



 **SynbActive<sup>®</sup>**



**MetSyn**

**Take care of you!**

 **SynBalance**  
LIFEWIDE PROBIOTICS

# MetSyn

Probiotic complex designed for metabolic health composed by  
*L. plantarum* - PBS067; *L. acidophilus* - PBS066; *L. reuteri* - PBS072

- ▶ Enhancing lipid & carbohydrates metabolism
- ▶ Improvement of anthropometric parameters & quality of life
- ▶ Enhancing BSH activity involved in bile acid deconjugation
- ▶ Slowing down systemic intestinal inflammatory processes and oxidative stress
- ▶ Improvement of gastrointestinal symptoms and overall gut well-being



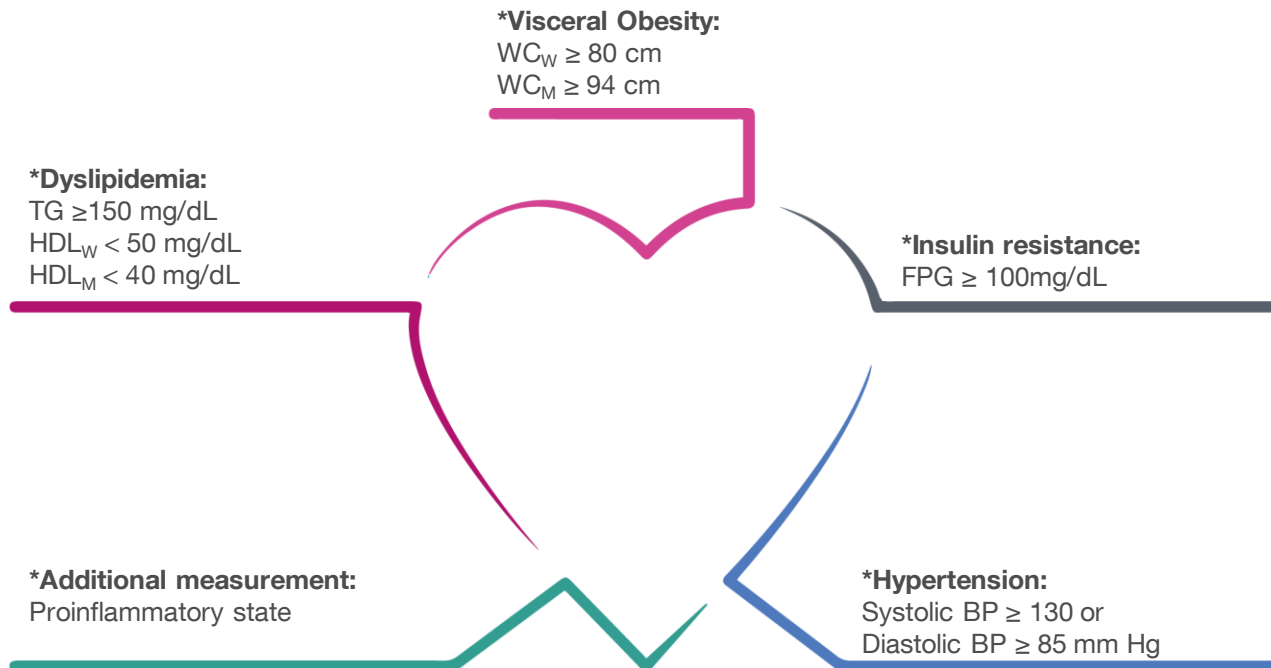
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**NUTRA**  
INGREDIENTS ASIA  
AWARDS 2022

WINNER  
**NUTRA**  
INGREDIENTS  
AWARDS 2021





# Metabolic Syndrome criteria



Metabolic Syndrome is a set of conditions that can increase the risk of:

- Type 2 diabetes
- CV disease
- NAFLD
- Osteoarthritis
- Stroke

# Biological target – Insulin Resistance and Obesity

In obesity, **pro-inflammatory cytokines** (e.g., TNF- $\alpha$ , IL-6) and **free fatty acids** released from adipose tissue **disrupt insulin signaling** and impair endothelial function.

Under normal conditions, insulin regulates vascular tone by balancing **endothelin-1–mediated vasoconstriction** and **nitric oxide–mediated vasodilation**.

In obese individuals, **TNF- $\alpha$ –induced inhibition of nitric oxide synthesis** leads to **reduced vasodilation** and **unopposed vasoconstriction**, contributing to endothelial dysfunction.

These alterations in insulin action at both **metabolic and vascular levels** result in **insulin resistance**, compensatory **hyperinsulinemia**, and progressive **metabolic imbalance**.

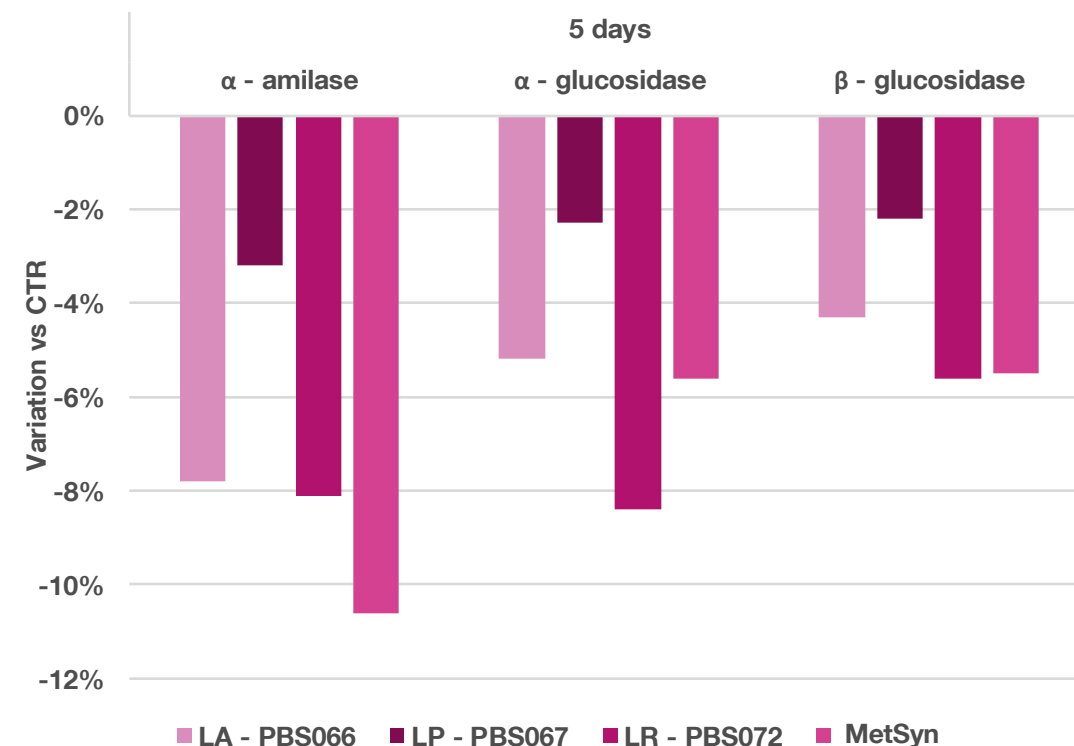




In-vitro

# Carbohydrate metabolism Enzymatic model

- $\alpha$ -amylase,  $\alpha$ -glucosidase and  $\beta$ -glucosidase are enzymes involved in the digestion-absorption of carbohydrates and hydrolyzation of oligosaccharides to release glucose.
- Probiotic strains are **effective in modulating the carbohydrate digestion** and reducing the absorption of sugars through the inhibition of  $\alpha$ -amylase,  $\alpha$ -glucosidase and  $\beta$ -glucosidase activity.



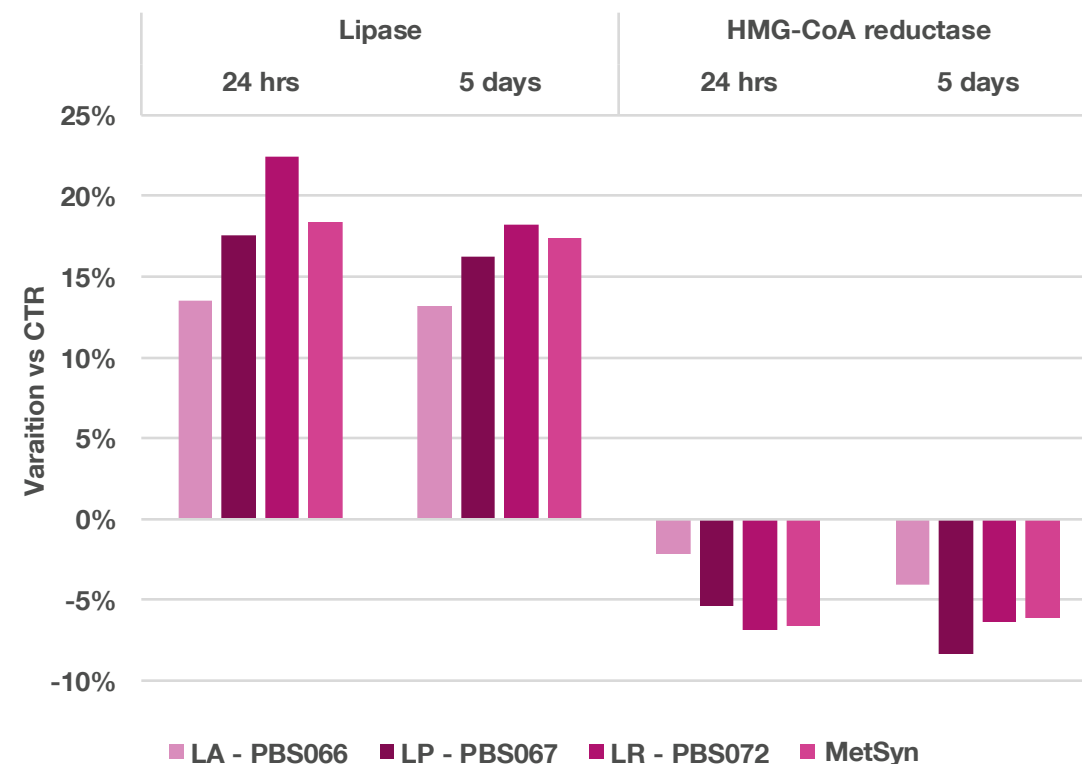
**Protocol:** enzymatic activity of  $\alpha$ -amylase was evaluated by Lugol reactive assay,  $\alpha$ -glucosidase and  $\beta$ -glucosidase were evaluated by Fehling assay.



