

# Challenge test-based resilience as a measure for health



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## ABSTRACT

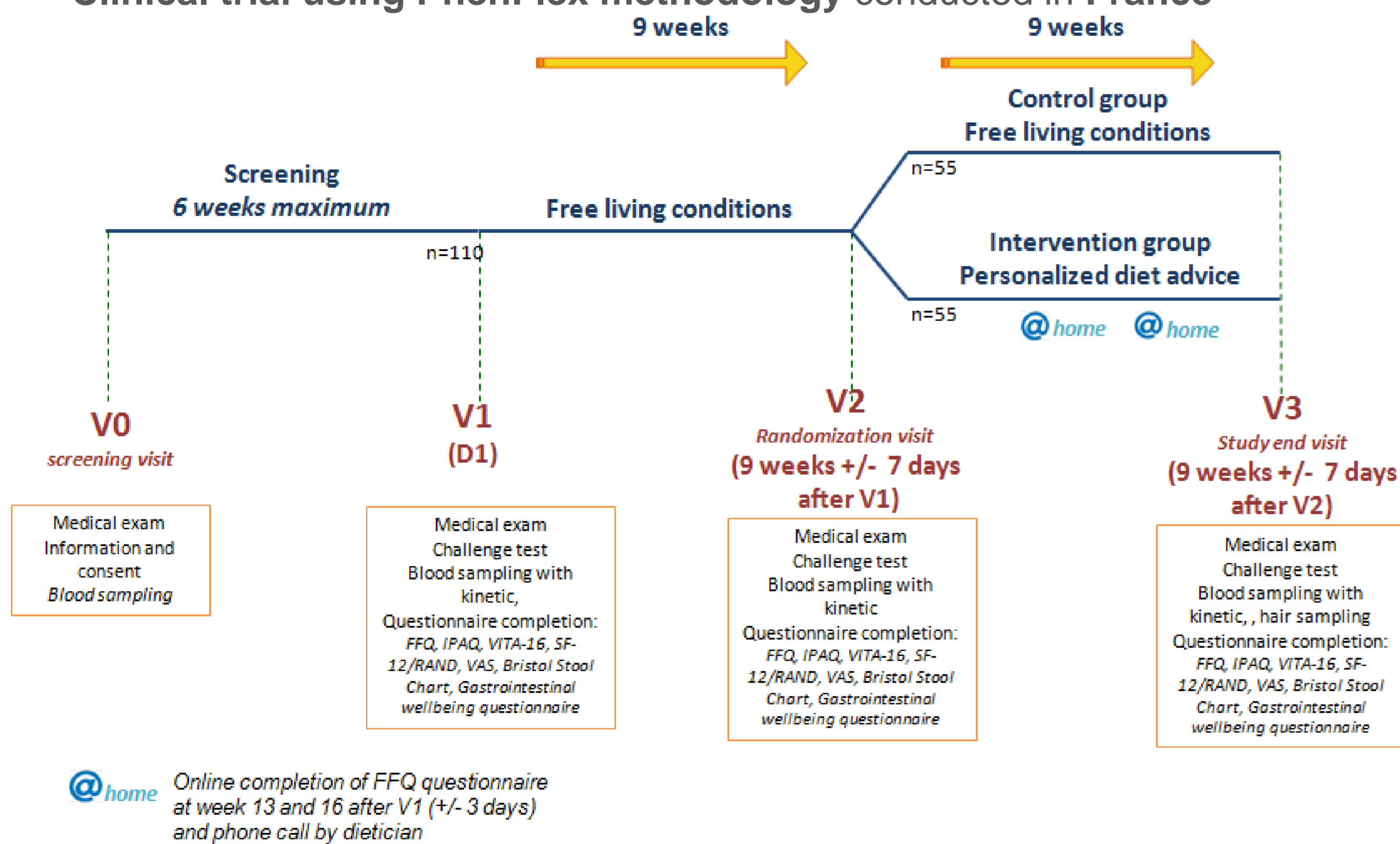
The **quantification of health effects** of food and nutrients remains a hurdle in the innovation pipeline of many food companies. “**Optimal health**” is increasingly defined in terms of ability to adapt to daily challenges also termed ‘**resilience**’<sup>1</sup>. Health as a dynamic situation, addresses the constant efforts of physiology to maintain homeostasis of the body, thus acting like a **shock absorber**.

In new concepts of intervention studies, **resilience** is tested by applying dietary or other challenges, followed by determining the amplitude and recovery time of the responding markers. Any relevant quantifiable biological parameter can be combined as a ‘**composite biomarker**’. Ultimately, “improved resilience” is thought to become a new **EFSA-accepted claimable** health benefit of food. The use of the PhenFlex challenge test has already shown its interest in clinical studies, in particular on a healthy population<sup>4</sup> and in type 2 diabetes patients<sup>5</sup>.

