



## Research article

## Effects of zinc and probiotic co supplementation on lipid profile, waist circumference, and body fat percentage in obesity women

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### ABSTRACT

Obesity is a state of excessive fat accumulation due to a prolonged imbalance between energy intake and expenditure. Zinc deficiency is crucial in the etiology of obesity/overweight, and is a consequence of excessive body weight as well. Hypozincemia worsens metabolic, immune, and oxidative status in obesity. Increasing zinc intake through diet or supplementation may be a viable strategy to reduce obesity-related disorders or conditions. Probiotic strain *Lactobacillus casei* Shirota is a lactic acid bacterium that has benefits for boosting the immune system, as an antioxidant, and can reduce cholesterol levels. This study analyzed the effect of zinc supplementation, *Lactobacillus casei* (LCS) and their co-supplementation on lipid profile consisting of total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides (TG), waist circumference and body fat percentage in obese women. Eighty-four participants were randomized to four groups (zinc (30 mg/day), LCS (6.5x10<sup>9</sup> CFU/day), "zinc and LCS", and placebo) for 30 days. Lipid profiles, anthropometric indicators, and dietary intake were determined pre and post-intervention. In the zinc group, LCS group, and "zinc and LCS" group showed significant differences between pre and post-intervention in serum TC, LDL, HDL, and TG ( $p < 0.05$ ). On anthropometric indicators, all groups showed significant differences between pre and post-intervention on waist circumference and body fat percentage ( $p < 0.05$ ). The beneficial effects of "zinc and LCS" co-supplementation were reported for the changes of some lipid profiles (TC, LDL, HDL, TG), BMI, weight, waist circumference, and body fat percentage.

**Keywords:** Zinc, *Lactobacillus casei*, Lipid profiles, Waist circumference, Body fat percentage, Obesity.

### INTRODUCTION

Obesity is a condition of excessive fat accumulation due to an imbalance between energy intake and energy expenditure for a long time [1]. Obesity has become a global problem, because its prevalence increases every year, not only in developed countries but also in developing countries. The 2018 Basic Health Research (Riskesdas) reported that the prevalence of adult obesity in Indonesia increased from 14.8% in 2013 to 21.8% in 2018. The prevalence of obesity in women (29.3%) was higher than that in men (14.5%). The highest prevalence of obesity in the adult population in Makassar city was

24.05%. One of the main causes of obesity is excessive food intake and low physical activity. The proportion of physical inactivity in Makassar city was 31.92%. The proportion of Fatty/Cholesterol Food Consumption Habits of the Population  $\geq 1$  time per day in Makassar City was 35.5%. It was recorded that 13.3% of people did not consume vegetables and fruit per day in a week in Makassar City [2].

Micronutrient imbalances are also significant contributors to obesity, but positive energy balance has been shown to be the main contributing factor. Overweight or obese people are more likely than

normal-weight people to develop micronutrient deficiencies while consuming excessive amounts of energy [3]. Obese people may have low serum zinc concentrations because they are under chronic oxidative stress, which increases the synthesis of glucocorticoids and decreases zinc transporters [4, 5]. Furthermore, cytokines secreted by adipose tissue can also increase the expression of the zinc transporter, changing the body's distribution of zinc [6].

As a cofactor of numerous enzymes and an antioxidant with anti-inflammatory qualities, zinc is a trace element that provides health advantages in many areas of metabolism [7-9]. Lipid metabolism is significantly influenced by zinc [10]. Zinc supplementation has been shown to improve various lipid profiles, according to the results of some trials or meta-analyses of trials, while several studies did not support this claim [11-13].

In addition to being a cause of obesity and overweight, zinc deficiency is a side effect of being overweight. Hypozincemia deteriorates obesity-related immunological, oxidative, and metabolic health. According to Syane et al, increasing zinc intake by food and/or supplementation may be a practical tactic to lessen problems or symptoms connected to obesity [14].

Probiotics are thought to play a further role in the pathophysiology of obesity. It has been investigated how probiotics, particularly *Lactobacillus* and *Bifidobacterium*, might balance the gut microbiota and treat obesity in order to better understand how they affect gut dysbiosis. Induction of/protection from metabolic endotoxemia, modulation of bile acid metabolism, and synthesis of short-chain fatty acids are the three main ways by which gut microbiota balance may modulate body weight. Furthermore, starch, unabsorbed sugars, cellulosic and non-cellulosic polysaccharides, and mucins which have a direct impact on lipid metabolism and energy production ferment to form short-chain fatty acids. Overall, the gut microbiota can impact the energy balance since it also regulates the gut's ability to absorb nutrients [15].