In-vitro

# Lipid metabolism Enzymatic model

- Modulation of lipolysis and cholesterol biosynthesis as biological markers of hyperlipidemia and hypercholesterolemia.
- MetSyn showed to **enhance lipid mass exploitation** and also to modulate the enzyme involved in cholesterol biosynthesis.



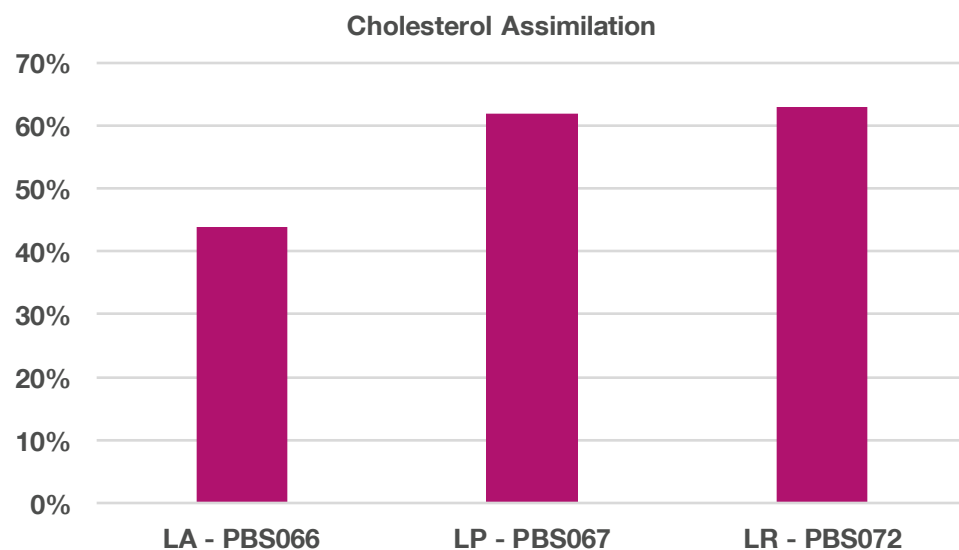
**Protocol:** enzymatic activity was assayed by colorimetric method evaluating the synthesis of fatty acids (lipase) and Mevalonic acid (HMG-CoA reductase)



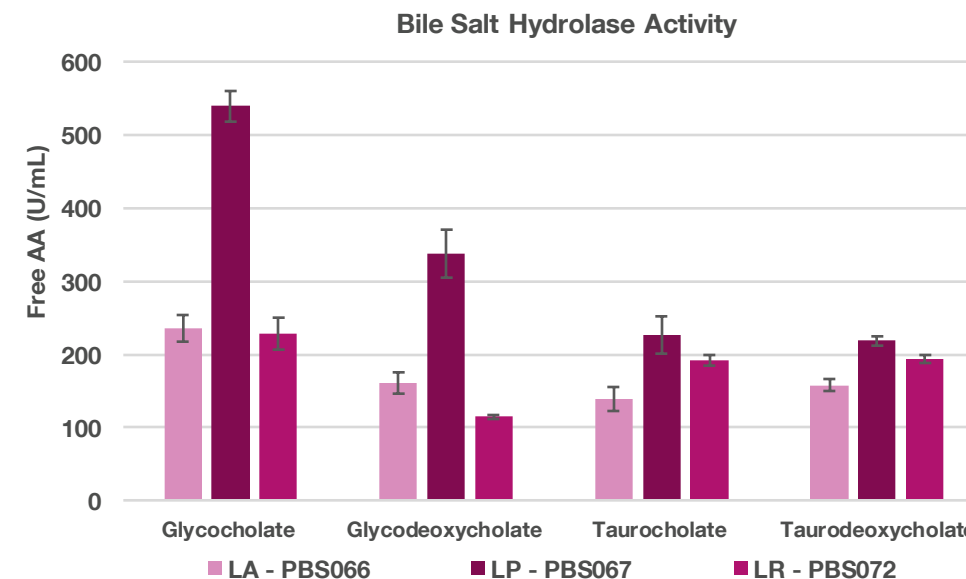
# Lipid metabolism

## Cholesterol control

- MetSyn strains demonstrated to modulate cholesterol levels by several mechanism as assimilating cholesterol for their own metabolism or enhance the activity of bile salt hydrolase.



**Protocol:** Probiotics ability to assimilate / co-precipitate cholesterol from MRS-Thio broth medium supplemented with 100 ug/mL Cholesterol and 0.3% oxgall. The remaining cholesterol was measured by spectrophotometric method.



**Protocol:** Evaluation of BSH activity after cells incubation with bile salt substrate (20mM) for 24 hours. BSH activity was determine by colorimetric measure of deriving free aminoacids.



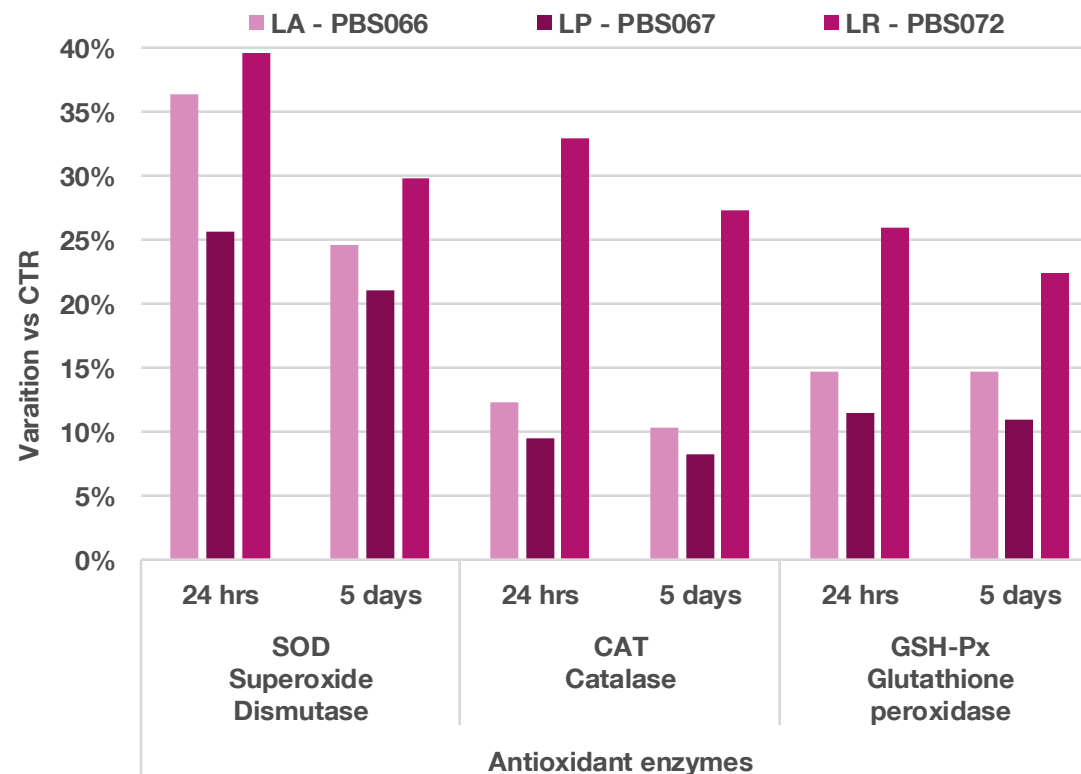


In-vitro

# Protection from oxidative stress

## Enzymatic model

- The antioxidant power of MetSyn was proven through positive modulation of antioxidant enzymes.
- The activity of the enzymes is strongly improved helping the reduction of the oxidative stress.



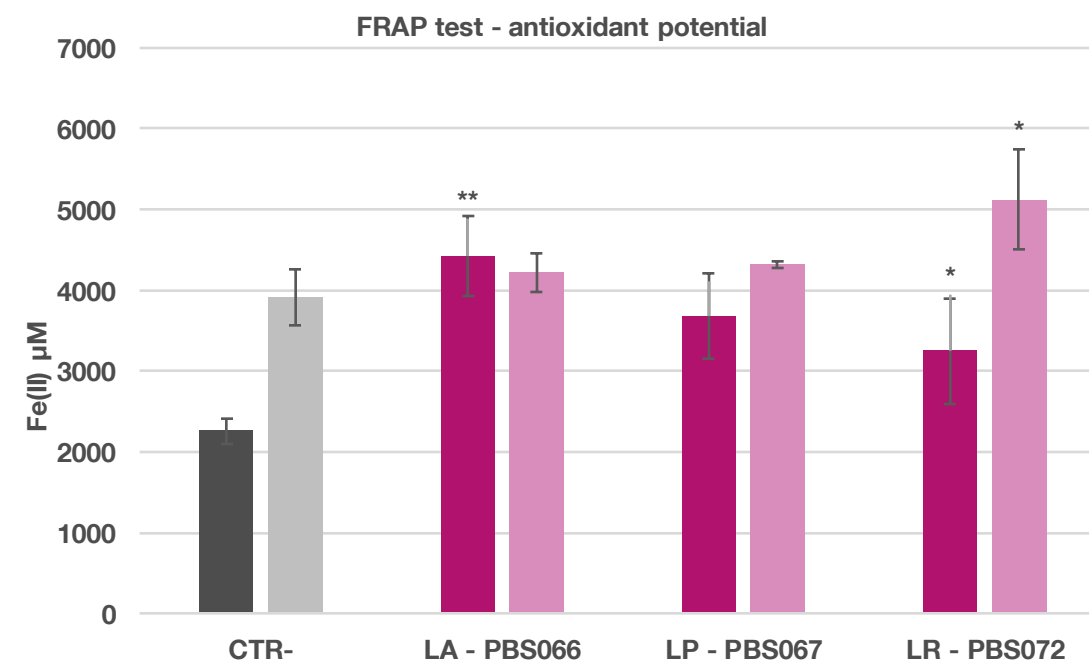
**Protocol:** Spectrofluorometric assay for the evaluation of the enzymatic activity of SOD as described by Flohè and Otting (1984), of CAT as described by Aebi (1984) and of GPx as described by Flohè and Gunzler (1984).



# Protection from oxidative stress

## FRAP model

- The antioxidant power was confirmed through the protection of cell culture from the oxidative stress.
- MetSyn demonstrates a strong synergic antioxidant potential.



I. Presti, G. D'Orazio, M. Labra, et al., "Evaluation of the probiotic properties of new Lactobacillus and Bifidobacterium strains and their in vitro effect".  
*Applied Microbiology and Biotechnology*, 2015, 99:13, 5613.

