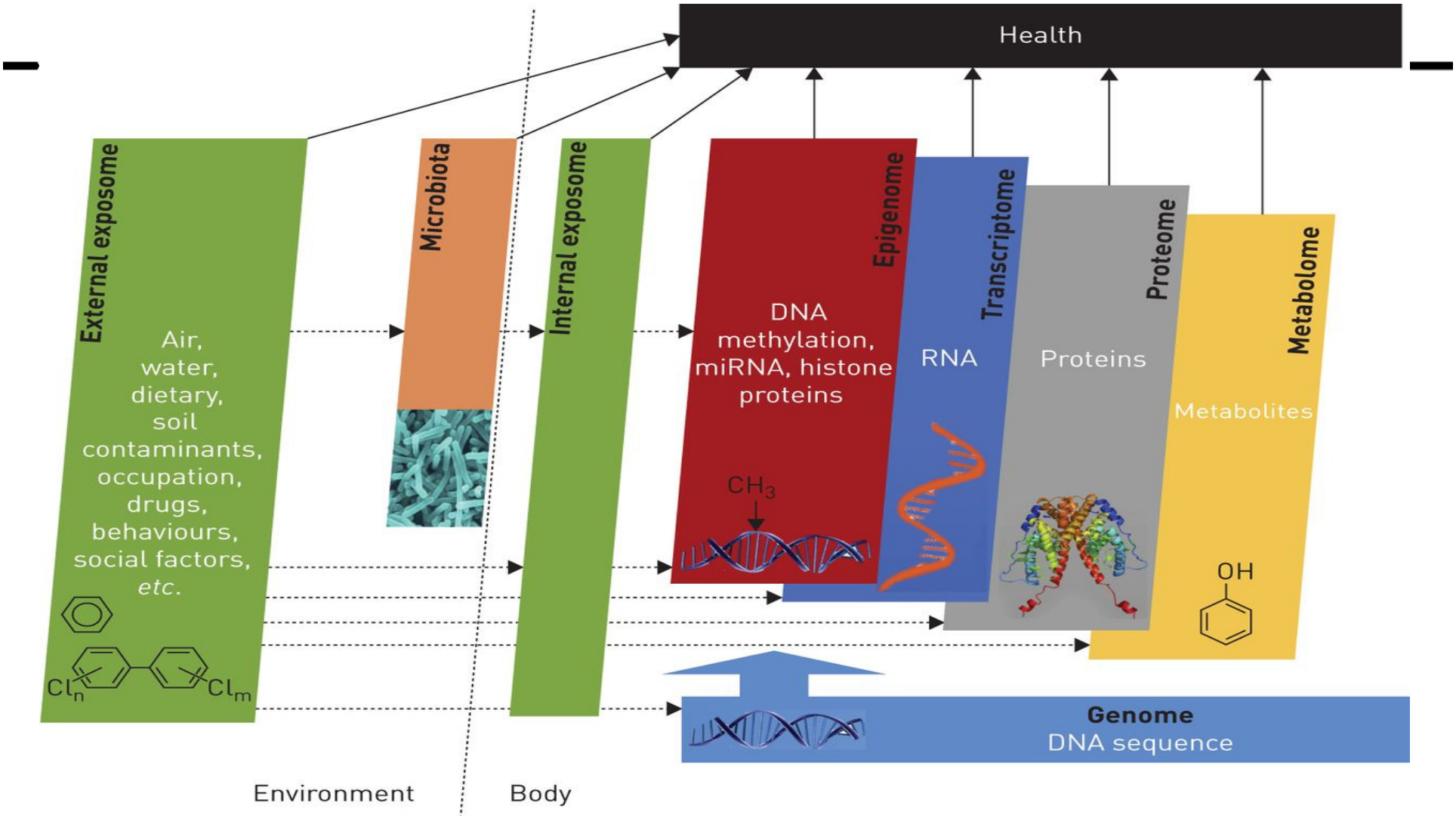
- What is my optimal nutrition
  - What is my health?
  - What do I know about my health

- How can I act upon it?
- About applications in disease
- The (business) way forward

Different from the inside…

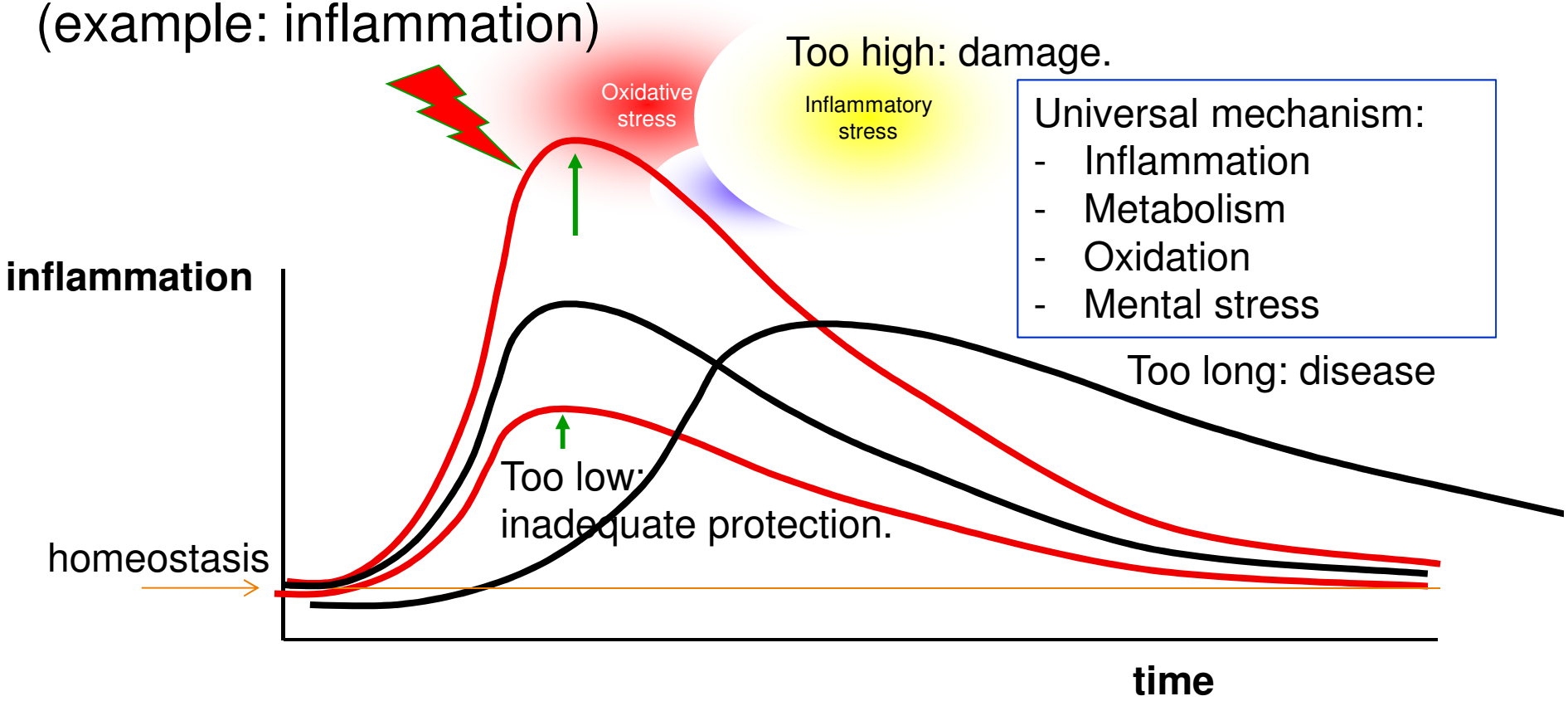


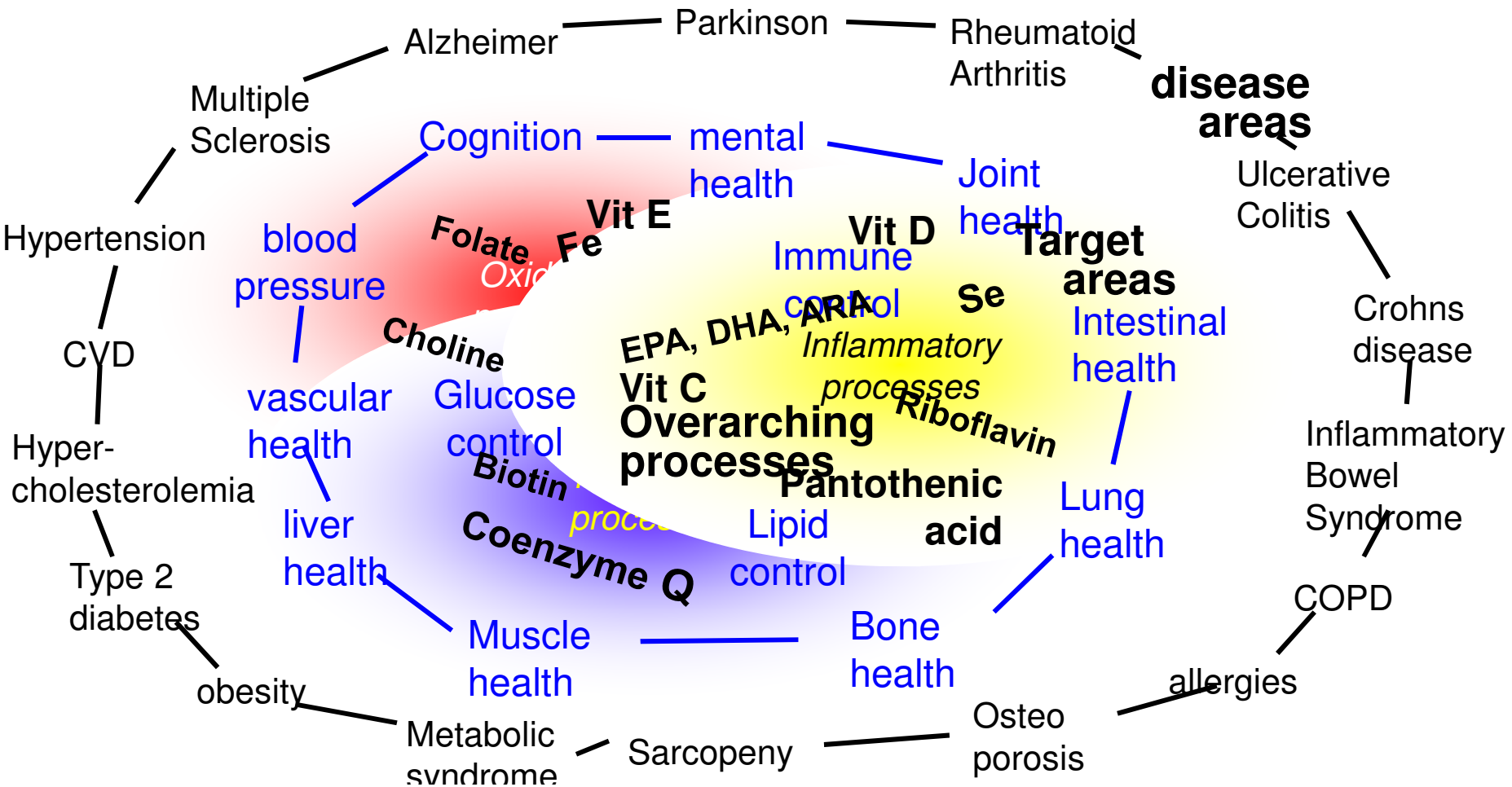
Different from the outside…


Health
External exposome
Air, water, dietary, soil contaminants, occupation, drugs, behaviours, social factors, etc.
Microbiota
Internal exposome
Epigenome
DNA methylation, miRNA, histone proteins
CH3
Transcriptome
RNA
Proteome
Proteins
Metabolome
Metabolites
OH
Cln
Clm
Genome
DNA sequence
Environment
Body