Zinc and *Lactobacillus* in obese women can be used to increase the body's resistance to free radicals. Probiotic strain *Lactobacillus casei Shirota* is a lactic acid bacteria that has the benefit of improving the immune system, as an antioxidant, and can reduce cholesterol levels. The mechanism of cholesterol reduction can occur because lactic acid present in probiotic drinks can degrade cholesterol into coprostanol. Coprostanol is a substance that cannot be absorbed by the intestines. Thanks to *Lactobacillus*, coprostanol, and the remaining cholesterol can be excreted through feces. In other words, the amount of cholesterol absorbed by the body is low. A report on this subject explains that the reduction of cholesterol by lactic acid bacteria (*Lactobacillus*) can reach about 27-38% [16]. Previous studies describe the positive effects of probiotic supplementation, namely a reduction

in BMI, total body fat, markers of metabolic disorders, an increase in the number of beneficial intestinal microorganisms, and higher levels of short-chain fatty acids [17].

The effects of probiotics and zinc in the gastrointestinal tract are similar, namely immunomodulating effects. Zinc has other effects, such as protecting pathogenic germs and maintaining barrier integrity. In addition, zinc affects the regeneration and function of intestinal villi, which will affect the formation of disaccharidase enzymes, namely lactase, sucrose, and maltase, which affect sodium (Na) and glucose transport [18].

On the one hand, the results of the effect of *Lactobacillus casei* or zinc were inconsistent in previous studies, and on the other hand, there was no trial to evaluate the effect of zinc and *Lactobacillus casei* co-supplementation on lipid profiles in obesity. The present multi-arm, parallel-group, randomized, double-blind placebo-controlled phase 2 clinical trial aimed to evaluate the effect of zinc and *Lactobacillus casei* co-supplementation along with loss-weight diet on serum lipid profiles (TG, LDL, HDL, TC), waist circumference, and body fat percentage in overweight or obese healthy women.

## MATERIAL AND METHODS

This randomized, double-blind, placebo-controlled clinical trial was performed on 84 healthy obese participants. Inclusion criteria were the age range of 30-50, nonsmoking, body mass index (BMI) > 25 (Kg/m<sup>2</sup>), be willing on 500 kcal calorie restriction. While exclusion criteria included pregnancy, breastfeeding, and postmenopausal among women. Those who took zinc and *Lactobacillus casei* supplements during the previous three months, as well as those utilizing medications that may interact with serum lipid profiles and weight reduction, were not included in the study. Participants were asked to provide written informed permission after being informed about the purpose of the study.

Using a random block technique generated by Random Allocation Software (RAS), the eligible participants were randomized at random to intervention-placebo groups [19]. Based on data from the same study, the sample size was established [20]. The confidence level was set at 95% and the formula  $N = [(Z1-\alpha/2 + Z1-B) 2 (SD12+SD22)] / \Delta^2$  was used to calculate the 21 samples in each group (accounting for a drop-out rate of 40%). For one month, the Zinc group (n=21) received a 30 mg zinc gluconate tablet per day. Dosages were selected based on the previous studies [21, 22]. The *Lactobacillus casei* (LCS) group (n=21) had received a 6.5x10<sup>9</sup> CFU/day, the co-supplementation group had received both a zinc gluconate tablet and 6.5x10<sup>9</sup> CFU *Lactobacillus casei* per day, while the placebo group (n=21) had nothing. Throughout the trial, all participants aside from the placebo group were instructed to limit their regular calorie intake to 500 kcal. to guarantee that the participants would follow the instructions. Blood

samples were obtained at the start and finish of the trial while subjects were fasting for 12 hours. Data on demographics was gathered using surveys. With no shoes on and minimal clothing, body weight and body fat % were determined using a bioelectrical impedance analysis (BIA) device (TANITA BC-542). A stadiometer (Seca) was also used to measure height without shoes. Weight (in kilos) divided by height (in meters squared) yielded the BMI. A stadiometer (Onemed) was used to measure waist circumference (WC). Using the Thermo Scientific™ Indiko™ plus Clinical Chemistry Analyzer, the serum concentrations of triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and LDL-C were measured.