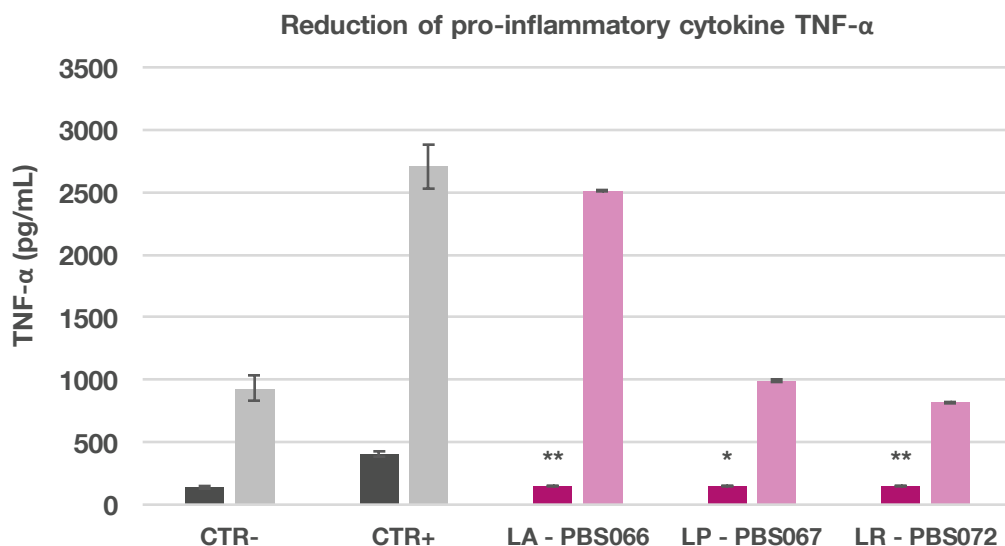
**Protocol:** Protection from inflammatory stress induced by sodium dodecyl sulphate, antioxidant power (AOP) & reducing properties. Murine model: Fibroblasts line (BALB/c3T3, clone A31). Outcomes at 24h (acute, darker) and 5dd (chronic, lighter). CTR+: SDS/ CTR-: no treatment



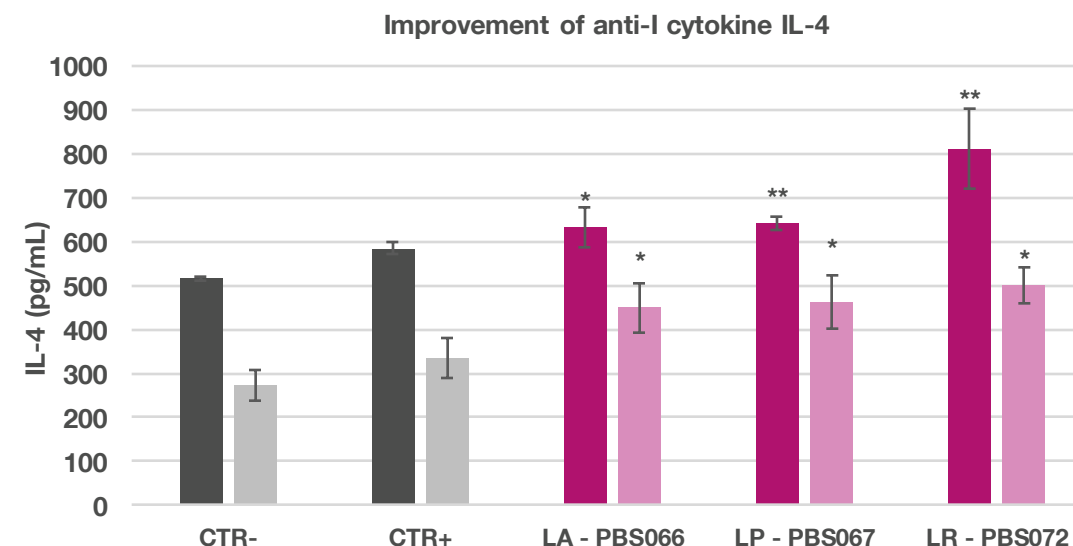
In-vitro

# Modulation of systemic inflammation

➤ MetSyn is effective in slowing down the inflammatory status activated by TNF- $\alpha$  both in early and late responses.



➤ MetSyn helps to activate the immunity response by improving IL-4 cytokine release.



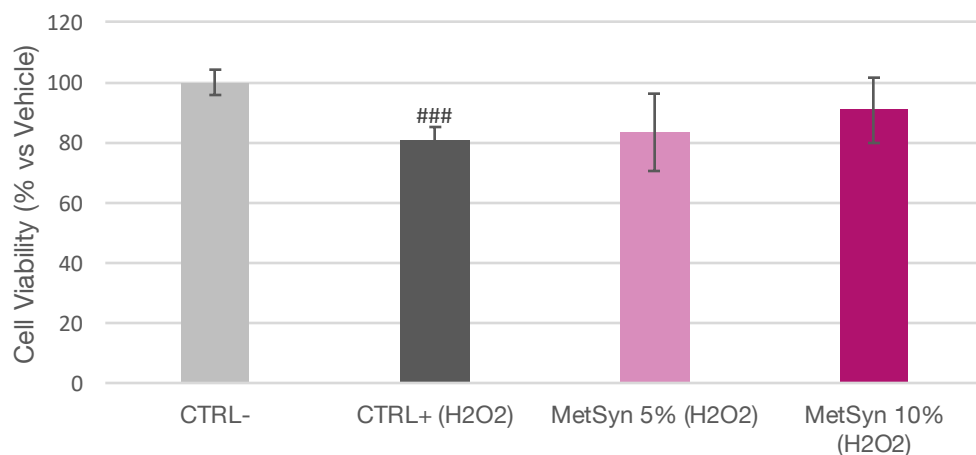
**Protocol:** Inhibition of pro-inflammatory TNF-alpha. Improvement of anti-inflammatory IL-4. Murine model: Fibroblasts line (BALB/c3T3, clone A31). Outcomes at 24h (acute, darker) and 5dd (chronic, lighter). CTR+: SDS/ CTR-: no treatment  
I. Presti, G. D'Orazio, M. Labra, et al., "Evaluation of the probiotic properties of new Lactobacillus and Bifidobacterium strains and their in vitro effect". *Applied Microbiology and Biotechnology*, 2015, 99:13, 5613.



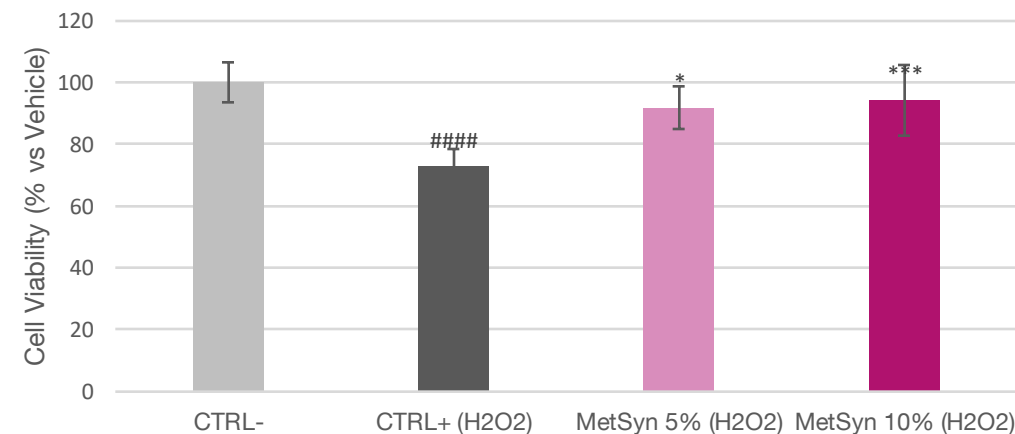
# Protection from oxidative stress HASMC and HAEC

- To evaluate the potential protective effects of bacterial metabolites derived from *L. plantarum*-PBS067, *L. acidophilus*-PBS066 and *L. reuteri*-PBS072 against the harmful stimuli on the vascular district, assays were carried out on Human Aortic Endothelial Cells (HAEC) and Human Aortic Smooth Muscle Cells (HASMC). The antioxidant power of MetSyn was proven to assess its ability to mitigate vascular damage.
- MetSyn showed a protective effect on cell viability at different concentration, especially on HAEC.

### Cell Viability (HASMC)



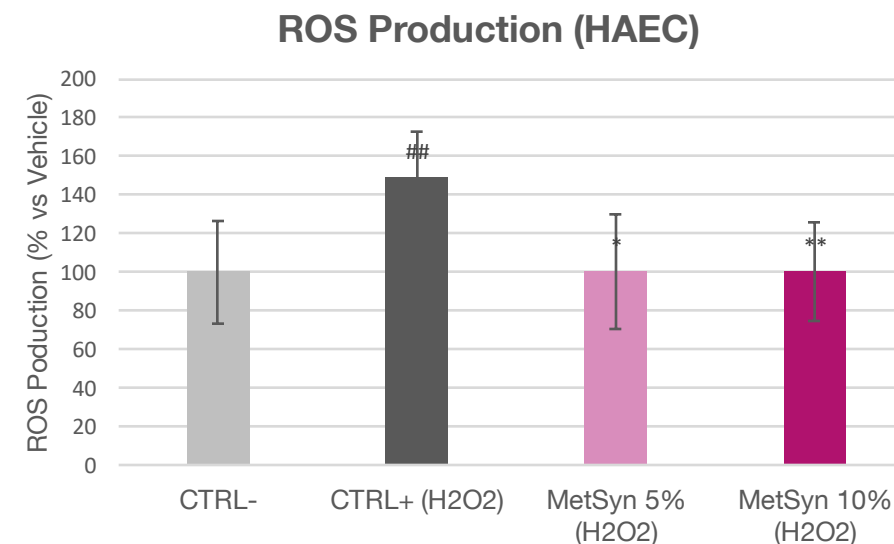
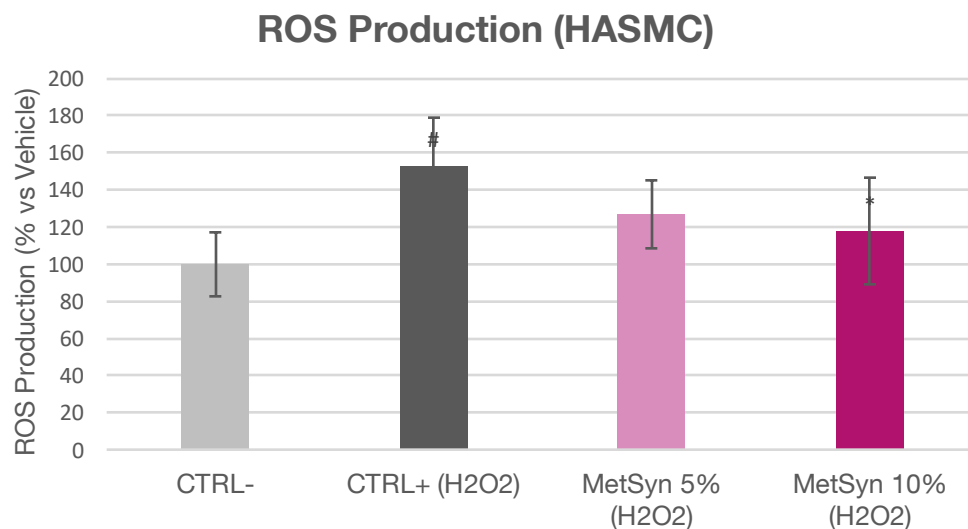
### Cell Viability (HAEC)