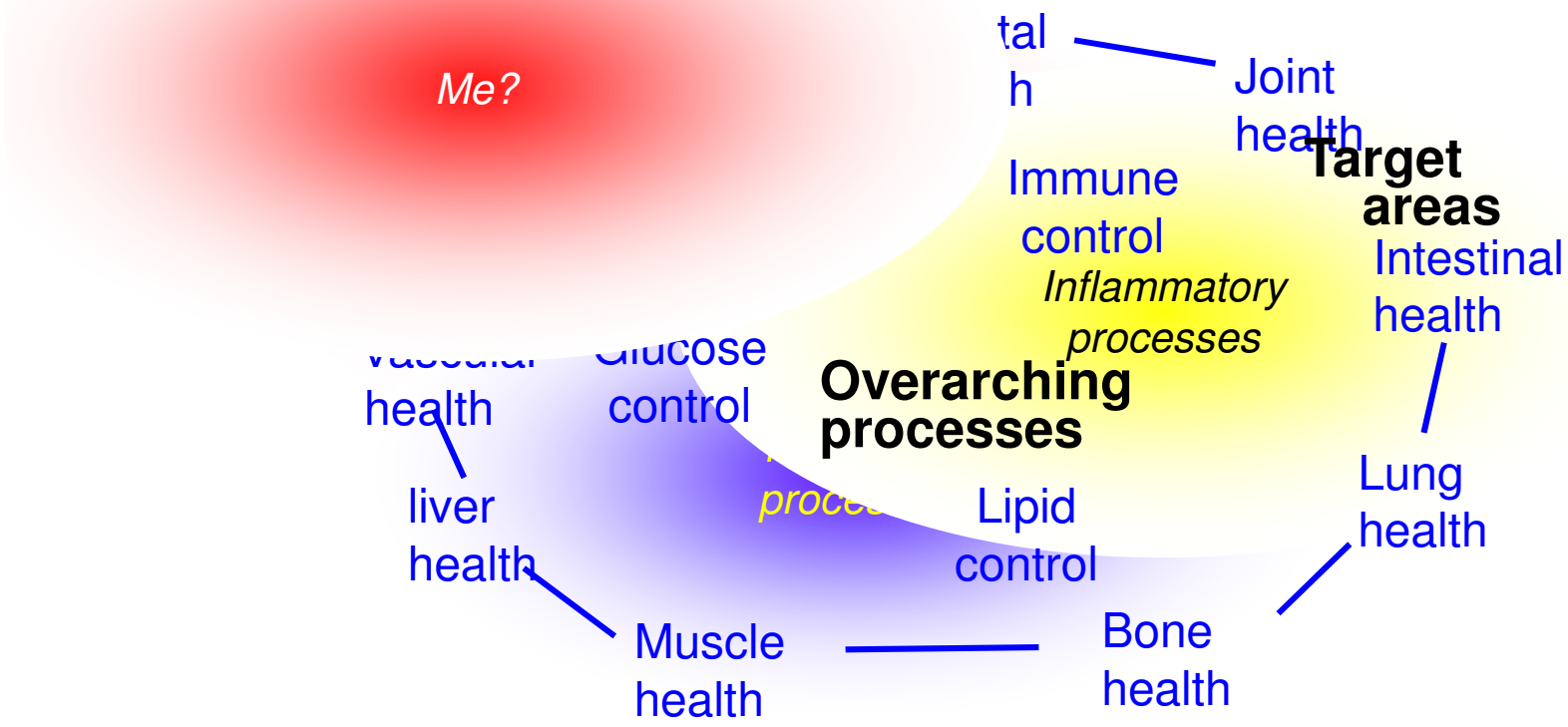
Health is not static but “the ability to adapt”

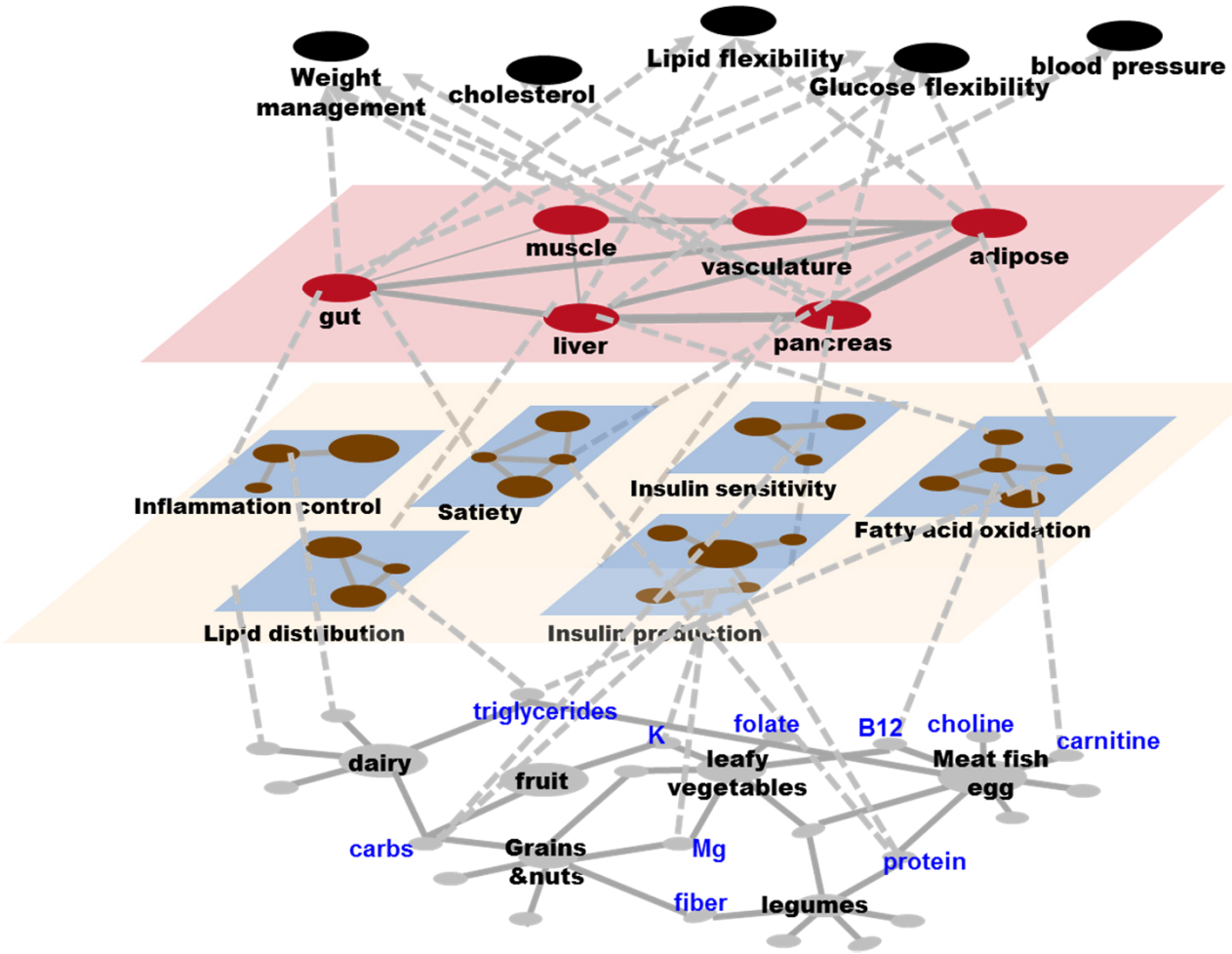
(example: inflammation)




Alzheimer
Parkinson
Rheumatoid Arthritis
Multiple Sclerosis
disease areas
Cognition
mental health
Joint health
Ulcerative Colitis
Hypertension
blood pressure
Folate
Fe
Vit E
Vit D
Target areas
Immune control
Se
Intestinal health
Crohns disease
CVD
Choline
EPA, DHA, ARA
Inflammatory processes
Vit C
Overarching processes
Riboflavin
Hyper-cholesterolemia
vascular health
Glucose control
Biotin
Pantothenic acid
Lung health
Inflammatory Bowel Syndrome
liver health
Lipid control
Coenzyme Q
Type 2 diabetes
COPD
Muscle health
Bone health
obesity
allergies
Metabolic syndrome
Sarcopeny
Osteo porosis