#### Statistical Analysis

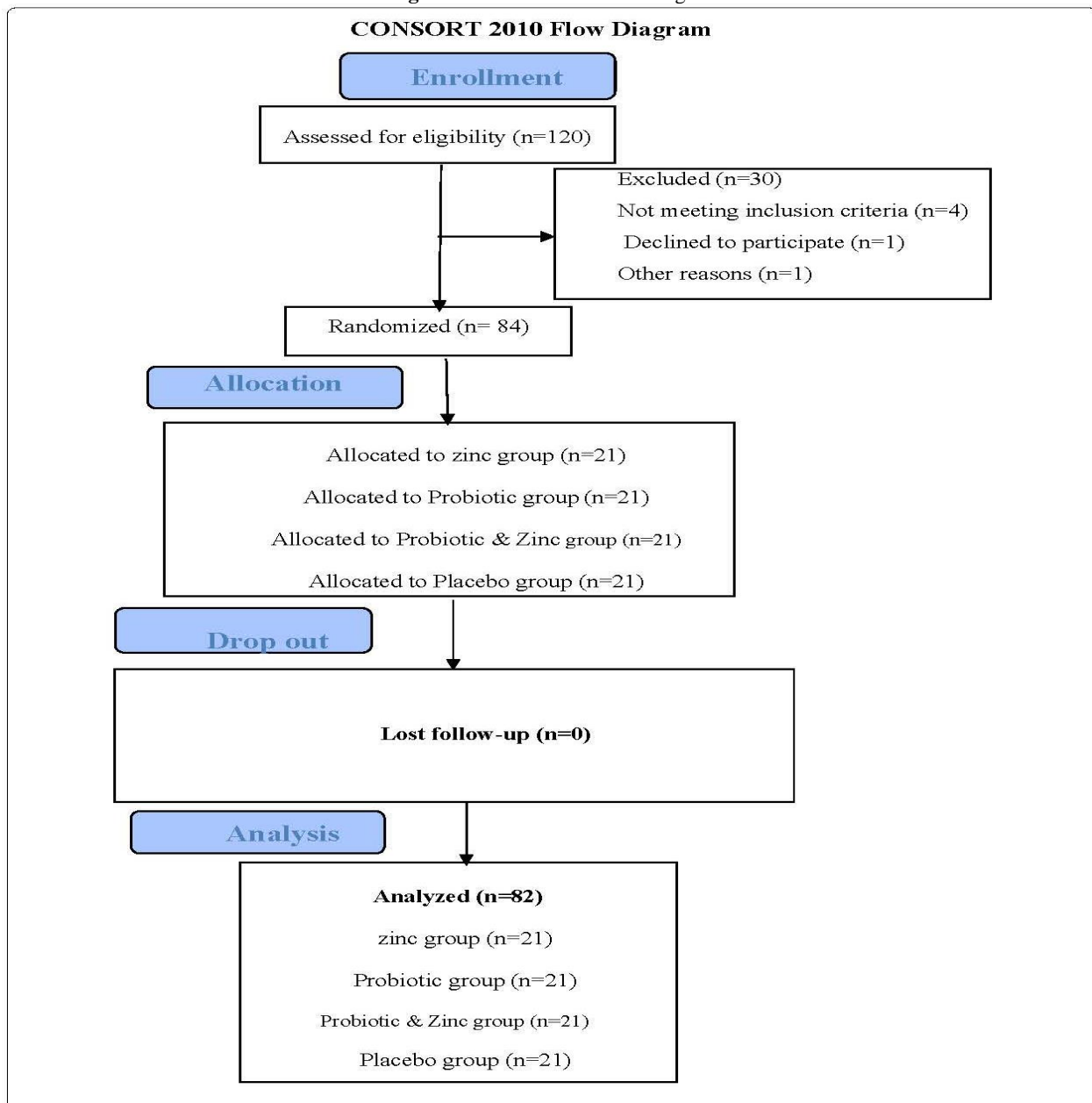
All analyses were performed using a statistical software package (SPSS), version 22.0 (SPSS, Inc). Statistical significance was determined at  $p < 0.05$ . Normal distribution and the homogeneity of

variances for quantitative variables were checked by Kolmogorov–Smirnov test and Leven’s tests, respectively. Data were reported as mean  $\pm$  standard deviation (SD) and median (interquartile range) for normally and non-normally distributed data, respectively. Within-group comparisons were performed using a paired-sample t-test. Between-group comparisons for variables were carried out using a one-way ANOVA and Kruskal–Wallis for normally and non-normally distributed data, respectively. The changes (pre-post intervention) were calculated based on the difference of variables from the baseline (pre-intervention) to the end (post-intervention) of the study.