**Protocol:** To mimic oxidative stress, hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) was applied at a concentration of 200 µM for 2 hours to HASMCs, and at 100 µM for 2 hours to HAECs. The supernatant was pre-incubated at the selected concentrations for 1 hour prior to H<sub>2</sub>O<sub>2</sub> exposure. Cell viability following H<sub>2</sub>O<sub>2</sub>-induced oxidative damage and the protective effects of MetSyn in HASMCs and HAECs was then evaluated. # Statistical significance vs CM-SMC (HG corning). \* Statistical significance vs CM-SMC (HG corning) + H<sub>2</sub>O<sub>2</sub> 200 µM/ 100 µM.

# Inhibition of ROS Production HASMC and HAEC

- Reactive Oxygen Species (ROS) are responsible for impairing endothelial function, promoting inflammation and oxidative stress, and facilitating atherosclerosis and thrombosis in the vascular district.
- MetSyn showed the ability to reduce the production of ROS in response to a pro-oxidative stimulus on both HASMC and HAEC.



**Protocol:** Both HASMCs and HAECs were subjected to the same oxidative stimulus protocol (200  $\mu$ M H<sub>2</sub>O<sub>2</sub> for HASMCs, 100  $\mu$ M for HAECs) following 1-hour pre-incubation with the supernatant at 5% and 10%0%. ROS levels were measured using dihydroethidium (DHE), a fluorescent probe specific for superoxide anion. Fluorescence intensity at 605 nm correlates with intracellular O<sub>2</sub><sup>•-</sup> levels. # Statistical significance vs CM-SMC (HG corning). \* Statistical significance vs CM-SMC (HG corning) + H<sub>2</sub>O<sub>2</sub> 200  $\mu$ M/ 100  $\mu$ M.

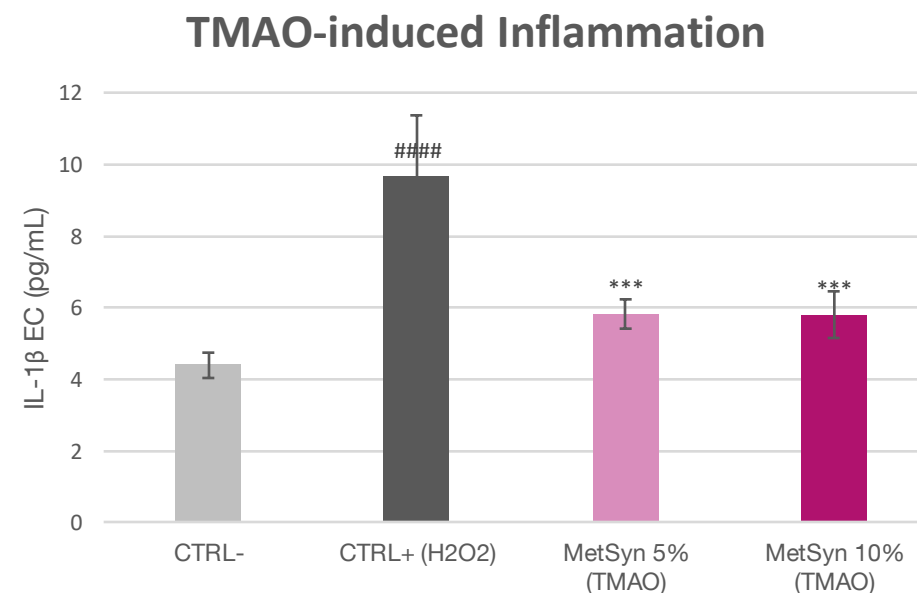


In-vitro

# Modulation of TMAO-Induced Inflammation HASMC

- Pro-inflammatory cytokines drive vascular damage by promoting inflammation, disrupting endothelial integrity, and accelerating atherothrombosis.
- MetSyn showed the ability to significantly limit the production of pro-inflammatory IL-1 $\beta$  induced by Trimethylamine N-oxide (TMAO) on HASMC.

**Protocol:** Cells were pre-incubated with the supernatant containing the metabolites at 5% and 10% for 1 hour prior to the addition of TMAO (600  $\mu$ M). TMAO was incubated for 24 hours to assess IL-1 $\beta$  production. At the end of each treatment period, cells were lysed using 1% Triton solution. The lysates were centrifuged at 8000g for 10 minutes, and the resulting supernatants were collected for the quantitative analysis of IL-1 $\beta$ . # Statistical significance vs CM-SMC (HG corning). \* Statistical significance vs CM-EC (HG corning) + TMAO 600  $\mu$ M.



# Clinical study design - Metabolic syndrome



## EVALUATED PARAMETERS:

- Anthropometric evaluation
- Lipid and glyceamic hematochemical markers
- Inflammatory markers
- Quality of Life

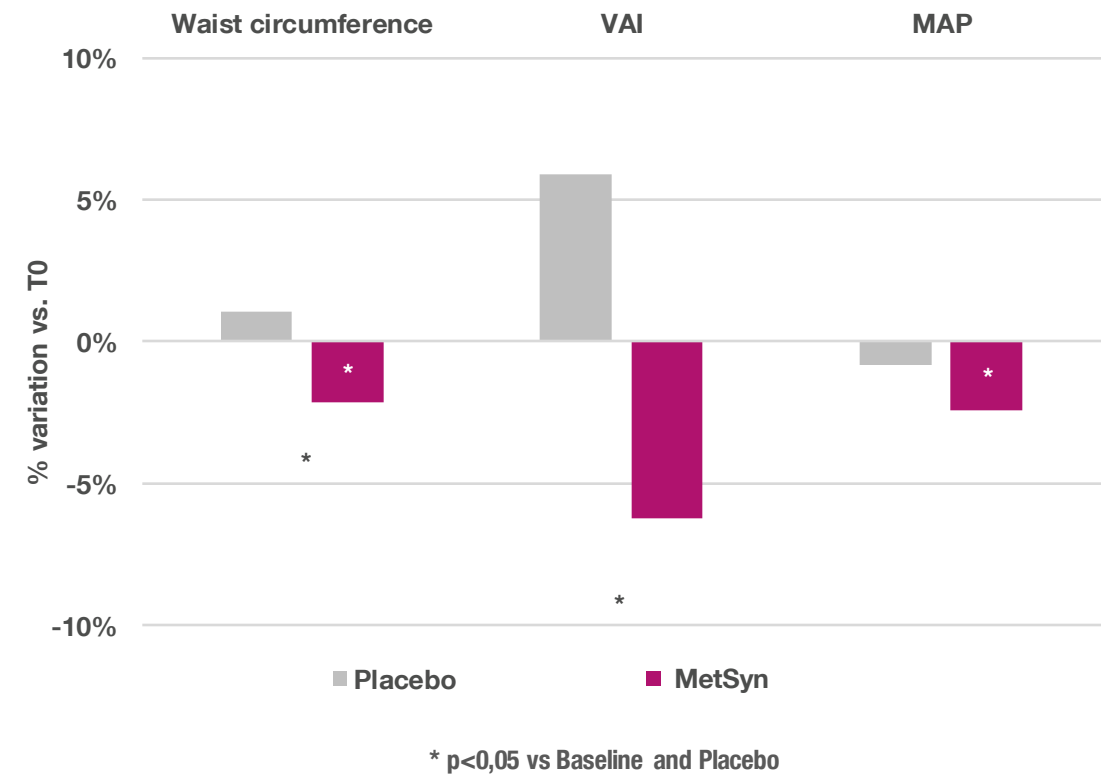
Cicero, Arrigo FG, et al. "Impact of a short-term synbiotic supplementation on metabolic syndrome and systemic inflammation in elderly patients: a randomized placebo-controlled clinical trial." European journal of nutrition (2020)."



Human

## Improvement of obesity markers

- MetSyn group perceived a better waist circumference reduction compared to the placebo, as well as visceral adipose index.
- Slight decrease of MAP (mean arterial pressure) has been reported.
- MetSyn strains demonstrated also to relieve from gastrointestinal symptoms as constipation and bloating.