heme and what should I eat to



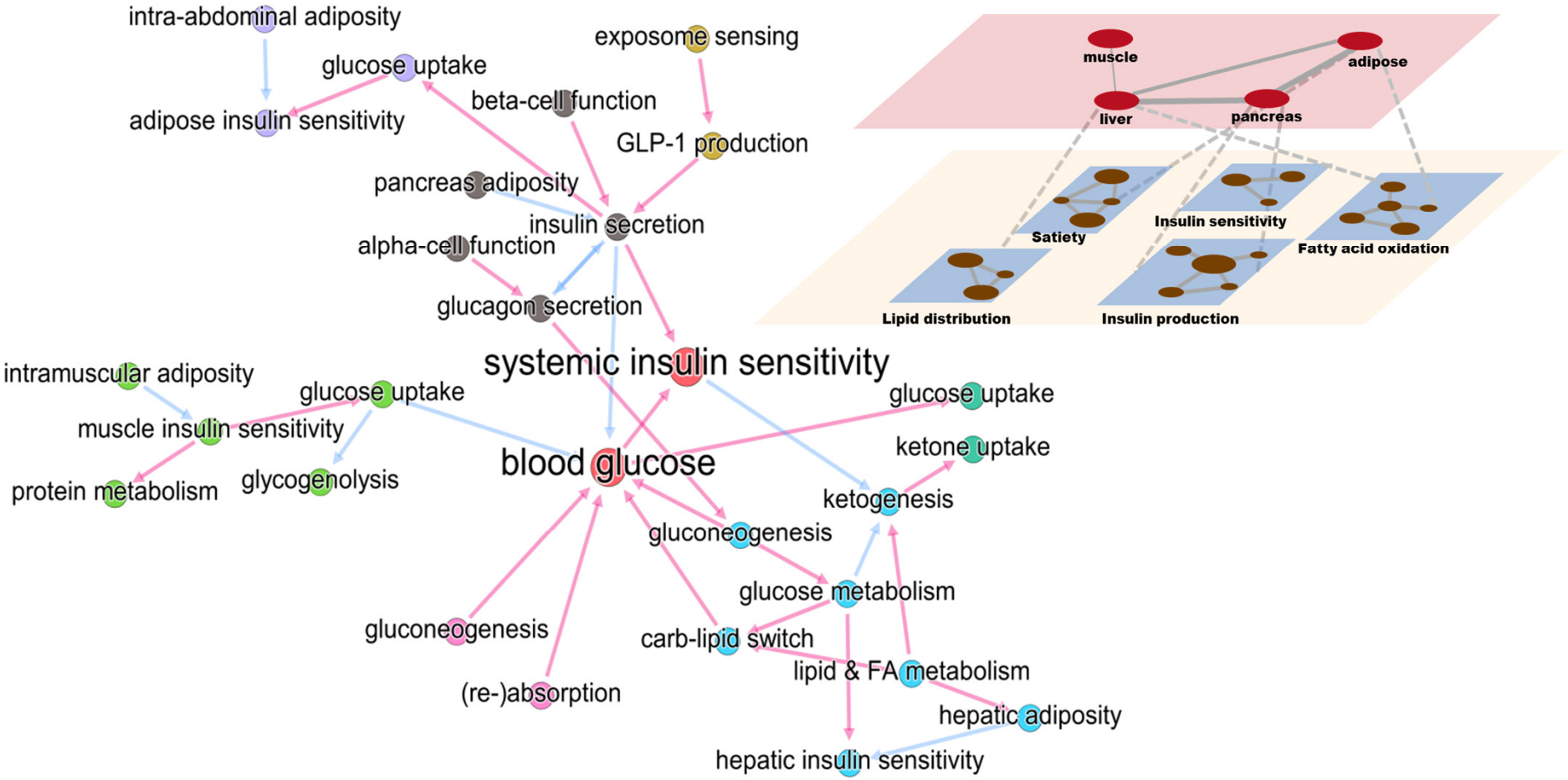


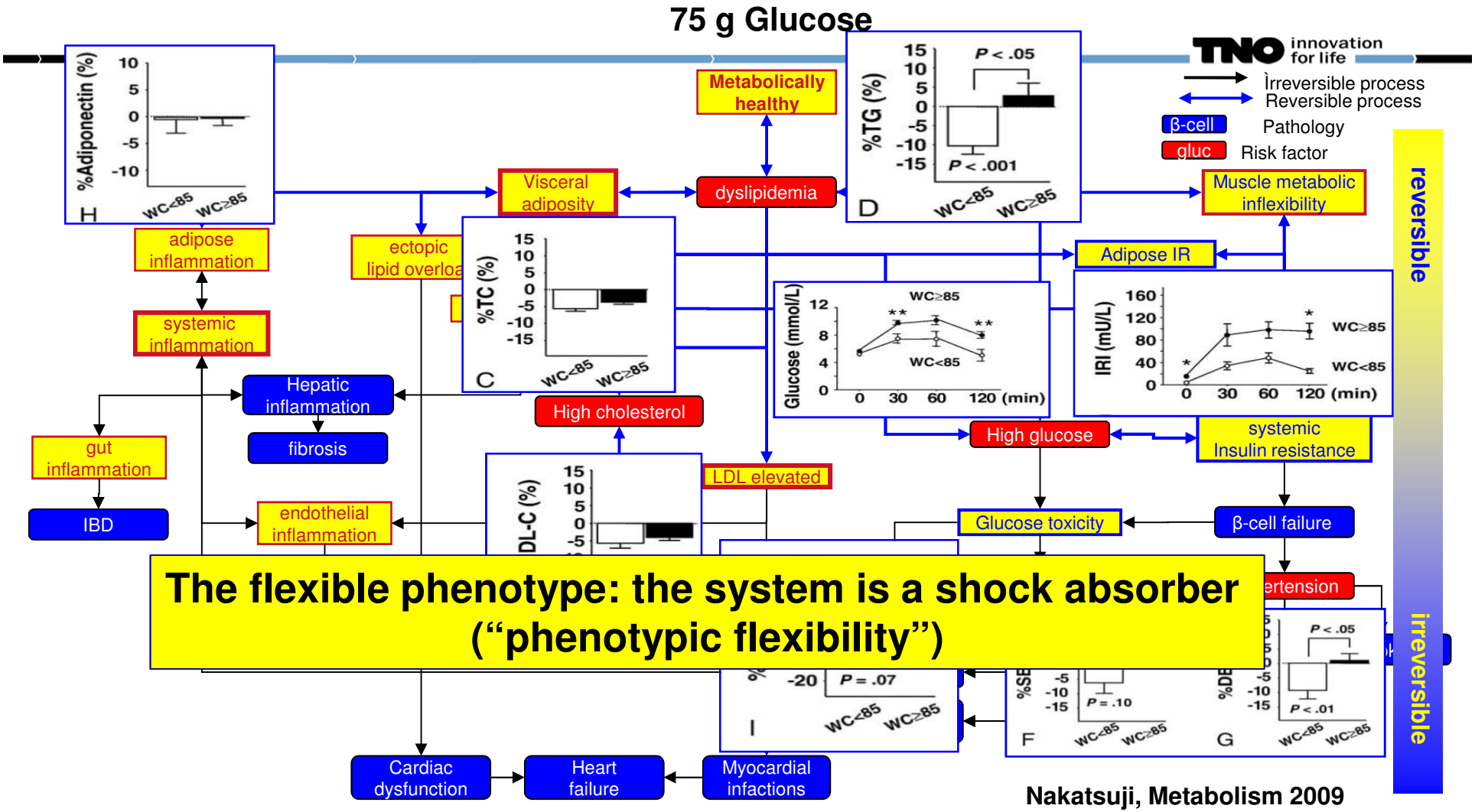
personalized nutrition based consumer goals

organs

flexibility processes and sub-processes

nutrients
(connected in diets)


intra-abdominal adiposity
glucose uptake
adipose insulin sensitivity
exposome sensing
beta-cell function
GLP-1 production
pancreas adiposity
insulin secretion
alpha-cell function
glucagon secretion
systemic insulin sensitivity
intramuscular adiposity
glucose uptake
muscle insulin sensitivity
protein metabolism
glycogenolysis
blood glucose
glucose uptake
ketone uptake
ketogenesis
gluconeogenesis
glucose metabolism
gluconeogenesis
carb-lipid switch
lipid & FA metabolism
(re-)absorption
hepatic adiposity
hepatic insulin sensitivity
muscle
adipose
liver
pancreas
Satiety
Insulin sensitivity
Fatty acid oxidation
Lipid distribution
Insulin production



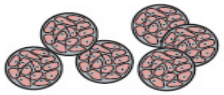
The flexible phenotype: the system is a shock absorber ("phenotypic flexibility")

Nakatsuji, Metabolism 2009

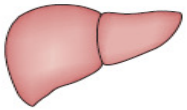
Phenotypic Flexibility as biomarker of health

134 biomarkers report on challenge responses in organs

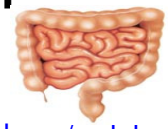
Brain
- Secondary messengers
- Trp, Tyr, Phe, Met



Pancreas
- Disposition index
- C-peptide
- Insulin
- Glucagon
- HOMA-B



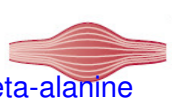
Liver
- Ketone bodies
- Central metabolism
- ALAT, ASAT, ALP, GGT
- CRP
- TG
- Liver IR index
- Liver IS index



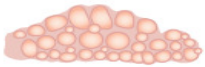
Gut
- Fructose, ribulose / xylulose
- GIP, GLP-1
- Indole-3-proprionic acid

Metabolic challenge

- Matsuda index, HbA1C, HOMA-IR
- glucose, 1,5-anhydroglucitol
- Glutathione ratio, uric acid, vit E
- mannose, ribose, glycine, pseudo uridine
- *RQ measures*




Muscle
- Lactate, beta-alanine
- Muscle IR index
- Branched chain amino acids & derivatives
- 1-methylhistidine, 3-methylhistidine
- 4-hydroxyproline, 4-oxoproline



Adipose tissue
- Glycerol, NEFA & specific FFA
- MG, DG
- Leptin, adiponectin
- Estimated SCD activity
- C16:1 FFA
- Adipose IR index

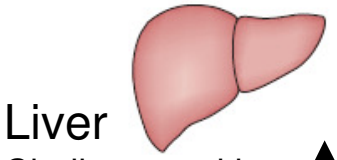
Kidney
- Creatinin
- Asp, Glu, Orn, Urea
- Albumin

Vasculature
- Cholesterol, HDL, LDL
- SAA, sICAM, sVCAM

PhenFlex challenge:
- **75 g glucose**
- **60 g palmoic oil**
- **20 g protein**

Blue = responding
Green = not responding
Back = could not be determined

Personalized (Micro)nutrient Recommendations
related to systems flexibility



Liver
Choline, carnitine

low grade inflammation

vitD, VitE, Mg,
ω-3 fatty acid, flavonoids,
curcuminoids

Catechins?