#### RESULTS

A total of 84 participants completed the 30 days of the trial. No one lost the follow-up. Figure 1 shows the flow diagram of the study.

Figure 1: Consort 2010 Flow Diagram



As set out in Table 1, the general and clinical characteristics of the participants were not found any significant difference between the four groups at the baseline.

**Table 1:** General and Clinical characteristics of the participants at the baseline

Variable	Placebo (n = 21)	Zinc (n = 21)	LCS (n = 21)	Zinc and LCS (n = 21)	P-value
Age (year)	35,90 ± 2,76	35,86 ± 3,12	36,15 ± 3,39	36,14 ± 3,39	0,979 <sup>a</sup>
Weight (kg)	74,44 ± 11,64	74,80 ± 8,35	77,72 ± 13,74	73,98 ± 7,4	0,868 <sup>b</sup>
BMI (kg/m <sup>2</sup> )	32,65 ± 5,15	31,96 ± 3,86	33,87 ± 5,89	31,49 ± 3,47	0,592 <sup>b</sup>
Waist circumference (cm)	99,19 ± 6,68	99,62 ± 6,73	102,57±7,21	98,76 ± 7,55	0,102 <sup>b</sup>
Body fat percentage (%)	43, 14 ± 5,82	42,99 ± 4,86	45,30 ± 7,21	41,66 ± 2,74	0,301 <sup>b</sup>
Total cholesterol (mg/dl)	205,21±38,36	227,43±41,9	209,05±38,56	219,59±42,05	0,180 <sup>b</sup>
HDL-C (mg/dl)	48,19 ± 8,42	51,73 ± 8,75	50,41 ± 8,33	51,15 ± 9,6	0,548 <sup>b</sup>
LDL-C (mg/dl)	120,39 ± 51,71	145,39±36,58	124,38±41,29	139,39±50,09	0,548 <sup>b</sup>
Triglyceride (mg/dl)	183,15 ± 92,02	151,52±32,47	171,34±63,42	145,23±90,49	0,301 <sup>b</sup>

Data are presented as mean± standard deviation (SD) for quantitative variables

<sup>a</sup> P-value was calculated for the comparison variables between four groups using a one-way analysis of variance (one-way ANOVA)

<sup>b</sup> P-value was calculated for the comparison variables between four groups using Kruskal–Wallis P-value< 0.05 was considered significant

BMI body mass index, HDL-C high-density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol

The dietary intake of participants is shown in Table 2. Participants of both groups ate slightly less than their prescribed goal. There was no between group difference in energy intake.