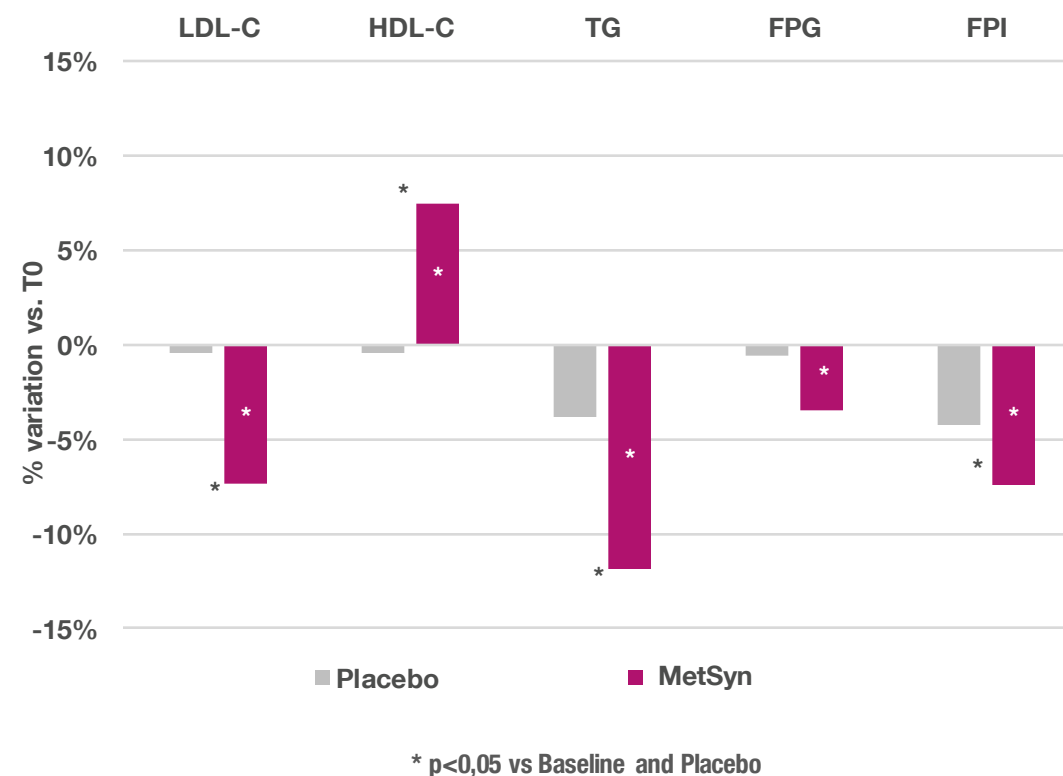




Human

# Modulation of metabolic profile

- All **dyslipidemic markers were improved** in MetSyn group during the treatment: especially TG and LDL-C were statistically reduced and HDL-C increased with respect to placebo.
- Fasting plasma insulin (FPI) and fasting plasma glycaemia (FPG) significant decreased in the active group with respect to placebo.

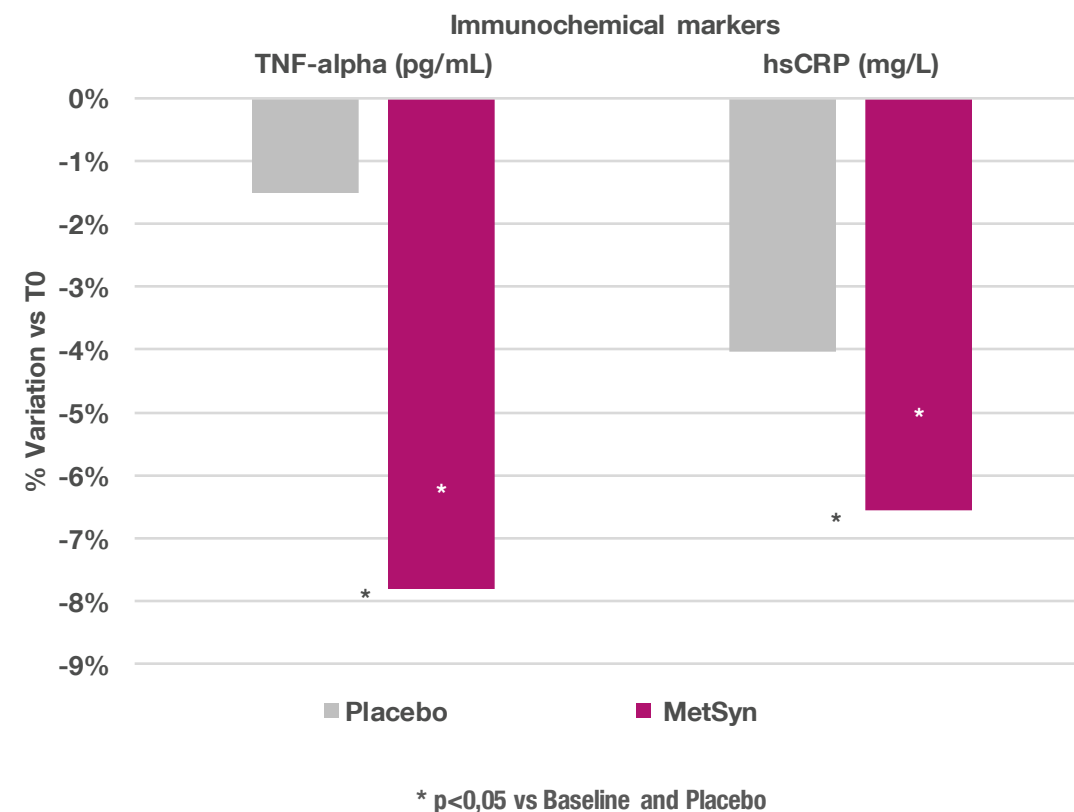




Human

# Reduction of systemic inflammation

- **Low-grade systemic inflammation** is linked with both **insulin resistance** and **endothelial dysfunction** and provides a connection between inflammation and metabolic processes.
- **C-reactive protein** is a **CVD marker**, higher levels are linked with an higher risk. **TNF- $\alpha$**  is **overproduced** by adipose tissue due to the anti-inflammatory actions of insulin.
- MetSyn group perceived a strong significant reduction of the inflammatory markers, showing its positive influence on chronic inflammation.



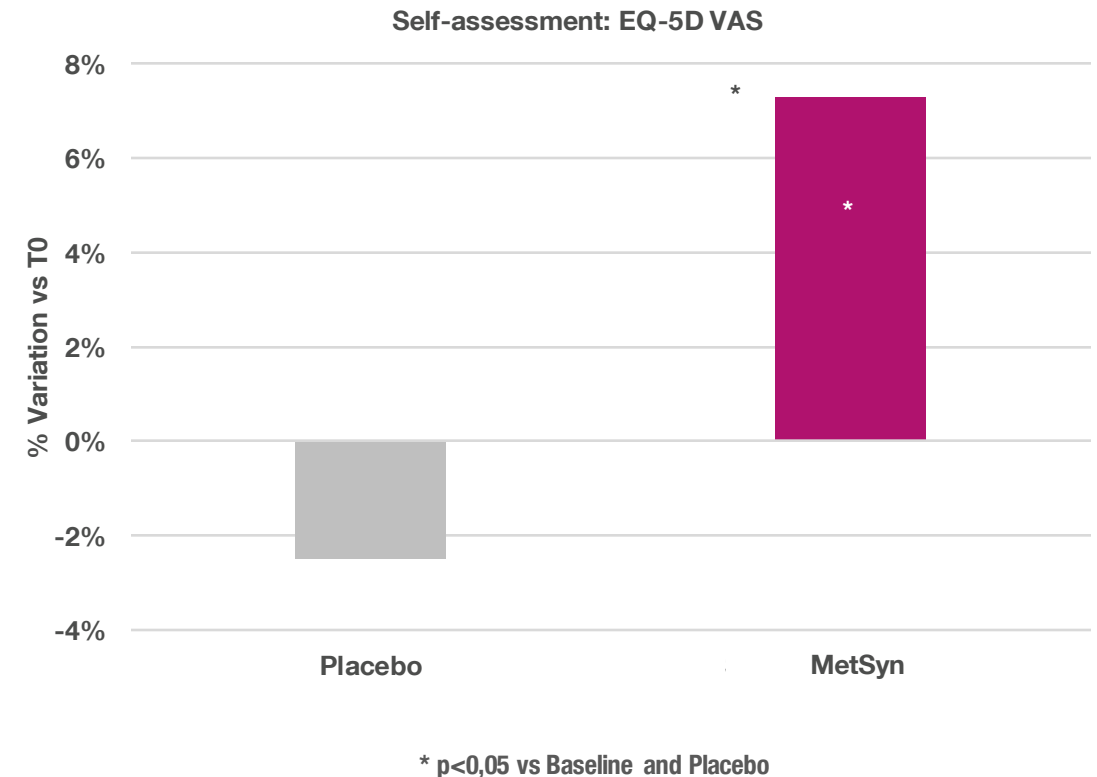


# Improvement of quality of life

Self-assessment quality of life questionnaire based on the following macro-areas:

- Physical capacity
- Self-esteem
- Daily habits
- General discomforts
- Anxiety – depression

Self-perception is significantly improved in MetSyn group, showing a strong effect of the treatment with respect to the sole lifestyle changes.

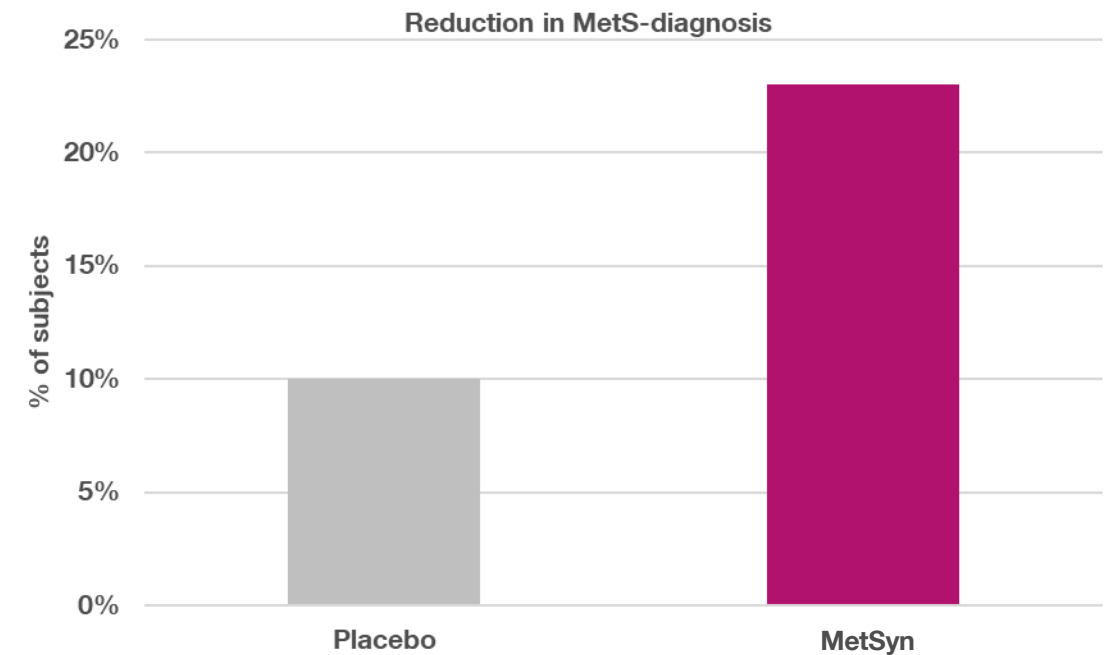




Human

# Diagnosis of metabolic syndrome

- At the end of the study, the number of patients not complying with the MetS diagnosis anymore, significantly **increased in MetSyn group (23%)**, compared with the placebo (10%).