Vasculature
vitC, K, cocoa flavanols,
NO-producing nutrients,
lycopene

Pancreas
Leucine, vitK, vitD, Mg

Metabolic challenge

Quercetin, Se, Zn, …

time

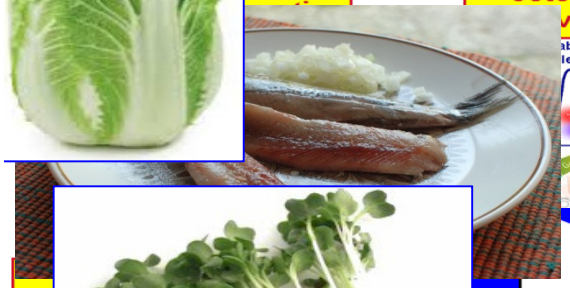
Visceral adiposity

Stannols,fibre

ectopic overload

Adipose IR

glycemic index



Type 2 diabetes subgroups react differently on different diets

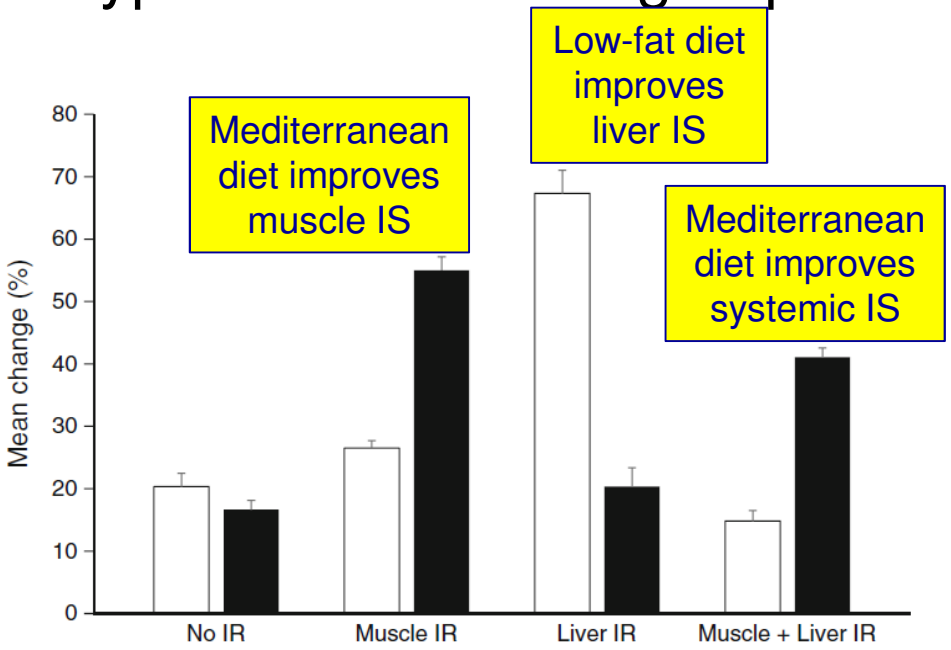
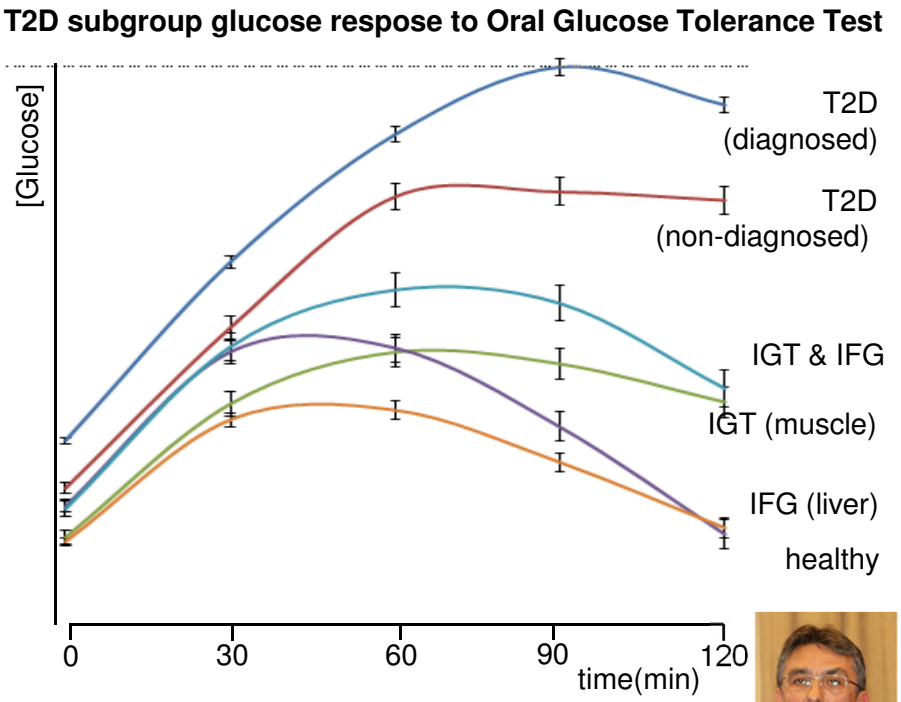
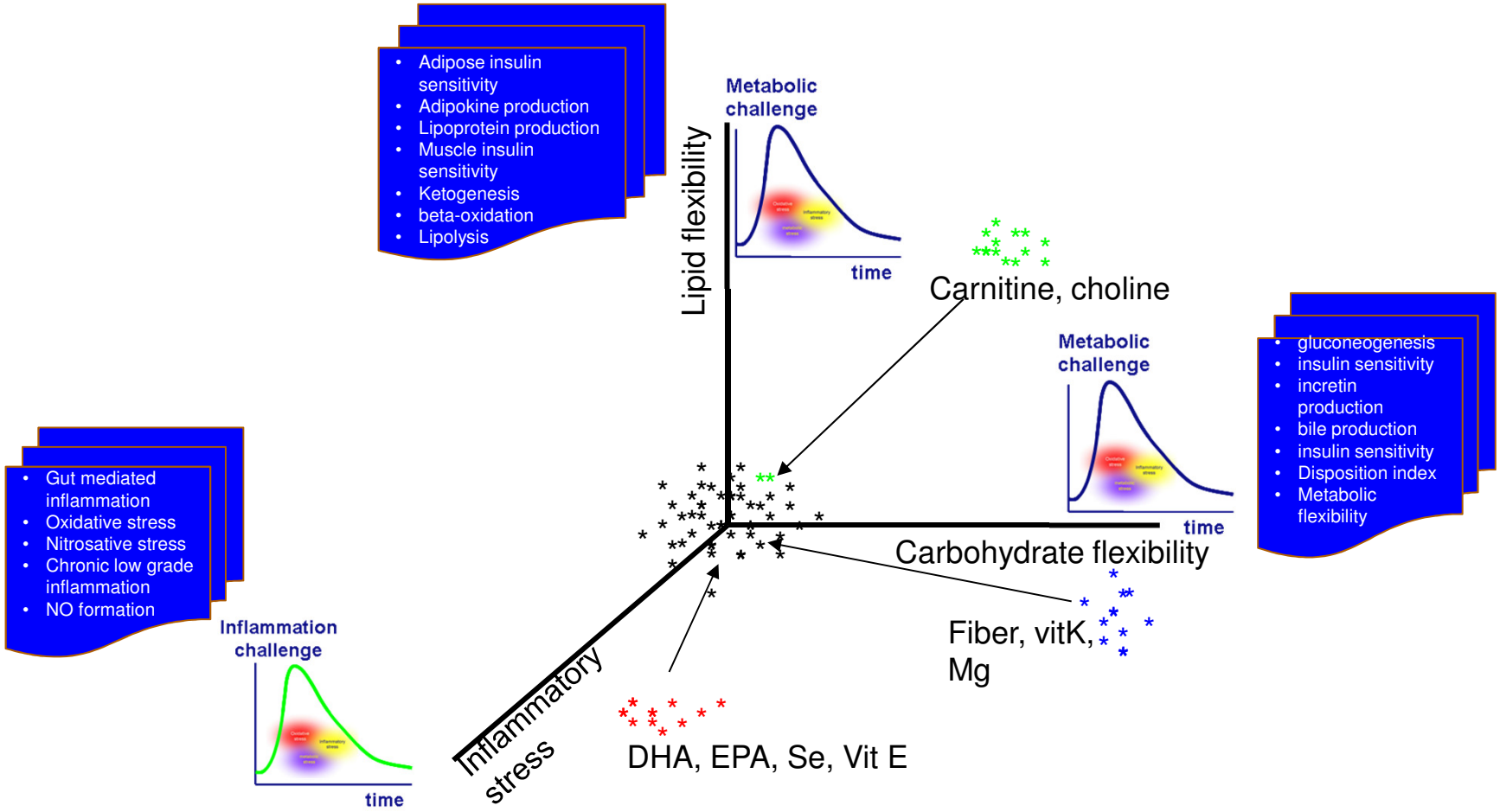


Fig. 1 Mean percentage change in values of disposition index between baseline and after 2 years of follow-up by IR phenotype. *$p<0.05$ between low-fat diet (white bars) and Mediterranean diet (black bars) in each IR subgroup analysed using a univariate model adjusted for age, sex, baseline BMI and change in weight