**Table 2:** Dietary characteristics of participants during the study

Variable	Placebo (n = 21)	Zinc (n = 21)	LCS (n = 21)	Zinc and LCS (n = 21)	P-value
TEE (%)					
Pre-intervention	174,96±16,68	172,11±36,58	171,26±16,32	169,91±11,63	0,623 <sup>f</sup>
Post-intervention	172,23±16,03	129,81±9,31	128,04 ± 12,00	129,05 ± 7,75	0,000 <sup>e</sup>
P-value	0,028 <sup>c</sup>	0,000 <sup>d</sup>	0,000 <sup>c</sup>	0,000 <sup>c</sup>	
Fat (% of energy)					
Pre-intervention	32,83 ± 3,58	32,36 ± 0,83	31,52 ± 4,01	32,09 ± 4,16	0,759 <sup>f</sup>
Post-intervention	31,75 ± 2,93	20,30±3,23	24,77 ± 4,04	23,85 ± 3,04	0,000 <sup>e</sup>
P-value	0,317 <sup>c</sup>	0,000 <sup>c</sup>	0,000 <sup>c</sup>	0,000 <sup>d</sup>	
Fiber (g/day)					
Pre-intervention	9,41 ± 1,63	9,22 ± 1,32	9,35 ± 1,19	9,43 ± 1,10	0,951 <sup>e</sup>
Post-intervention	9,30 ± 0,75	10,93 ± 6,67	9,59 ± 1,70	9,85 ± 1,32	0,001 <sup>e</sup>
P-value	0,800 <sup>c</sup>	0,000 <sup>c</sup>	0,480 <sup>c</sup>	0,254 <sup>c</sup>	
Cholesterol (g/day)					
Pre-intervention	223,61 ± 46,66	208,70±41,24	213,00 ± 38,65	201,79 ± 36,36	0,376 <sup>e</sup>
Post-intervention	209,89±30,37	90,79 ± 27,21	123,15 ± 37,35	117,60 ± 27,58	0,000 <sup>f</sup>
P-value	0,306 <sup>c</sup>	0,000 <sup>d</sup>	0,000 <sup>d</sup>	0,000 <sup>d</sup>	
MUFA (g/day)					
Pre-intervention	29,75 ± 5,71	29,59 ± 5,42	30,47 ± 5,89	30,48 ± 5,58	0,932 <sup>e</sup>
Post-intervention	29,20 ± 4,03	13,09 ± 2,89	16,23 ± 3,14	15,52 ± 2,50	0,000 <sup>e</sup>
P-value	0,742 <sup>c</sup>	0,000 <sup>c</sup>	0,000 <sup>c</sup>	0,000 <sup>c</sup>	
PUFA (g/day)					
Pre-intervention	21,93 ± 3,59	22,19 ± 4,46	20,75 ± 4,69	21,27 ± 3,81	0,691 <sup>f</sup>
Post-intervention	21,72 ± 2,34	10,71 ± 2,06	13,80 ± 2,70	13,31 ± 1,89	0,000 <sup>e</sup>
P-value	0,821 <sup>c</sup>	0,000 <sup>d</sup>	0,000 <sup>c</sup>	0,000 <sup>d</sup>	
Zinc (mg/day)					
Pre-intervention	9,01 ± 0,94	9,02 ± 0,88	8,75 ± 0,94	8,68 ± 1,10	0,706 <sup>f</sup>
Post-intervention	8,95 ± 0,45	7,82 ± 5 0,61	7,66 ± 0,41	7,69 ± 0,37	0,000 <sup>f</sup>
P-value	0,792 <sup>c</sup>	0,001 <sup>d</sup>	0,000 <sup>c</sup>	0,001 <sup>d</sup>	

Data are presented as mean± standard deviation (SD) for quantitative variables and frequency (%) for qualitative variables

<sup>c</sup> P-value was calculated for the comparison variables within the group using a paired t-test

<sup>d</sup> P-value was calculated for the comparison variables within the group using the Wilcoxon Signed Ranks Test

<sup>e</sup> P-value was calculated for the comparison variables between four groups using one-way analysis of variance (one-way ANOVA)

<sup>f</sup> P-value was calculated for the comparison variables between four groups using the Kruskal Wallis Test

Table 3 shows the comparison of lipid profiles within the groups. The post-intervention serum lipid profiles of the zinc, LCS, and "zinc and LCS" groups showed a significant improvement, as shown in Table 3 (within-group comparisons).

**Table 3:** Comparisons of lipid profiles and anthropometric indicators of the Participants between and within the groups

Variable	Placebo (n = 21)	Zinc (n = 21)	LCS (n = 21)	Zinc and LCS (n = 21)	P-value
Total cholesterol (mg/dl)					
Pre-intervention	205,21±38,36	227,43±41,9	209,05±38,56	219,59±42,05	0,180 <sup>f</sup>
Post-intervention	205,87±43,06	200,11±36,62	196,10±40,35	192,38±26,16	0,416 <sup>f</sup>
P-value	0,931 <sup>d</sup>	<b>0,000<sup>c</sup></b>	<b>0,004<sup>d</sup></b>	<b>0,001<sup>c</sup></b>	
Change	0,67±41,75	-27,31±15,86	-13,95±18,66	-27,21±32,50	<b>0,039<sup>f</sup></b>
HDL-C (mg/dl)					
Pre-intervention	48,19 ± 8,42	51,73 ± 8,75	50,41 ± 8,33	51,15 ± 9,6	0,548 <sup>f</sup>
Post-intervention	46,21 ± 9,28	57,10 ± 10,67	68,77 ± 13,77	72,33 ± 10,97	<b>0,000<sup>f</sup></b>
P-value	0,122 <sup>c</sup>	<b>0,004<sup>c</sup></b>	<b>0,000<sup>d</sup></b>	<b>0,000<sup>c</sup></b>	
Change	-1,98 ± 5,61	5,37 ± 7,58	18,36±9,01	21,18±4,71	<b>0,000<sup>f</sup></b>
LDL-C (mg/dl)					
Pre-intervention	120,39 ± 51,71	145,39±36,58	124,38±41,29	139,39±50,09	0,234 <sup>e</sup>
Post-intervention	122,01 ± 42,47	119,18±32,38	97,71 ±44,19	93,52 ± 31,20	0,055 <sup>e</sup>
P-value	0,863 <sup>c</sup>	<b>0,000<sup>c</sup></b>	<b>0,000<sup>c</sup></b>	<b>0,000<sup>c</sup></b>	
Change	1,62 ± 42,41	-25,74±16,71	-26,67±19,57	-45,39±33,64	<b>0,000<sup>e</sup></b>
Triglyceride (mg/dl)					
Pre-intervention	183,15 ± 92,02	151,52±32,47	171,34±63,42	145,23±90,49	0,301 <sup>f</sup>
Post-intervention	188,26 ± 93,52	116,76±27,50	143,10±52,92	130,23±79,98	<b>0,015<sup>f</sup></b>
P-value	0,610 <sup>c</sup>	<b>0,000<sup>c</sup></b>	<b>0,003<sup>d</sup></b>	<b>0,042<sup>d</sup></b>	
Change	5,11 ± 45,22	-34,75±33,47	-28,24±34,84	-15,00±29,43	<b>0,003<sup>e</sup></b>