A **new study** is approved by Competent Authority and Ethics Committee to be conducted by **BIOFORTIS in France**, aimed to test this new concept on a **compromised population**. This study is conducted as part of the public-private PhenFlex-2 consortium\* involving **academia** as well as **worldwide industries**.

## Innovative Study Design

- Recruitment of a “compromised population” presenting two criteria of metabolic syndrome
- Assessment of “**FlexScore**” or “**metabolic age composite biomarker**” as tool to measure **health**
- **Clinical trial using PhenFlex methodology** conducted in **France**



## Objectives of the study

The aim is to evaluate the **efficacy of the ‘composite biomarker’** to measure:  
 - the health status defined by the metabolic resilience in 110 ‘**compromised**’ volunteers,  
 - the **health effect** after a 9-weeks period of **optimal diet** compared to a 9-weeks period of **free living conditions** within and between groups.

The **intervention group** will receive **personalized dietary** recommendations. The **control group** will **not** receive any **dietary** recommendation.

This study will also help us to show that the **composite biomarker has an added value** as compared to the traditional fasting single biomarkers which are used in the composite biomarker calculation.

This study, will take place at the **Clinical Investigation Unit of BIOFORTIS (FRANCE)**.

• **BASF, By-Health, Biofortis SAS, Ciro + BV, TNO, Roquette Frère SA, TKI AGRI & food**

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2- van Ommen, B., Keijer, J., Heil, S. G. and Kaput, J. (2009), Challenging homeostasis to define biomarkers for nutrition related health. *Mol. Nutr. Food Res.*, 53: 795–804. doi:10.1002/mnfr.200800390

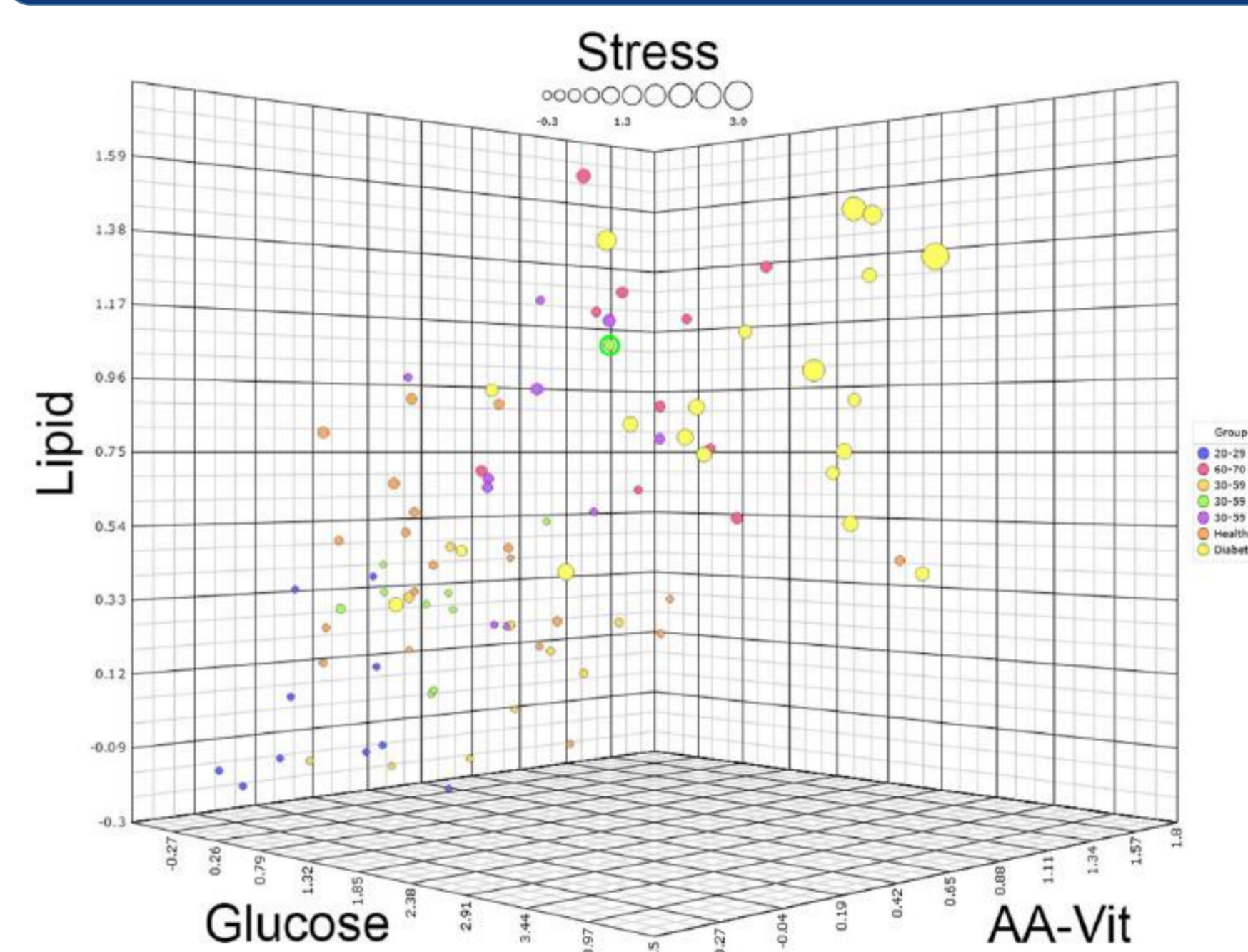
3- Stroeve JHM, van Wietmarschen H, Kremer BHA, van Ommen B, Wopereis S. Phenotypic flexibility as a measure of health: the optimal nutritional stress response test. *Genes Nutr.* 2015;10:459.