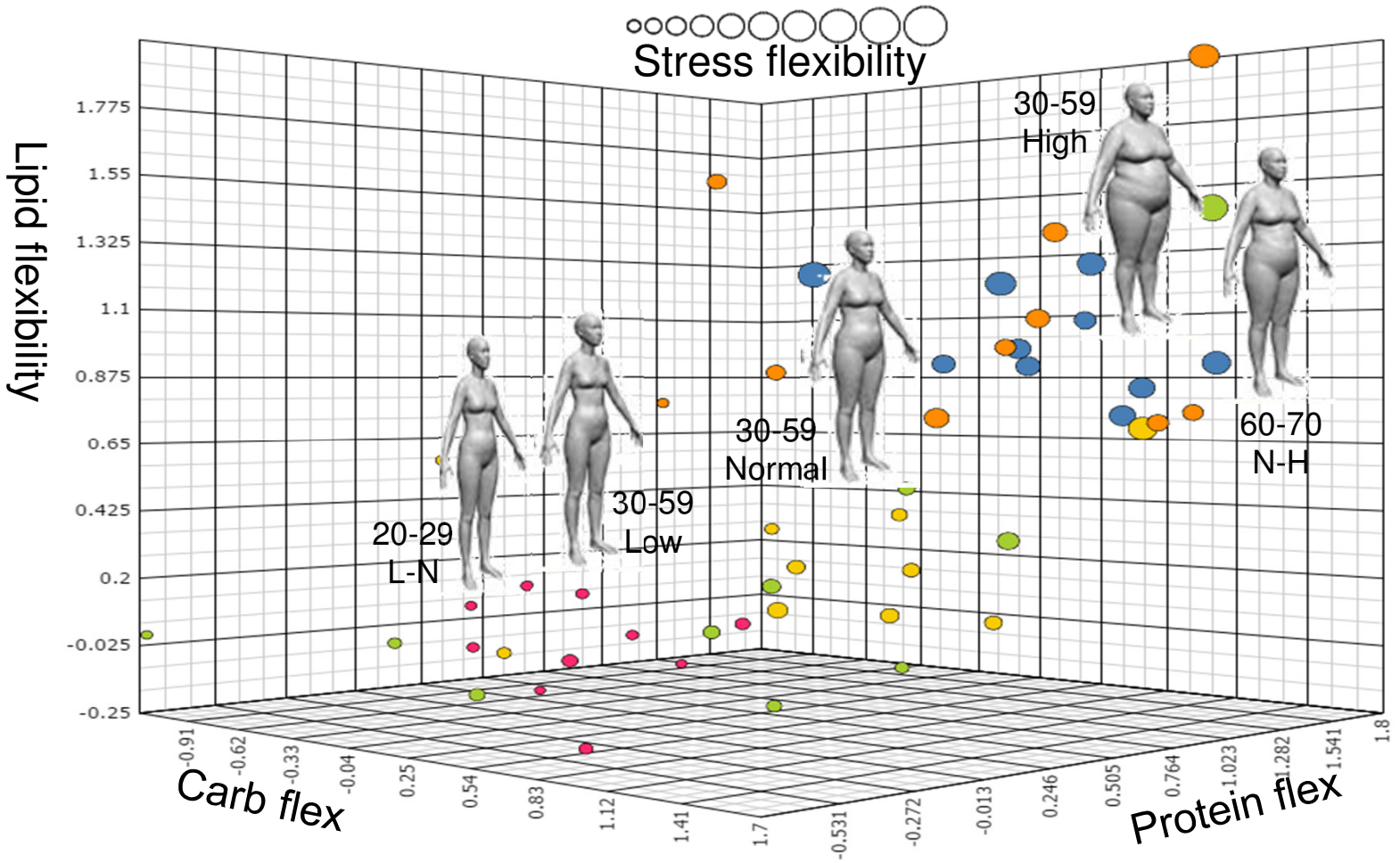


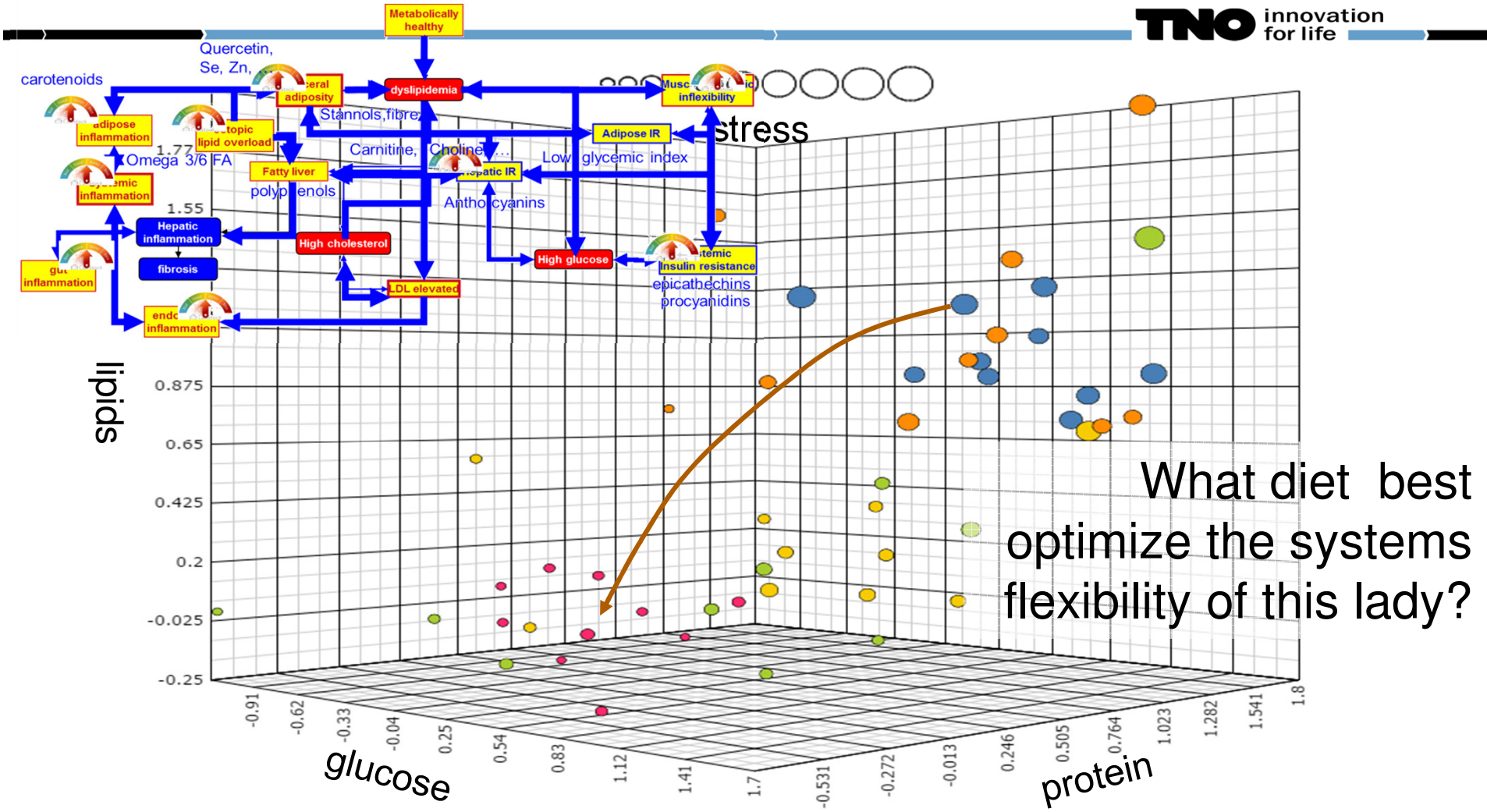
Blanco-Rojo, Diabetologia, Oct 2015

José Lopez-Miranda

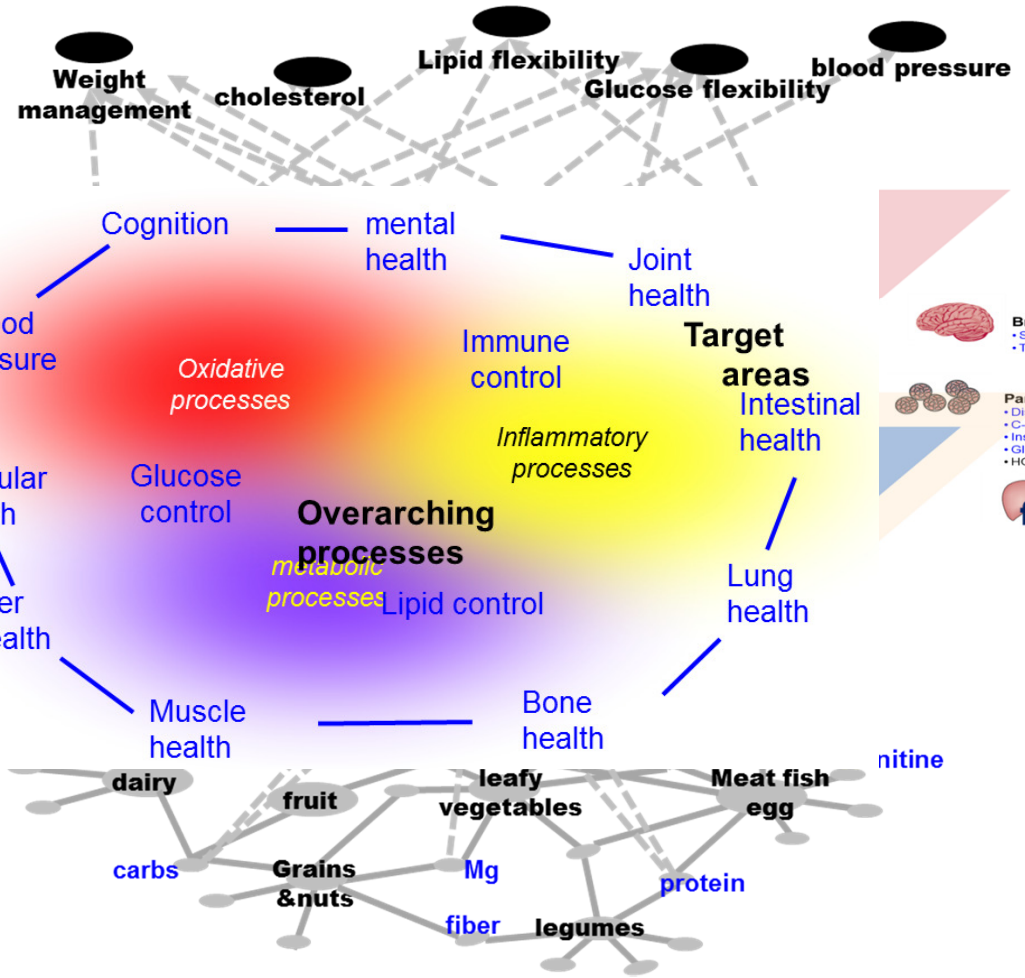

Adipose insulin sensitivity
Adipokine production
Lipoprotein production
Muscle insulin sensitivity
Ketogenesis
beta-oxidation
Lipolysis
Metabolic challenge
time
Lipid flexibility
Carnitine, choline
Metabolic challenge
time
gluconeogenesis
insulin sensitivity
incretin production
bile production
insulin sensitivity
Disposition index
Metabolic flexibility
Carbohydrate flexibility
Fiber, vitK, Mg
Gut mediated inflammation
Oxidative stress
Nitrosative stress
Chronic low grade inflammation
NO formation
Inflammation challenge
time
Inflammatory stress
DHA, EPA, Se, Vit E

Phenotypic flexibility of 50 healthy subjects in a “health space”

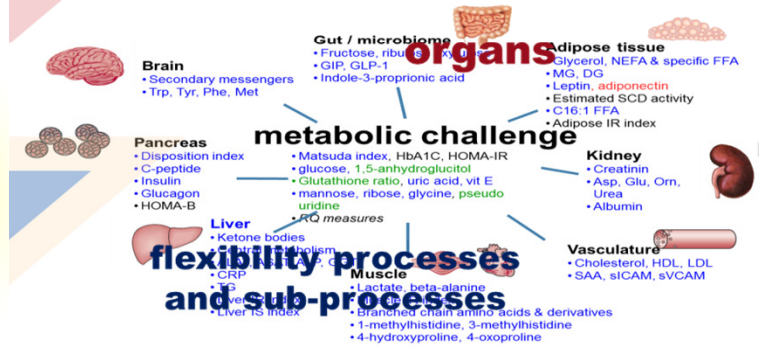




What diet best optimize the systems flexibility of this lady?



personalized nutrition based consumer goals



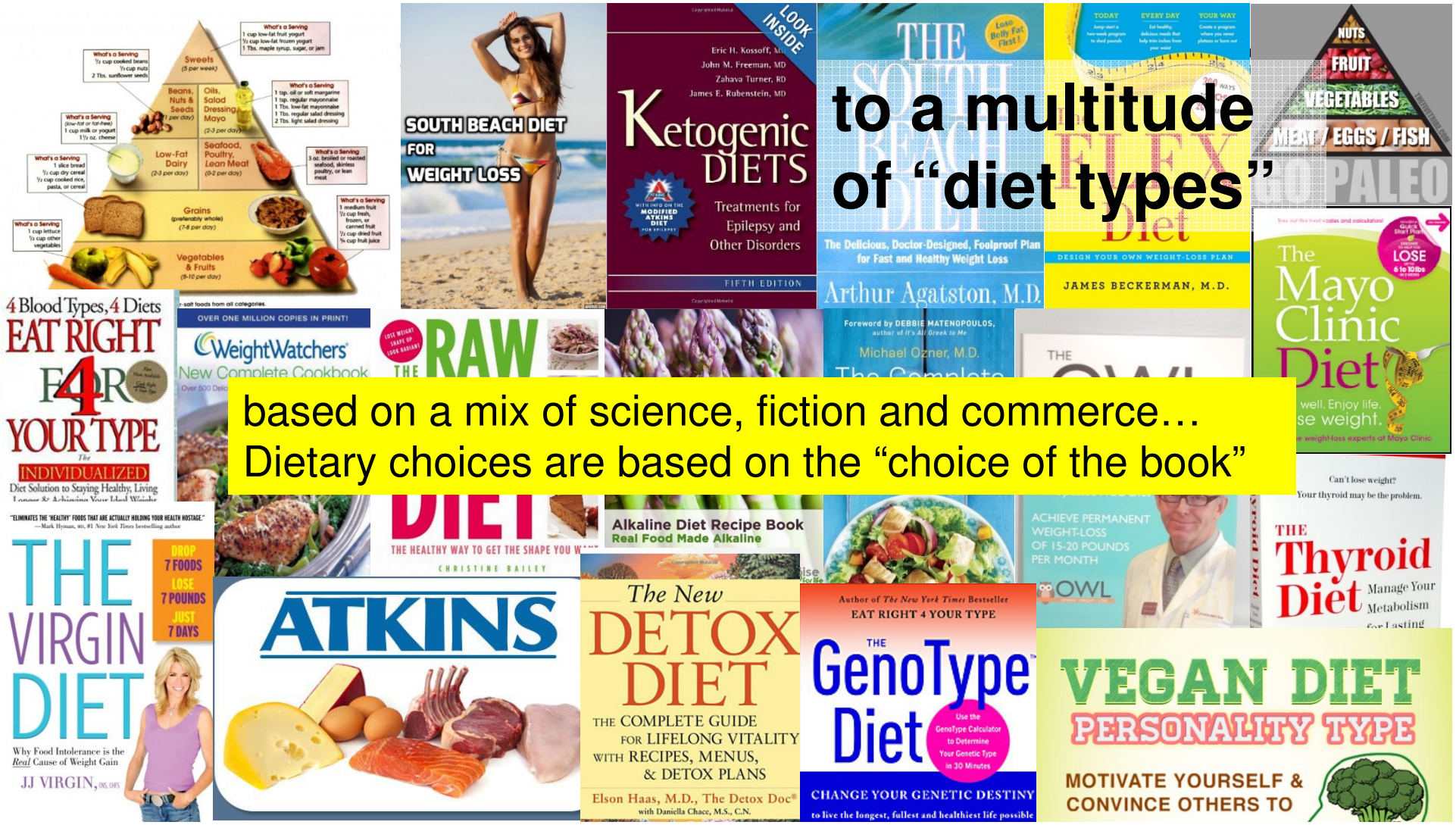
nitine

nutrients
(connected in diets)

So what`s the right diet for me?

From public Health dietary recommendations

dietary recommendations are mostly based on epidemiology: associations of the masses