Data are presented as mean± standard deviation (SD) for quantitative variables and frequency (%) for qualitative variables

<sup>d</sup>P-value was calculated for the comparison variables within the group using the Wilcoxon Signed Ranks Test

<sup>e</sup>P-value was calculated for the comparison variables between four groups using one-way analysis of variance (one-way ANOVA)

<sup>f</sup>P-value was calculated for the comparison variables between four groups using the Kruskal Wallis Test

The comparison of waist circumference and body fat percentage (%) within groups is depicted in Table 4. As set out in Table 4 (within-group comparisons), the anthropometric indicators on waist circumference and body fat percentage, in the four groups revealed a significant improvement for post-group.

**Table 5:** Comparisons of Anthropometry indicators of the Participants between and within the groups

Variable	Placebo (n = 21)	Zinc (n = 21)	LCS (n = 21)	Zinc and LCS (n = 21)	P-value
Waist circumference (cm)					
Pre-intervention	99,19 ± 6,68	99,62 ± 6,73	102,57±7,21	98,76 ± 7,55	0,102 <sup>f</sup>
Post-intervention	100,76±6,75	96,23 ± 6,94	100,90±7,19	96,29 ± 7,90	<b>0,014<sup>f</sup></b>
P-value	<b>0,004<sup>d</sup></b>	<b>0,000<sup>c</sup></b>	<b>0,000<sup>d</sup></b>	<b>0,000<sup>d</sup></b>	
Change	1,57 ± 2,04	-3,33 ± 1,98	-1,67 ± 0,73	-2,38 ± 0,92	<b>0,000<sup>f</sup></b>
Body fat percentage (%)					
Pre-intervention	43, 14 ± 5,82	42,99 ± 4,86	45,30 ± 7,21	41,66 ± 2,74	0,293 <sup>f</sup>
Post-intervention	43,37 ± 5,82	42,33 ± 4,91	44,92 ± 7,23	41,20 ± 2,76	0,271 <sup>f</sup>
P-value	<b>0,000<sup>d</sup></b>	<b>0,000<sup>d</sup></b>	<b>0,000<sup>d</sup></b>	<b>0,000<sup>c</sup></b>	
Change	0,23 ± 0,16	-0,58 ± 0,41	-0,37 ± 0,18	-0,46 ± 0,27	<b>0,000<sup>e</sup></b>

Data are presented as mean± standard deviation (SD) for quantitative variables and frequency (%) for qualitative variables

<sup>c</sup>P-value was calculated for the comparison variables within the group using a paired t-test

<sup>d</sup>P-value was calculated for the comparison variables within the group using the Wilcoxon Signed Ranks Test

<sup>e</sup>P-value was calculated for the comparison variables between four groups using one-way analysis of variance (one-way ANOVA)

<sup>f</sup>P-value was calculated for the comparison variables between four groups using the Kruskal Wallis Test

## DISCUSSION

While the tolerated limit of the greatest intake (40 mg/day) was less than in this investigation, the use of 30 mg/d zinc was more than the recommended amount (DRIs 8-11 mg/day) [23]. Despite lifestyle guidelines, a hypo caloric diet, and continued subject follow-up, there was no significant difference in dietary intake across the groups. The mean decrease in calorie intake in each group was roughly 500 kcal (the suggested values). Between the pre- and post-intervention periods, there was a change in weight and BMI toward improvement. Consequently, it might result from supplements' beneficial effects on weight and BMI [24, 25].