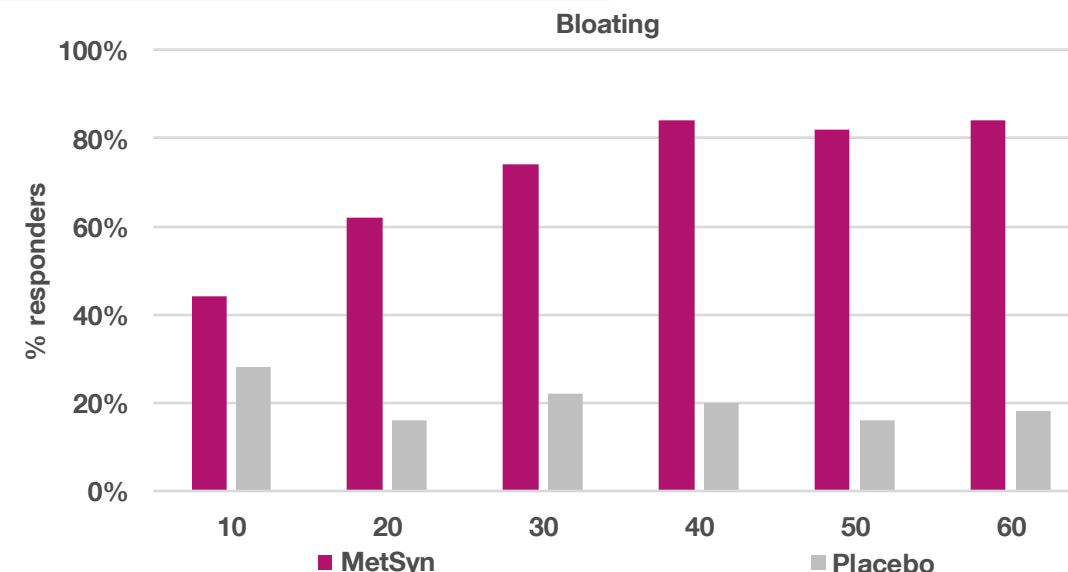
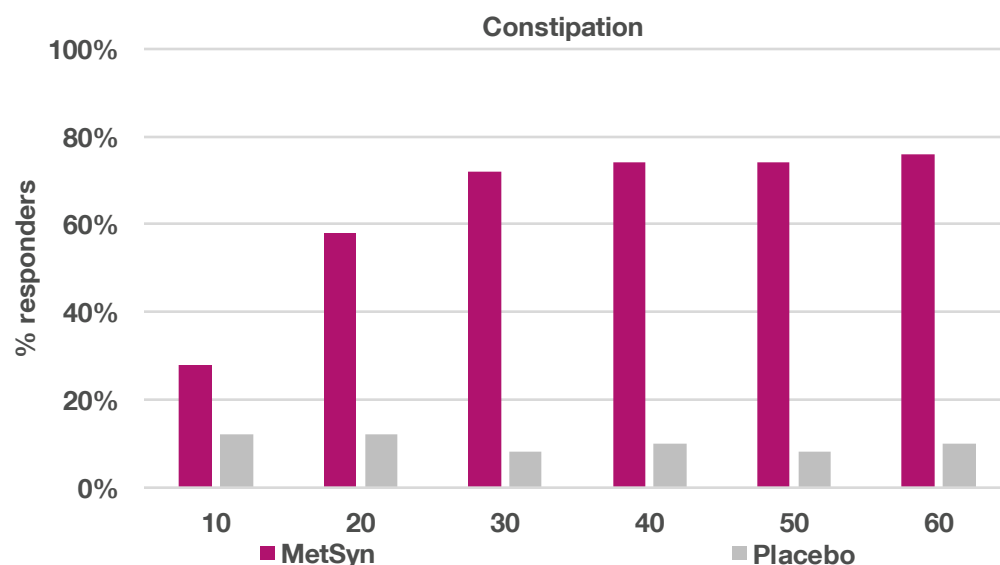


Human

# Improvement of gastrointestinal symptoms

- GI diseases are commonly found in overweight and obese people.
- Variation of symptoms during the active treatment (60 days) compared to placebo expressed as % of responders.

**RESPONDER:** subject reporting a decrease of symptoms of at least 30% compared to the basal condition.



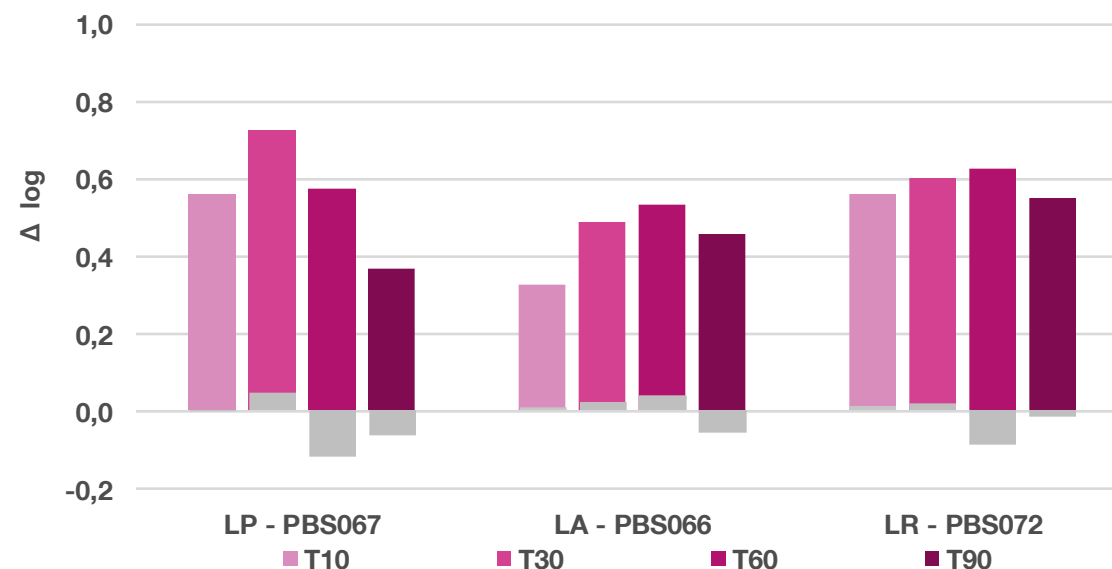
**Protocol:** Oral intake: 1B CFU/day/strain for 60 days. Subjects: 50/group. Inclusion criteria: patients with a condition similar to irritable bowel syndrome IBS. *Randomized, double blind, placebo controlled.* Method: collection of stools & HR-QOL questionnaire. Outcome: GI-tract colonization, clinical evaluation of symptoms. Analytical technique: Real time – qPCR. Analysis performed at T0, T10, T30, T60, T90 (30dd wash out). VAS score based on symptoms scale: Bloating, Abdominal pain, Constipation, Abdominal cramps, Flatulence, Data recorded for study group in active phase and follow-up period compared to placebo. V. Mezzasalma et al., "A Randomized, Double-Blind, Placebo-Controlled Trial: The Efficacy of Multispecies Probiotic Supplementation in Alleviating Symptoms of Irritable Bowel Syndrome Associated with Constipation" BioMed Research International,



# Clinical evidence of GI colonization

Quantification of strains with respect to T0 (confirmed by qPCR tests on blinded samples) during the treatment (60 days) and follow-up (additional 30 days):

- No significant increase in the placebo group (grey color) for any specie
- Selective, consistent and significant improvement of administered strains (magenta colors) in the study group



V. Mezzasalma et al., "A Randomized, Double-Blind, Placebo-Controlled Trial: The Efficacy of Multispecies Probiotic Supplementation in Alleviating Symptoms of Irritable Bowel Syndrome Associated with Constipation" BioMed Research International, 2016.

**Protocol:** Oral intake: 1B CFU/day/strain for 60 days. Subjects: 50/group. Inclusion criteria: patients with a condition similar to irritable bowel syndrome IBS. *Randomized, double blind, placebo controlled.* Method: collection of stools & HR-QOL questionnaire. Outcome: GI-tract colonization, clinical evaluation of symptoms. Analytical technique: Real time – qPCR. Analysis performed at T0, T10, T30, T60, T90 (30dd wash out).



# Clinical study design – Obesity (APAC)



## EVALUATED PARAMETERS:

- Body weight
- Body Mass Index
- HOMA Index and Visceral Adipose Index
- Waist and Hip circumference
- Blood parameters (HDL, LDL, TG, FI, FG, HbA1c)
- Obesity related Quality of Life (ORWELL-97)

Manuscript under preparation

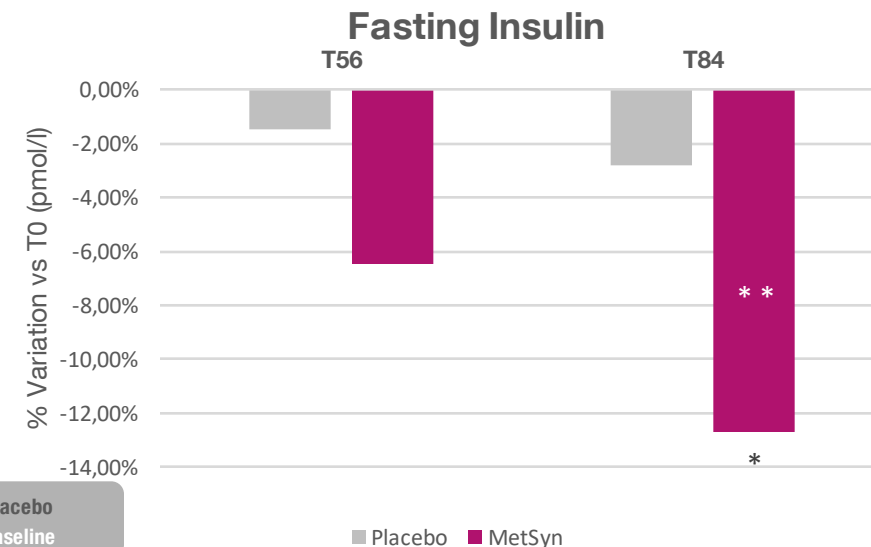
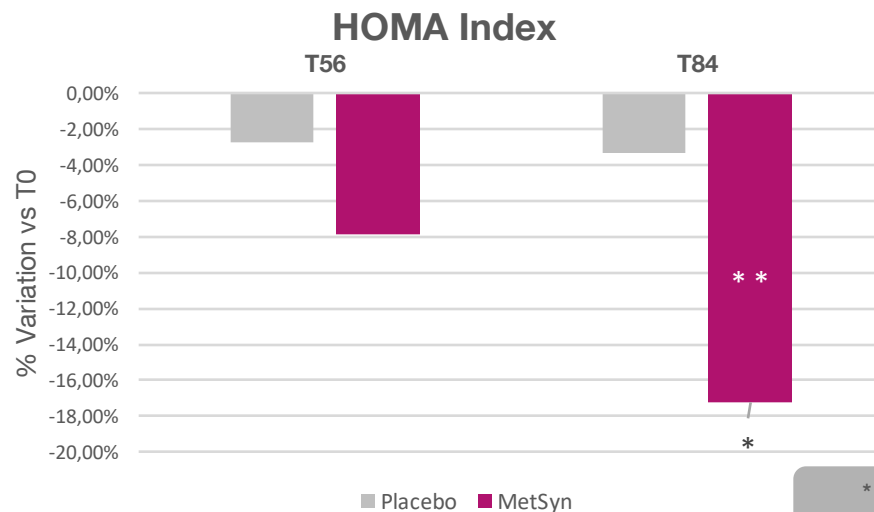




Human

## Improvement of insulin sensitivity & glycemic control

- MetSyn intake led to a **significant reduction in the HOMA index** compared to placebo, reflecting improved **pancreatic  $\beta$ -cell function** and decreased insulin resistance.
- In addition, **HbA1c, fasting plasma insulin, and fasting plasma glucose** were significantly reduced versus placebo, indicating better **glycemic control** and a lower risk of **metabolic complications**.