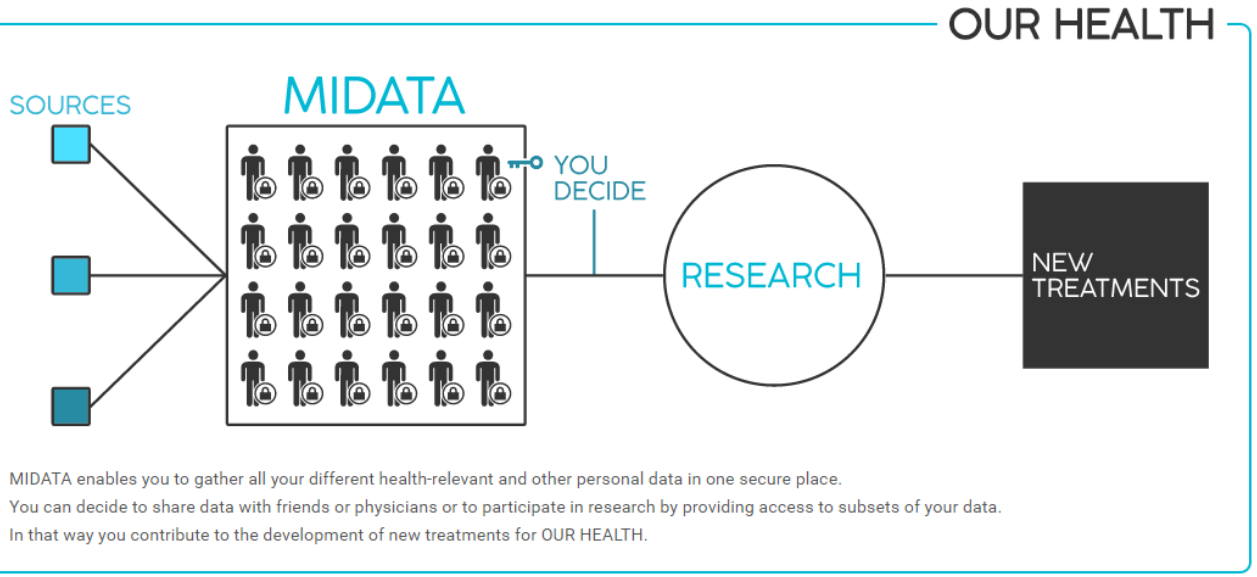

to a multitude of "diet types"
based on a mix of science, fiction and commerce…
Dietary choices are based on the "choice of the book"
Sweets
Beans, Nuts & Seeds
Oils, Salad Dressing, Mayo
Low-Fat Dairy
Seafood, Poultry, Lean Meat
Grains
Vegetables & Fruits
SOUTH BEACH DIET FOR WEIGHT LOSS
Ketogenic DIETS
Treatments for Epilepsy and Other Disorders
FIFTH EDITION
THE SOUTH BEACH DIET
The Delicious, Doctor-Designed, Foolproof Plan for Fast and Healthy Weight Loss
Arthur Agatston, M.D.
FLEX Diet
DESIGN YOUR OWN WEIGHT-LOSS PLAN
JAMES BECKERMAN, M.D.
NUTS
FRUIT
VEGETABLES
MEAT / EGGS / FISH
PALEO
The Mayo Clinic Diet
4 Blood Types, 4 Diets
EAT RIGHT 4 YOUR TYPE
The INDIVIDUALIZED Diet Solution to Staying Healthy, Living
OVER ONE MILLION COPIES IN PRINT!
WeightWatchers New Complete Cookbook
THE RAW DIET
THE HEALTHY WAY TO GET THE SHAPE YOU
CHRISTINE BAILEY
Foreword by DEBBIE MATENOPOULOS
Michael Ozner, M.D.
Alkaline Diet Recipe Book
Real Food Made Alkaline
ACHIEVE PERMANENT WEIGHT-LOSS OF 15-20 POUNDS PER MONTH
OWL
Can't lose weight?
Your thyroid may be the problem.
THE Thyroid Diet
Manage Your Metabolism
THE VIRGIN DIET
DROP 7 FOODS
LOSE 7 POUNDS
JUST 7 DAYS
Why Food Intolerance is the Real Cause of Weight Gain
JJ VIRGIN
ATKINS
The New DETOX DIET
THE COMPLETE GUIDE FOR LIFELONG VITALITY WITH RECIPES, MENUS, & DETOX PLANS
Elson Haas, M.D., The Detox Doc®
with Daniella Chace, M.S., C.N.
Author of The New York Times Bestseller
EAT RIGHT 4 YOUR TYPE
THE GenoType Diet
Use the GenoType Calculator to Determine Your Genetic Type in 30 Minutes
CHANGE YOUR GENETIC DESTINY
to live the longest, fullest and healthiest life possible
VEGAN DIET
PERSONALITY TYPE
MOTIVATE YOURSELF & CONVINCE OTHERS TO

Information overflow?

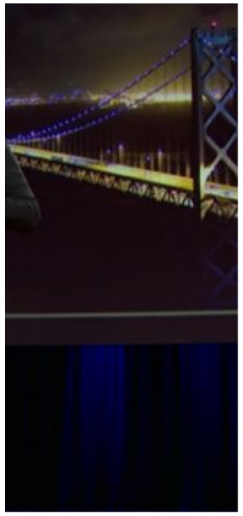
Misleading Information?

MIDATA.COOP

MY DATA – OUR HEALTH



MIDATA enables you to gather all your different health-relevant and other personal data in one secure place.
You can decide to share data with friends or physicians or to participate in research by providing access to subsets of your data.
In that way you contribute to the development of new treatments for OUR HEALTH.



this year, but is just coming to light now.

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The real value of MY health data: how can this data work for me?

Health Data Cooperative as legal entity that valorizes my own health data.

COOPERATIVE
Citizen-owned
Citizen-controlled

MyDataOurHealth

Developers

Doctors

Schools & daycare

Hospitals

Research

food industry

Infant formula producers

Education

Retail

Farmers market

Government

Health Service Providers

Ernst Hafen, ETH Zurich


CONSTANT
CRAVERS
They want to eat all the time


FEASTERS
Once they start, they can't stop

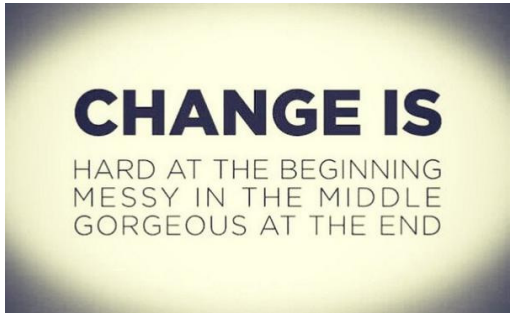

EMOTIONAL
EATERS
People who eat for
psychological reasons

DISCIPLINE

...is just choosing between
what you want now and what you want most.

Four Behavioural changes phases

Initial response	Continued response	maintenance	habit
Initial effort to change behavior	Continue effort to establish behavior	Sustained effort to continue newly established behavior	Self pertetuating pattern of behavior

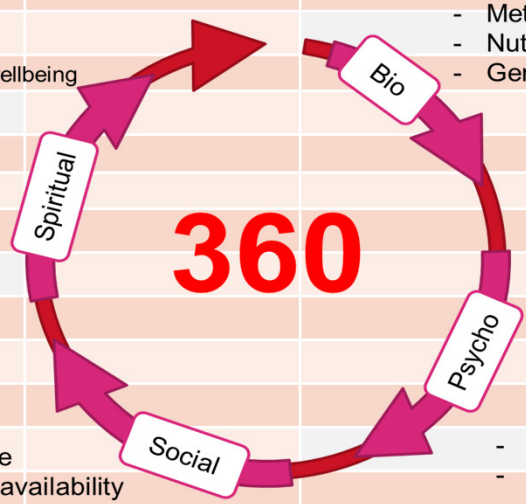


Rothman (2009) Disentangling behavioural initiation and behavioural maintenance

Each person deserves the right method for the right phase

Behavior Change Technique (93 different techniues)	Initial response	Continued response	Maintenance	Habit
Prompt practice	360 DEGREES DIAGNOSIS			
Stress management				
General communication skills training				
Environmental restructuring				
Model/demonstrate the behavior				
Goal setting (outcome)				
Relapse prevention/coping planning				
Facilitate social comparison				
Goal setting (behavior)				
Action planning				
Provide feedback on performance				
Barrier identification/problem solving				
Provide instruction				
Teach to use prompts/cues				
Provide normative information about others' behavior				
Plan social support/social change				

- Eudaimonic wellbeing
- Life goals
- Worldview
- Religion
- Mindfullness
- Gratefullness



- Metabolic status and flexibility
- Nutrition intake
- Genetics

- Peer pressure
- Food /sports availability
- Family habits
- Work environment
- Health literacy

- Dietary preferences
- Nutrition intake
- Stress resilience
- Personality type
- Coping styles

Example of individual approach based on 360°

Behavior Change Technique	Initial response	Continued response	Maintenance	Habit
Prompt practice				
Stress management				■
General communication skills training				
Environmental restructuring			■	
Model/demonstrate the behavior				
Goal setting (outcome)	■			
Relapse prevention/coping planning				
Facilitate social comparison				
Goal setting (behavior)				
Action planning	■			
Provide feedback on performance				
Barrier identification/problem solving				
Provide instruction				
Teach to use prompts/cues			■	
Provide normative information about others' behavior				■
Plan social support/social change				

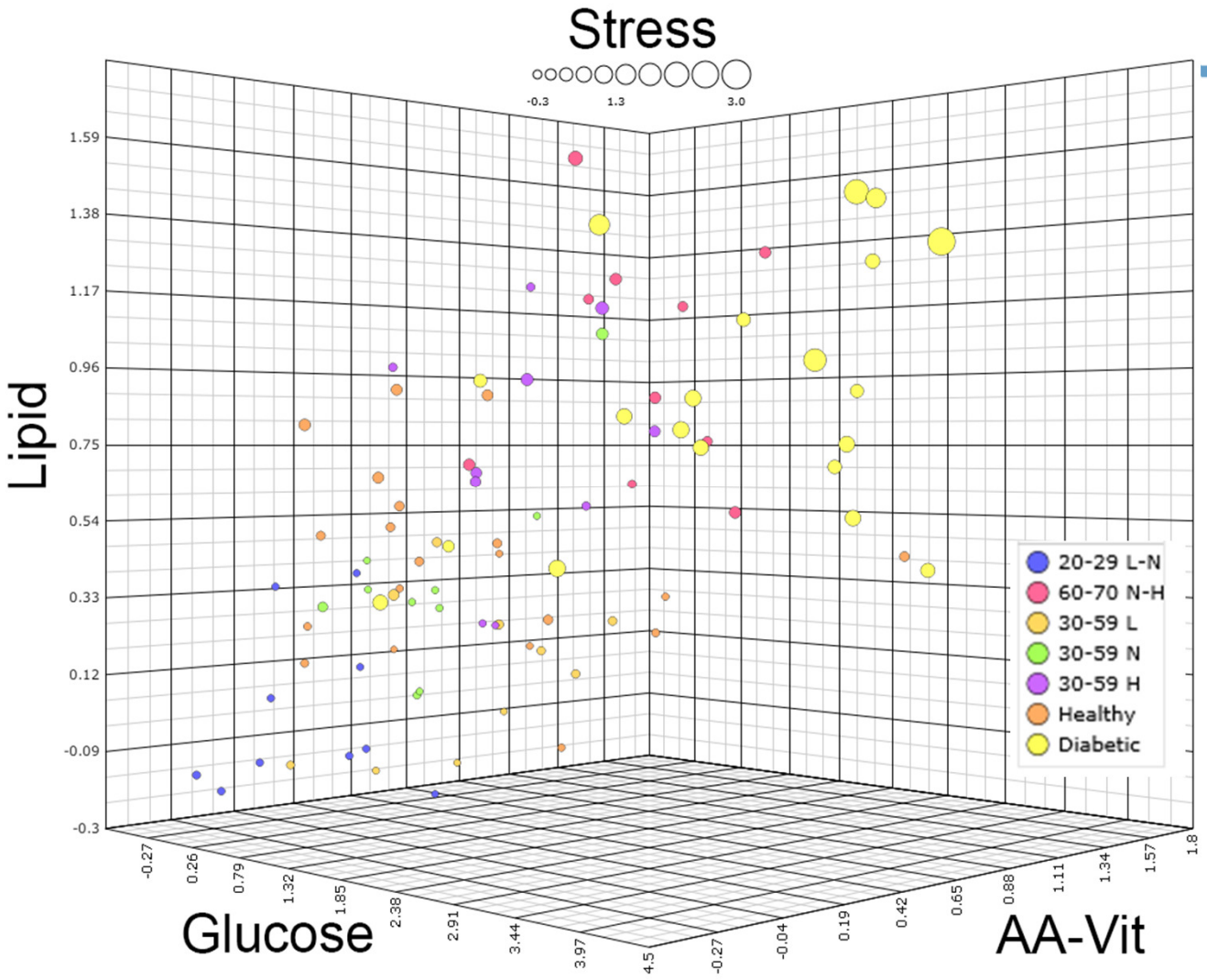
Personalized selection of behavioural change sequences

Bottomline

- The technology is there to come
- The science is good enough to introduce
- The data ownership is an issue
- “Personalized” will change society but society also needs to change
- Food services will replace food products

TYPE 2 DIABETES IS A MAJOR AND GROWING PROBLEM

- At the end of 2016, nearly one million people in the Netherlands were suffering from the lifestyle disease Type 2 Diabetes Mellitus (T2D). Around 55,000 people develop this disease each year.
- T2D has a huge impact on people's lives. Each day, they have to take various medicines, or inject insulin. They often feel very tired, and the illness even stops some people from working. In the long term, T2D can have serious effects, such as nerve damage, cardiovascular disease and blindness.
- The medical costs involved, plus the loss of labour productivity, mean that T2D costs society a great deal of money.