Zinc supplementation was shown to improve several blood lipid levels (TC, HDL, LDL, and TG) in various populations in earlier studies [11, 12, and 26]. Additionally, the results of a meta-analysis by Asbaghi et al. demonstrated the positive effects of zinc supplementation on HDL in both studies with lengths of time greater

than or equal to 12 weeks. Furthermore, only studies lasting 12 weeks or less showed a reduction in blood TG, TC, and LDL following zinc administration. Interestingly, they noted that at dosages lower than 100 mg, the effects of zinc supplementation were greatest [11].

Zinc may influence serum lipid levels through a variety of molecular processes. The following are the suggested mechanisms of zinc action, both direct and indirect: Zinc has the ability to influence several aspects of insulin synthesis and secretion: (1) it can regulate the activity of pancreatic  $\beta$ -cells by affecting the expression of the transporter; (2) it can increase insulin sensitivity or insulin resistance by phosphorylating insulin-receptor substrates at the adipocytes [7]; (3) it can inhibit lipolysis in adipose tissues, which reduces the amount of fatty acids released and ultimately regulates lipoprotein synthesis (liver secretion of VLDL and LDL) from the liver; and (4) it can influence the gene expression of enzymes involved in hepatic lipid homeostasis,

which in turn regulates lipid synthesis and utilization in mitochondria and peroxisomes [27].

Probiotic supplements have been shown to lower body weight, BMI, and fat percentage [28]. To lessen the intestinal absorption of cholesterol, probiotics have the ability to bind cholesterol. Probiotics may also lessen the amount of bile salts that are circulated through the enterohepatic system, which would force the liver to resynthesize bile salts by mobilizing more cholesterol [29-31]. This would lower cholesterol levels. Currently, two distinct mechanisms by which gut microorganisms control blood lipid levels are known. One way is through controlling the metabolism of bile acids, which influences other metabolic processes and modifies blood lipid levels [32]. Probiotics can influence anthropometric indices and body composition through a number of mechanisms, including: (a) decreasing adipocyte size by increasing fatty acid oxidation and lowering lipid absorption; (b) inhibiting adipogenesis by producing conjugated linoleic acid (CLA); (c) increasing satiety-inducing glucagon-like peptide-1 (GLP-1) and peptide YY (PYY) secretion; (d) increasing satiety by increasing the synthesis of short-chain polyunsaturated fatty acids; and (e) modulating the expression of fasting-induced adipose factor (FIAF), which appears to promote adipose tissue lipolysis and subsequently lipids being redirected from storage to the circulation [33-38]. Bacterial fermentation produces short-chain fatty acids (SCFAs), which include acetate, butyrate, and propionate. These compounds serve as energy substrates and as appetite and satiety regulators. By activating the G- protein-coupled receptors GPR41 and GPR43 on intestinal epithelial cells, SCFAs also have a role in the regulation of energy metabolism and insulin sensitivity in peripheral organs [39].

After the intervention, there was a significant decrease in the anthropometric measurements of waist circumference and body fat percentage indices. Numerous studies have also demonstrated that specific bacterial strains, like *Lactobacillus* and *Bifidobacterium spp.*, can reduce BMI, waist circumference, and percentage body fat when combined with prebiotics [40,41]. According to research by Minami et al., pre-obese adults could effectively reduce body fat with the aid of the probiotic strain *Bifidobacterium breve B-3*. According to the study, participants' body fat mass and percentage of body fat significantly decreased after 12 weeks of treatment [42]. Furthermore, a prior investigation has illustrated the capacity of *Lactobacillus gasseri* BNR17 to decrease waist circumference and visceral fat formation in individuals with obesity [43].

The richness, or the diversity and abundance, of microbial species found in the gut, is a crucial feature of the gut microbiota that has been the subject of extensive investigation. Studies demonstrating that people who are overweight or obese typically have a less

diversified gut microbiome than those with a healthy body weight have contributed to the expanding body of data linking gut microbial richness with obesity [44, 45]. Moreover, a greater diversity of gut bacteria has been linked to improved health outcomes, whereas a reduced diversity has been connected to a number of illnesses, including obesity. Research has demonstrated that the gut microbiota of obese people typically exhibits lower alpha diversity, suggesting a less varied and well-balanced microbial population [46-48]. It is believed that this imbalance in the gut microbiota influences hunger regulation, energy metabolism, and inflammation, all of which have a role in the development of obesity. When given for eight weeks to people with high body mass index, *Lactobacillus acidophilus*, *Lactobacillus casei*, and *Bifidobacterium lactis* reduced inflammatory indicators and body fat percentage [49]. These results imply that probiotics may be able to reduce inflammation and enhance a number of health-related factors.