\* Statistical significance vs Placebo  
\* Statistical significance vs Baseline

**HOMA Index:** The HOMA index is a mathematical model that estimates insulin resistance (HOMA-IR) and pancreatic  $\beta$ -cell function (HOMA- $\beta$ ) based on fasting glucose and insulin levels. A higher HOMA-IR value indicates greater insulin resistance.

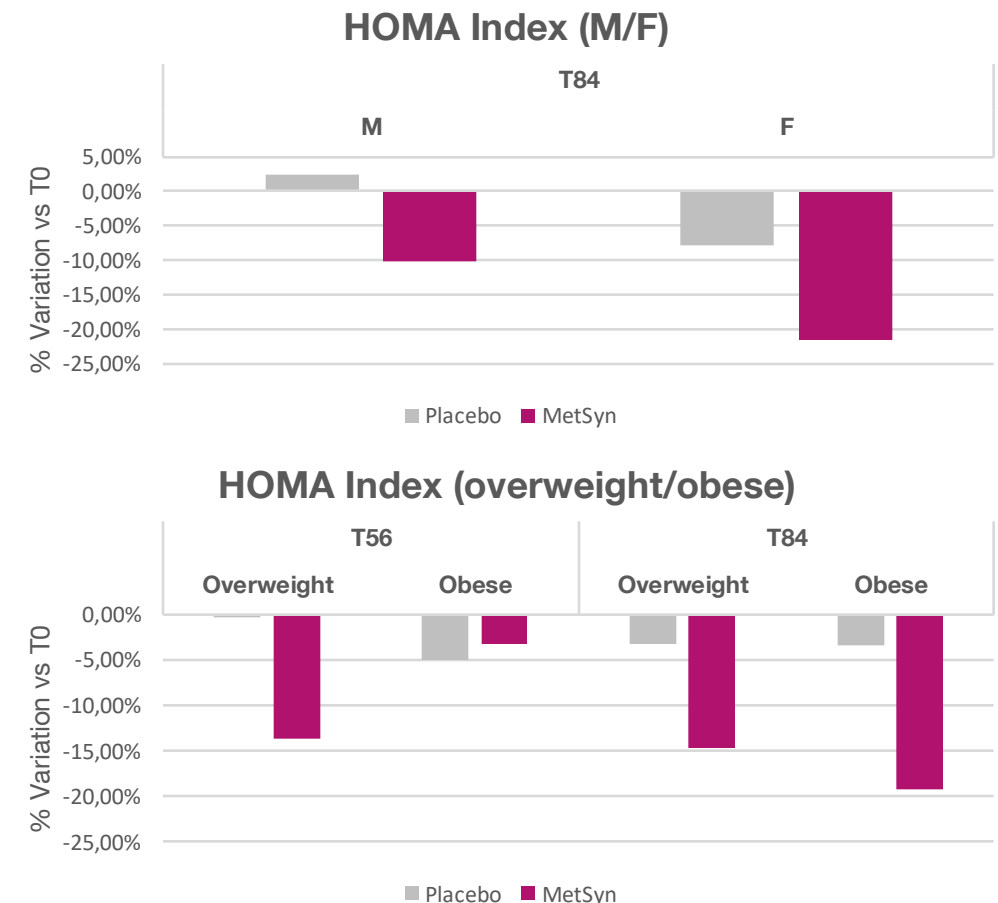


Human

# Insulin sensitivity modulation: Subgroup Analysis

- MetSyn intake improved insulin sensitivity across all subgroups, with **women showing greater reductions** in HOMA-Index than men, especially after extended administration (T84), suggesting a stronger or more sustained response in females.
- When stratified by weight, **overweight participants responded earlier**, with a notable decrease in HOMA-Index, whereas **obese participants showed a delayed but more pronounced improvement** over time.

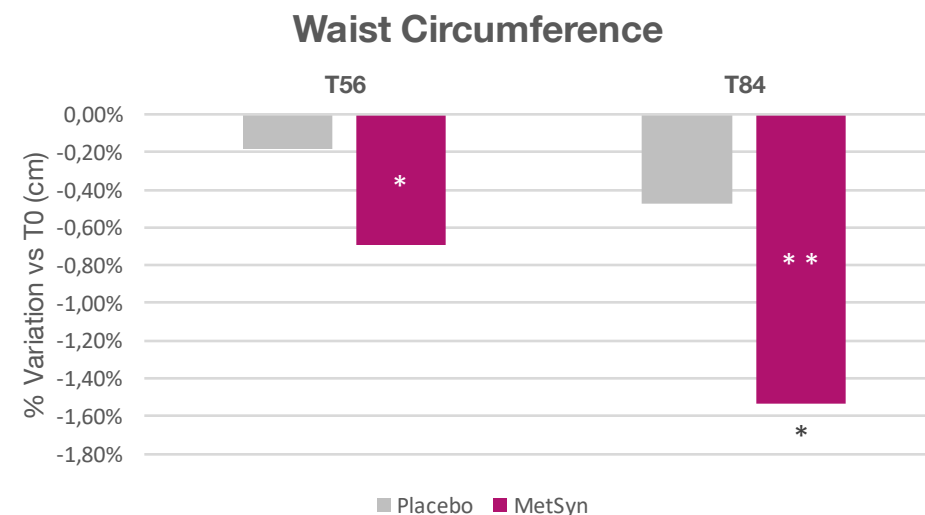
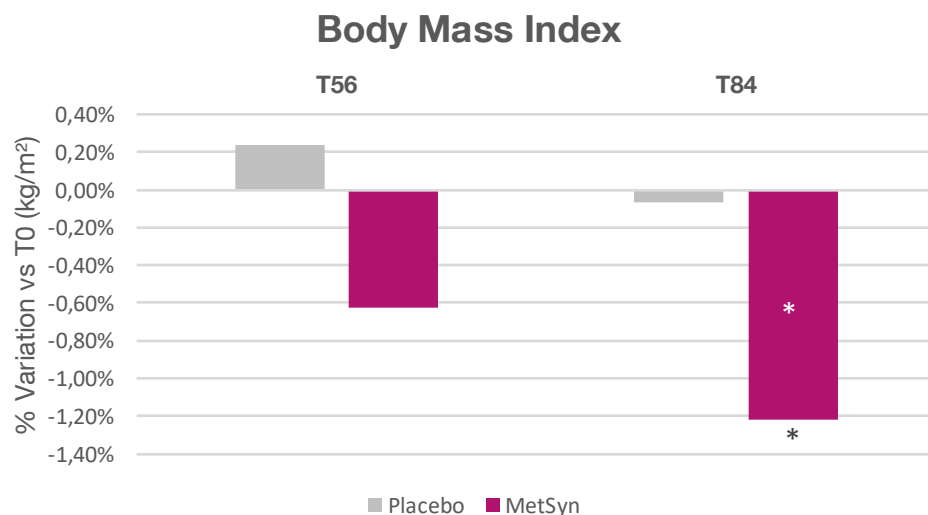
These findings indicate that **timing and magnitude of response can differ by sex and weight status**, highlighting the importance of personalized approaches in metabolic interventions.





# Improvement of anthropometric parameters

- MetSyn group showed reduction of anthropometric parameters, such as **body weight** (- 0,97 kg) and **Body Mass Index** compared to the placebo.
- Additionally, MetSyn led to a decrease in body fat distribution parameters, such as **waist and hip circumferences** (-1,50 and -0,90 cm respectively), reflecting a reduction in abdominal fat and contributing to an improved cardiometabolic profile.