TNO innovation for life

70 “healthy subjects”
20 type 2 diabetics

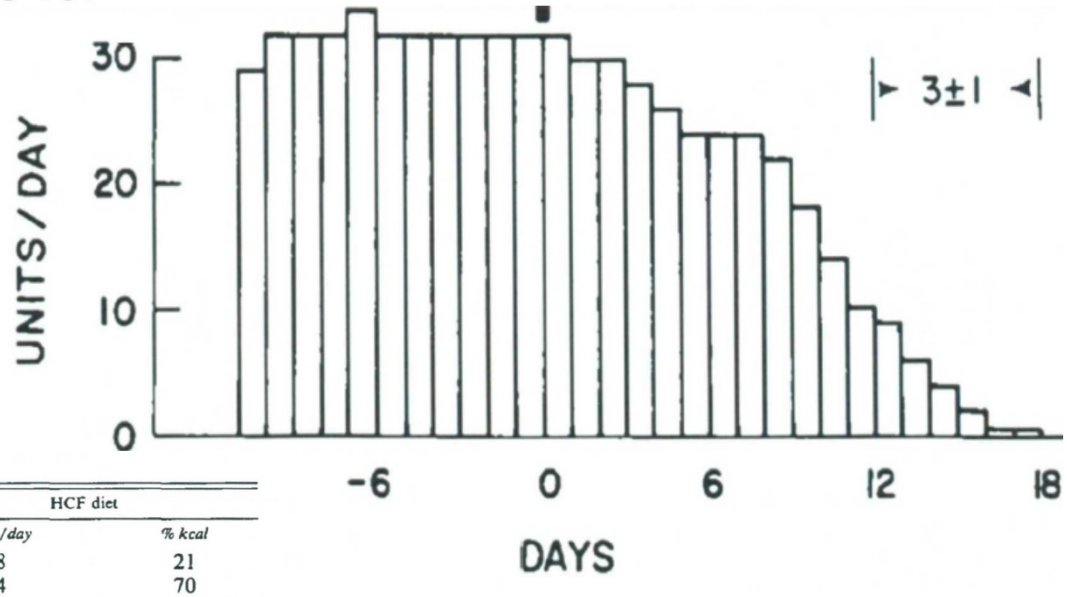
➔ A continuum!

Both metabolic health and disease can be viewed from a “regaining flexibility” view.

Cliffhanger
Can we cure type 2 diabetes using the same approach?

High-carbohydrate, high-fiber diets for insulin-treated men with diabetes mellitus[1, 2]

James W. Anderson, M.D. and Kyleen Ward, R.D.



Composition of diets[a]

	Control diet		HCF diet	
	g/day	*% kcal*	*g/day*	*% kcal*
Protein	92	20	98	21
Carbohydrate, total[b]	191	43	314	70
Simple	79		91	
Complex	112		223	
Fat, total	74	37	18	9
Saturated	26		5	
Monosaturated	39		5	
Polyunsaturated fatty acids	9		8	
Cholesterol	0.48		0.065	
Plant fiber, total	26		65	
Insoluble	16		53	
Soluble	10		12	

[a] Values are given for representative 1800-kcal diets. [b] Total carbohydrate refers to available carbohydrate and does not include plant fiber (24).

The American Journal of Clinical Nutrition 32: NOVEMBER 1979, pp. 2312–2321

Is insulin resistance reversible?

TNO innovation for life

Intensive lifestyle coaching with advanced type 2 diabetes patients

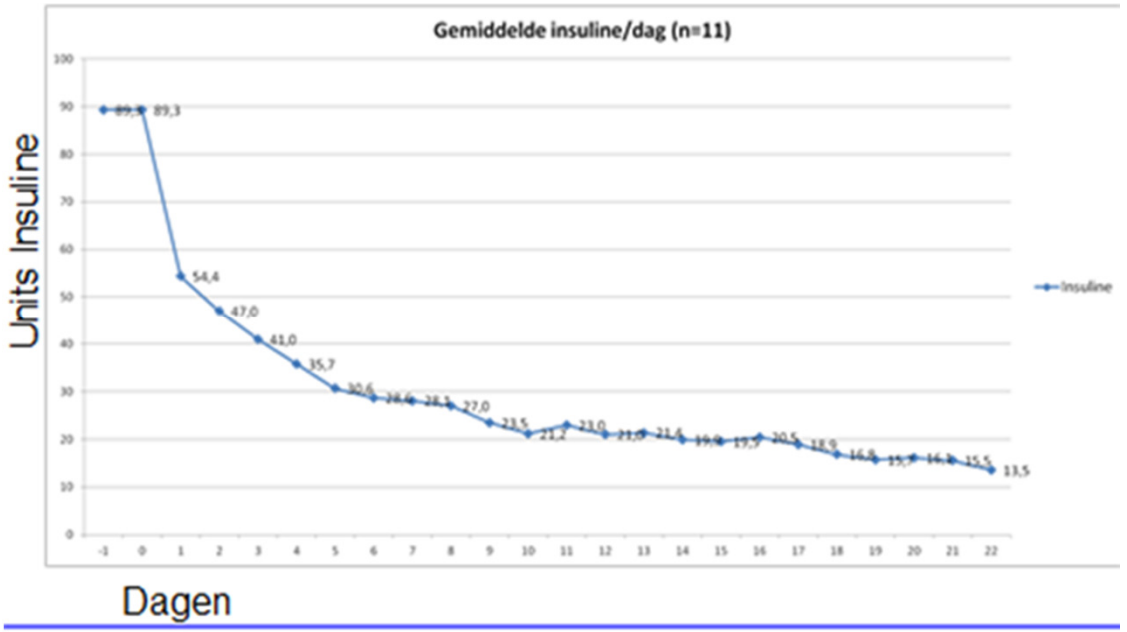
11 type 2 diabetic patients in advanced disease state entered into an intensive program of lifestyle coaching:

- Motivational coaching
- Physical activity
- Healthy diet

Insulin dosing was reduced with 80% in 3 weeks.

After three months, 10 out of 11 patients did not use insulin anymore.

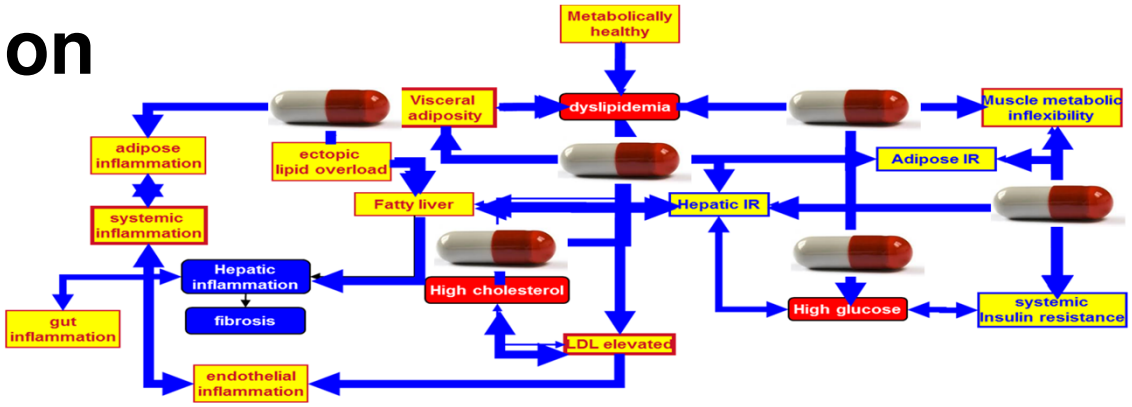
Average Insulin trend



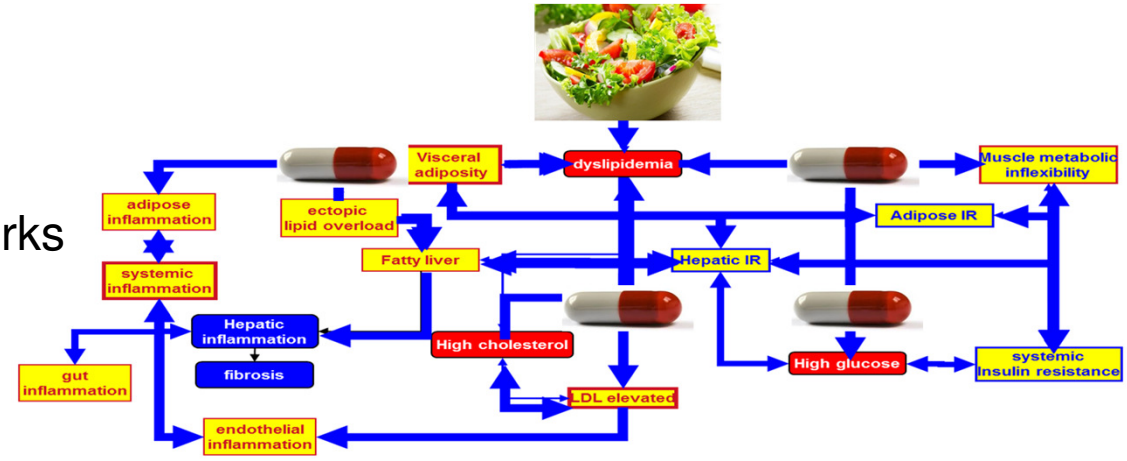
Health Coach Program
Revitalise Your Health

The role of medication

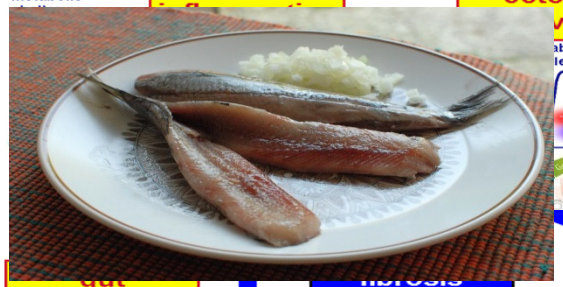
Now: suppress glucose:

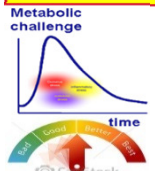


Sometimes: retreat if lifestyle works



Future: precision medicine and precision nutrition





carotenoids

Quercetin,
Se, Zn, …

Visceral adiposity

Stannols,fibre

adipose

ectopic

Fatty liver

polyphenols

Carnitine, Choline, …

Hepatic IR

Adipose IR

Low glycemic index

Anthocyanins

High cholesterol

LDL elevated

High glucose

systemic Insulin resistance

epicathechins
procyanidins

endothelial inflammation

Social system	Physiological system	Healthcare system

T2 Diabetes is a ‘systems disease’

Obesogenic environment Limited engagement with health status Social interactions are important for outcome	Multiple interacting physiological processes T2 Diabetes initiates when one or more biological processes lose flexibility	Conflicting stakeholder interests No focus on prevention Short term financial vision

T2 Diabetes needs a ‘systems solution’

Optimal coaching, participation and communication Integration of medical, social, economical and mental solutions	Diagnosis of all relevant processes and predispositions Goal: regain flexibility in all relevant processes, exploiting diet, lifestyle, medication and genetics where relevant	Patient empowerment Implement in regional setting Acceptance by accreditation