4- van den Broek, T. J. *et al.* Ranges of phenotypic flexibility in healthy subjects. *Genes Nutr.* 12, 32 (2017).

5- Wopereis, S., Stroeve, J. H. M., Stafleu, A., Bakker, G. C. M., Burggraaf, J., van Erk, M. J., Pellis, L., Boessen, R., Kardinaal, A. A. F., van Ommen, B. (2017). Multi-parameter comparison of a standardized mixed meal tolerance test in healthy and type 2 diabetic subjects: the PhenFlex challenge. – PubMed

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## PhenFlex methodology

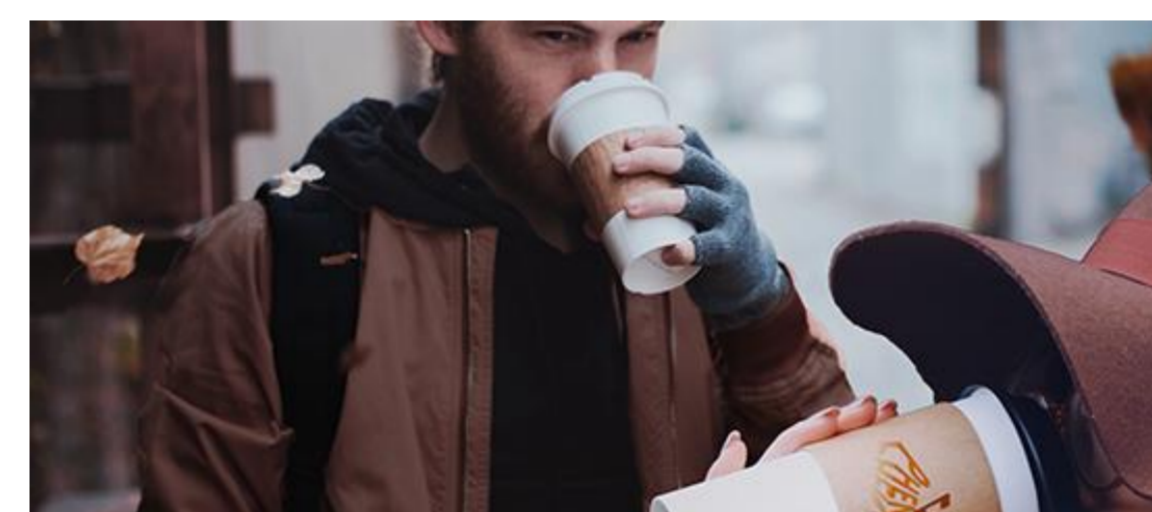


### “Health Space model”

As an example, the above depicted data visualization includes individual phenotypic flexibility of subjects from two different studies. This representation allows visualization of clusters representing different age categories next to a Diabetic cluster.

Groups are labeled using their respective **age** intervals as well as their **body fat %** intervals, **L** for low, **N** for normal, and **H** for high.