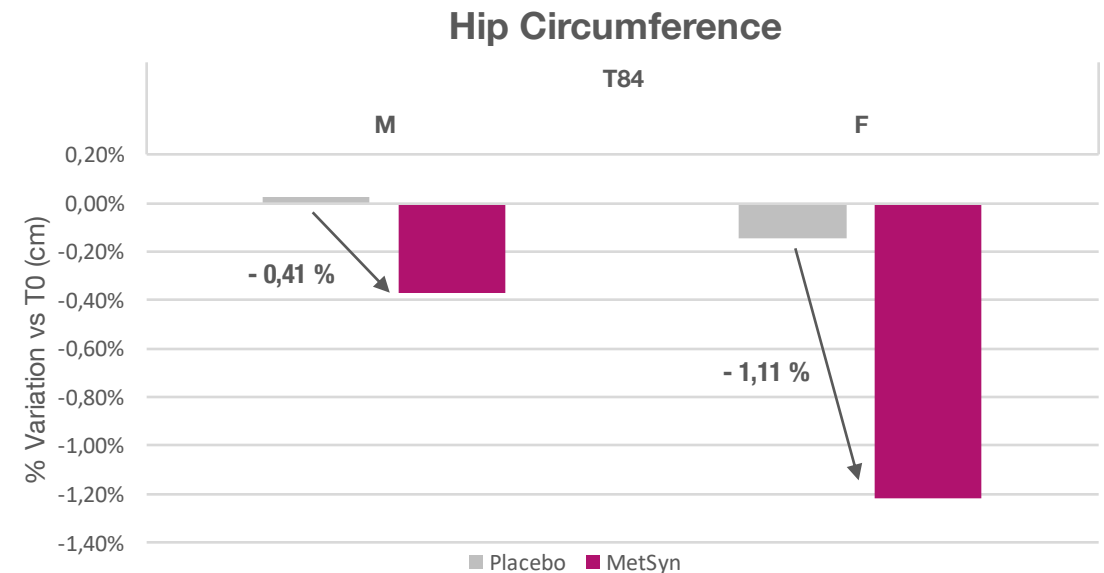
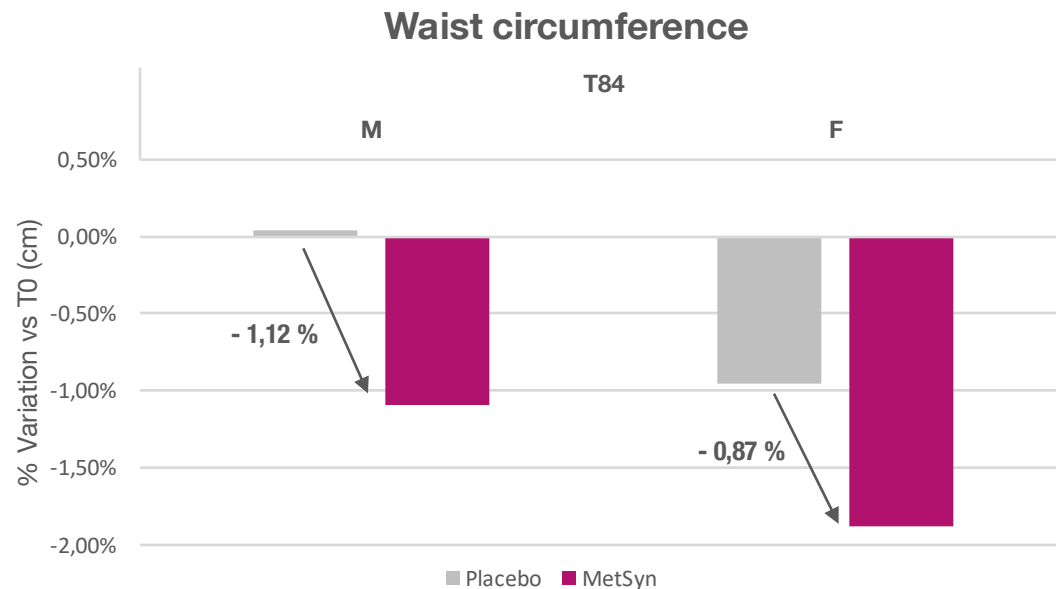




Human

# Waist and Hip circumferences: Subgroup Analysis

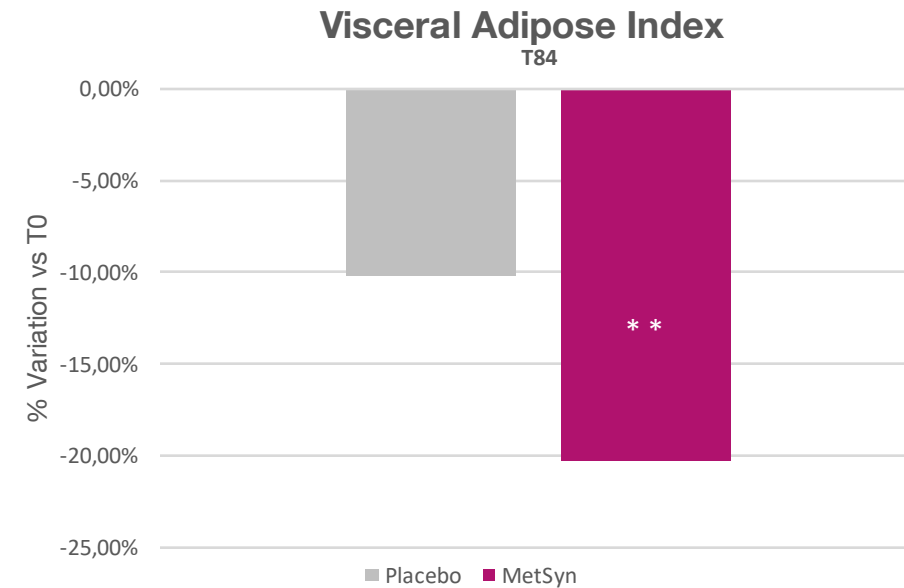
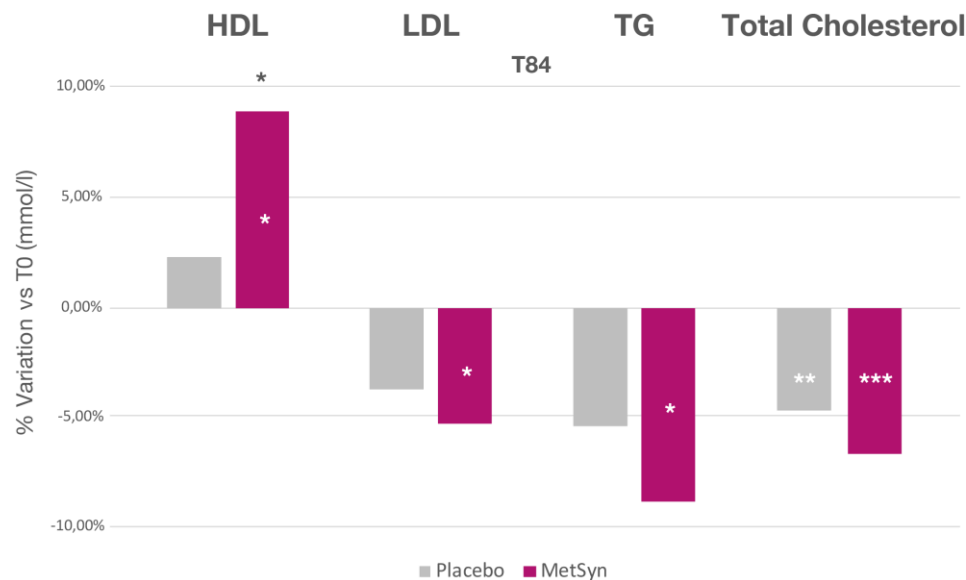
- MetSyn led to **greater waist circumference reduction in men** and **greater hip circumference reduction in women**, reflecting typical fat distribution patterns and targeting areas of adiposity most relevant to metabolic risk.
- Improvements were **consistent and positive in both genders**, highlighting overall effectiveness.





# Modulation of lipid profile

- Overall, **all dyslipidemic markers improved** in MetSyn group during the treatment at T84, with **HDL significantly increased** with respect to placebo.
- Moreover, this was accompanied by a significant reduction in both the **Visceral Adipose Index** and the **Conicity Index** compared to baseline (T0), indicating a decrease in abdominal fat accumulation and an improvement in **body fat distribution**, which may contribute to reduced **cardiometabolic risk**.



\* Statistical significance vs Placebo  
\* Statistical significance vs Baseline

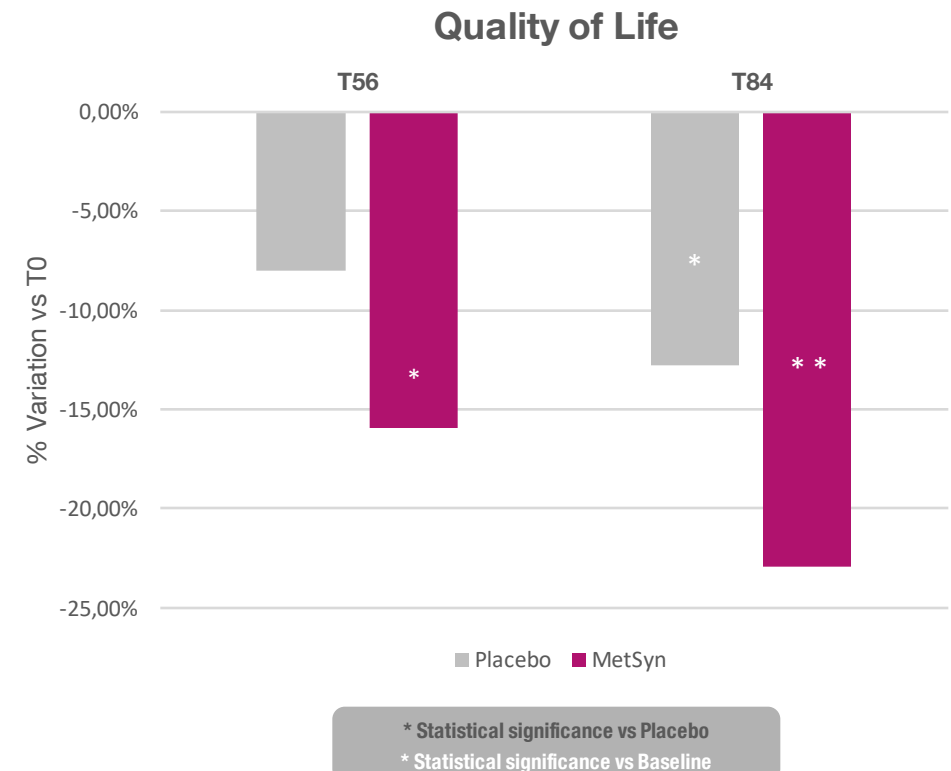


# Improvement of quality of life

Validated questionnaire to determine the influence of obesity on the Quality of Life, based on the following macro-areas:

- Physical health
- Lifestyle attitudes
- Daily habits
- Self-esteem
- Psychological/Emotional well-being

MetSyn group showed significant decrease in questionnaire scores, indicating reduced impact of body weight on physical, social, and psychological well-being.



# Summary

**Description:** Probiotic complex designed for cardiometabolic prevention composed by *L. plantarum* - PBS067, *L. acidophilus* - PBS066, *L. reuteri* - PBS072

**Dosage:** 6B CFU/Day (2B CFU/strain)

**Treatment:** 60 days



Capsules



Tablets



Sachets  
or sticks



Triphase  
vials



Bulk / Full  
service

## RESULTS:

- ✓ Control of carbohydrates digestion
- ✓ Modulation of lipid metabolism
- ✓ Protection from oxidative stress
- ✓ Inhibition of inflammatory stress
- ✓ Improvement of GI symptoms

## TYPICAL APPLICATIONS:

- ✓ Improvement of metabolic functions
- ✓ Decreased hyperglycemia
- ✓ Control of cholesterol synthesis
- ✓ Modulation of chronic inflammation
- ✓ Weight management





Discover more:



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