THE ‘LIFESTYLE AS MEDICINE’ TIMELINE

Aim: cure by lifestyle

Intense personalized lifestyle program

- Start motivational coaching
- Health literacy
- Optimal diet
- Physical activity
- Introduction e-health

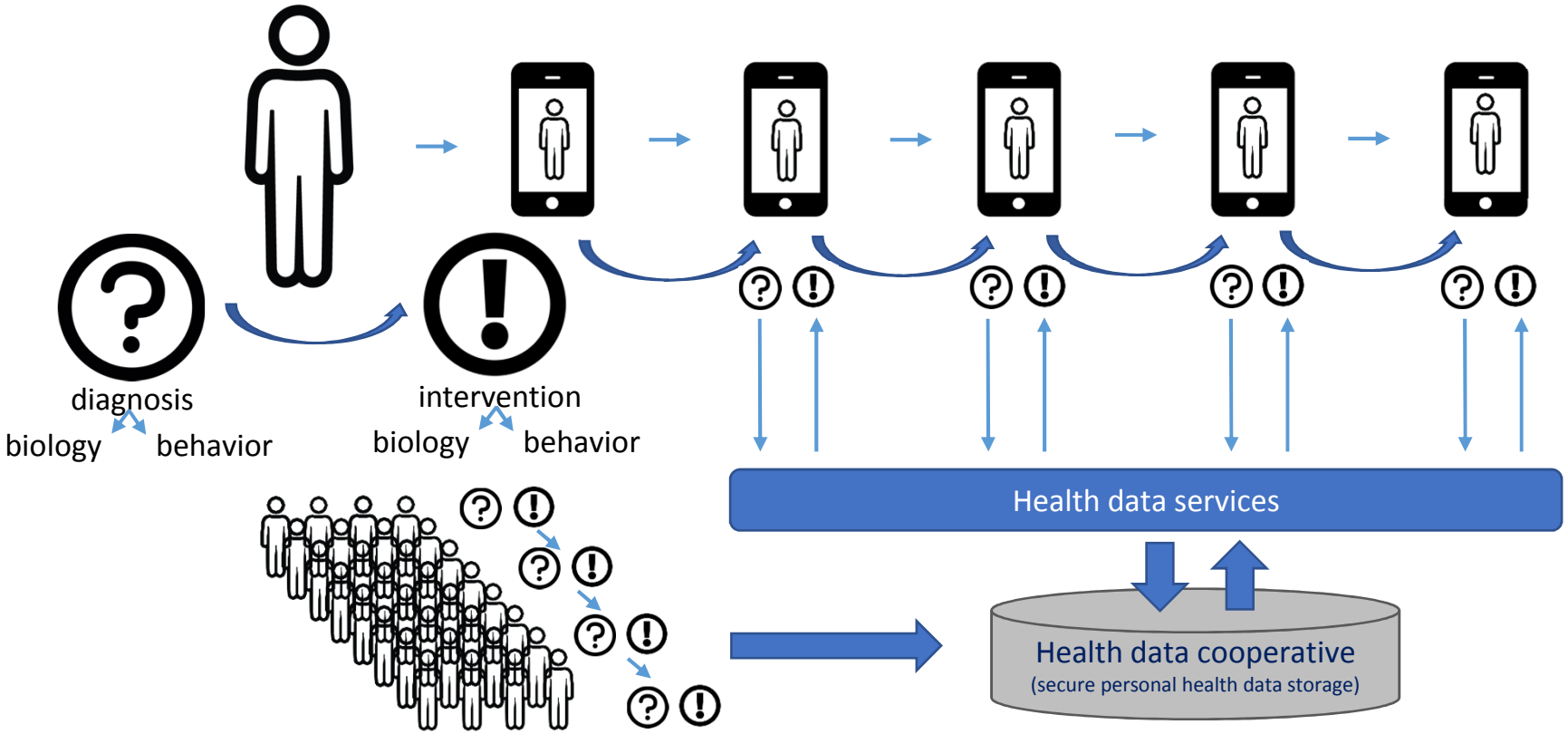
Aim: maintain changed lifestyle

All aspects of new lifestyle have settled into new habits

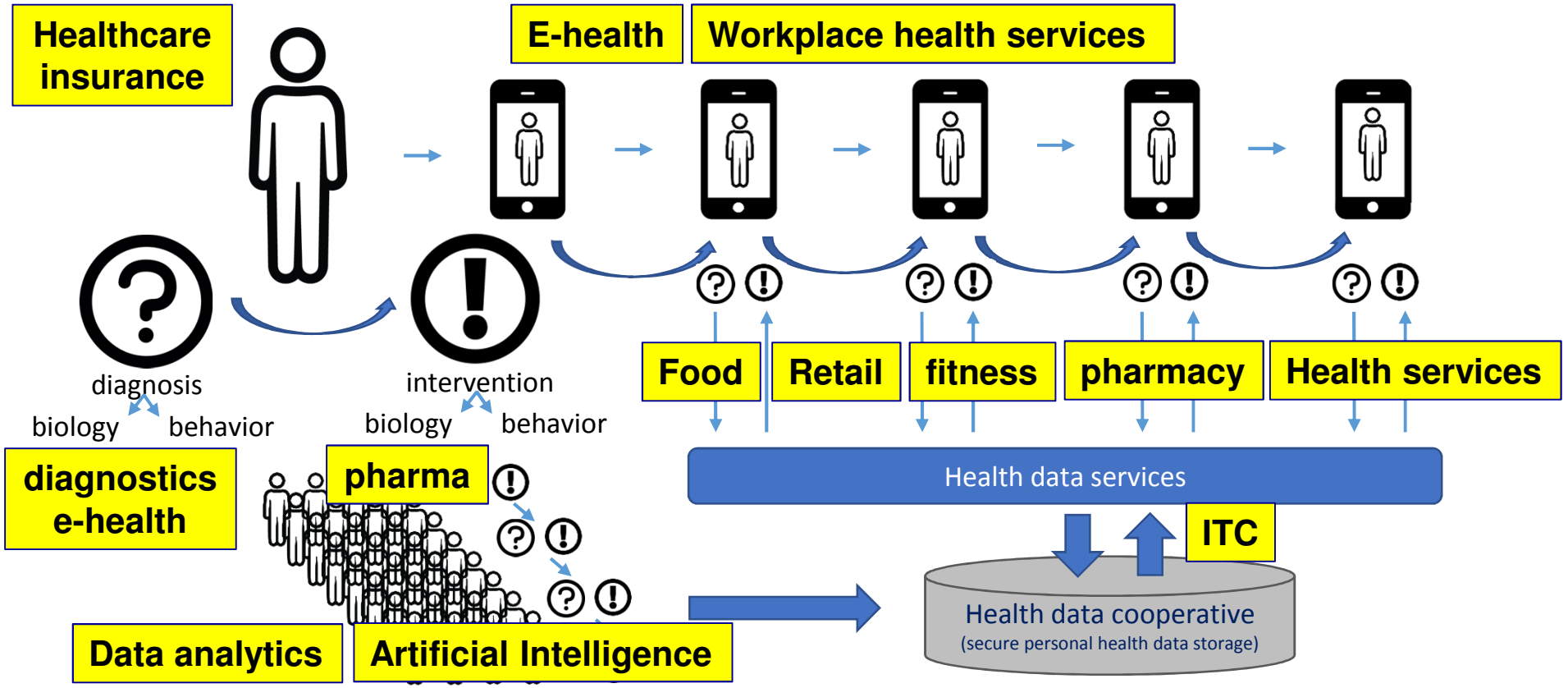
- All tools are personalized and connected to a sustainable support system
- Connected to one personal health data system (Health Data Cooperative)
- Social, economic and regulatory environment cooperates in habituation

The TNO life companion v1.0

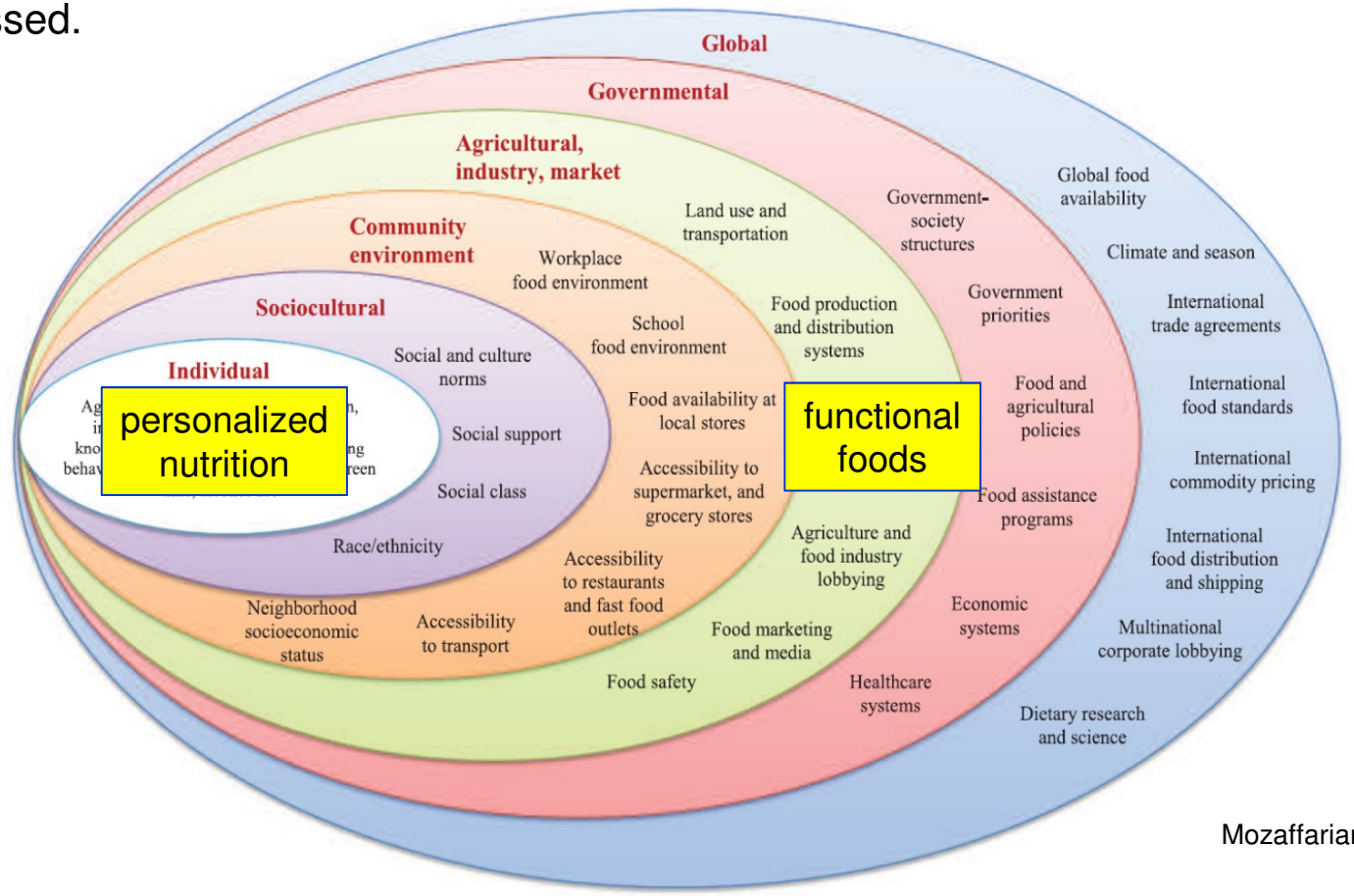
personalized advice timeline



The TNO life companion v1.0 – business opportunities



Diet related health can only be optimized in a systems approach where all relevant factors are addressed.



Mozaffarian, Circulation 2016