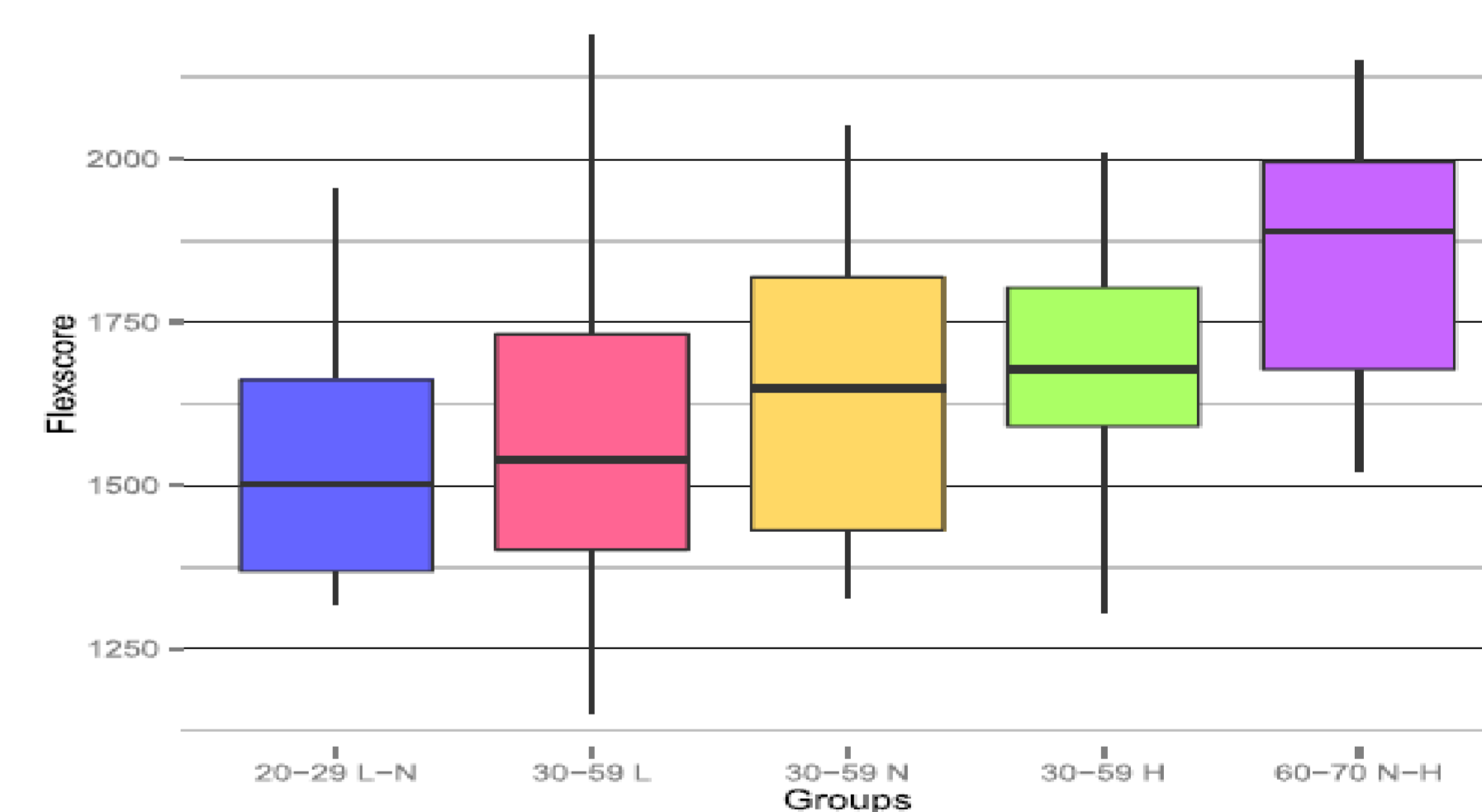
**FlexScore** is calculated from **selected biological features** with this multivariate statistical model.<sup>2</sup>



### PhenFlex Challenge Drink

is a 500 ml drink containing Palmolein, Glucose, and Casein causing a metabolic perturbation (920 kcal).

→ **Health Space Model combined with PhenFlex Challenge drink allow to calculate the FlexScore also called metabolic age.**



**FlexScore** also termed “**metabolic age**” increased with age and body fat %. Group labeling used the respective **age** and **body fat %** intervals; **L** for low, **N** for normal, and **H** for high<sup>2</sup>

## Conclusions

The **PhenFlex challenge test** is an **innovative tool** which has already been shown in clinical research and represents an appropriate response to:

- the **needs of many companies** wishing to assess their products,
- provides interesting perspectives in the understanding of **pathophysiological mechanisms**.

This methodology brings a **new way** to demonstrate the health effect of **food products**.

The objective assessment of improved resilience via standardised PhenFlex methodology within the **healthy population** is thought to become a new **EFSA-accepted claimable** health benefit of food.

**This study** allows to consolidate the application of this PhenFlex methodology on **compromised** subjects and highlight the **whole interest** of this approach.