Losing weight through diet may enhance host metabolism and reduce the chance of potential comorbidities linked to obesity. Findings on the effects of dietary weight loss on the composition and function of the microbiome from randomized trials have been equivocal, despite evidence to suggest that these benefits are due to modulations of the gut microbiome and related metabolites upon calorie restriction [50-52]. Small sample sizes, brief trial lengths, and a variety of microbiome evaluation methodologies employed in earlier research may be to blame for this, as well as the extreme and restrictive dietary strategies employed in numerous intervention trials to induce weight reduction [53, 54]. Furthermore, differentiating between brief fluctuations in the composition of the gut microbiome [54]. It has been difficult to discern intervention-associated changes since most previous research did not include recurrent gut microbiota surveys. Furthermore, it is unclear how long-term changes in the composition of the gut microbiome following weight reduction will last and how much they are related to changes in circulating metabolites, anthropometric, and clinical indicators in addition to body composition [55]. According to the study's findings, obese female adults who received zinc and *Lactobacillus casei* for a month had a decrease waist circumference, fat percentage and serum lipid profiles in their body when compared to a placebo. As such, it could be useful in preventing both macro and micro vascular problems. However, there were certain drawbacks, like a brief follow-up period. Future research could take into account extending the duration of the intervention and figuring out the safety and efficacy of zinc and *Lactobacillus casei* supplementation dosages. To the best of our knowledge, this was the first study in the area to look at the impact of co-supplementing with probiotics and zinc on adult obese women, and it can be considered as the strength of the study.



**CONCLUSION**

The study concludes that in the zinc group, LCS group, and “zinc and LCS” group showed significant differences between pre and post-intervention in serum TC, LDL, HDL, and TG ( $p < 0.05$ ). On waist circumference and body fat percentage, all groups showed significant differences between pre and post-intervention on waist circumference and body fat percentage ( $p < 0.05$ ). The beneficial effects of “zinc and LCS” co-supplementation were reported for the changes of some lipid profiles (TC, LDL, HDL, TG), BMI, weight, waist circumference, and body fat percentage.

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**REFERENCES**

1. Abdollahi S, Toupchian O, Jayedi A, et al, 2020. Zinc Supplementation and Body Weight: A Systematic Review and Dose-Response Meta-analysis of Randomized Controlled Trials. *Adv Nutr.* 2020. 11(2), Pages 398-411 Doi: <https://doi.org/10.1093/advances/nmz084>.
2. Mota Martins L, Soares de Oliveira AR, Clímaco Cruz KJ, et al, 2014. Influence of cortisol on zinc metabolism in morbidly obese women. *Nutr Hosp.* 29, Pages 57–63.
3. Feitosa MCP, de Sousa Lima VB, Moita Neto JM, et al, 2013. Plasma concentration of IL-6 and TNF- $\alpha$  and its relationship with zincemia in obese women. *Revista da Associação Médica Brasileira.* 59(5), Pages 429–434. Doi: [https://doi.org/10.1016/S2255-4823\(13\)70501-0](https://doi.org/10.1016/S2255-4823(13)70501-0).
4. Habib SA, Saad EA, Elsharkawy AA, et al, 2015. Pro-inflammatory adipocytokines, oxidative stress, insulin, Zn and Cu: interrelations with obesity in Egyptian non-diabetic obese children and adolescents. *Adv Med Sci.* 60(2), Pages 179–85. Doi: [10.1016/j.advms.2015.02.002](https://doi.org/10.1016/j.advms.2015.02.002).
5. Lynch CJ, Patson BJ, Goodman SA, et al, 2001. Zinc stimulates the activity of the insulin-and nutrient-regulated protein kinase mTOR. *Am J Physiol Endocrinol Metab.* 281(1), Pages E25–34. Doi: [10.1152/ajpendo.2001.281.1.E25](https://doi.org/10.1152/ajpendo.2001.281.1.E25).
6. Dunn MF, 2005. Zinc–ligand interactions modulate assembly and stability of the insulin hexamer—a review. *Biometals.* 18(4), Pages 295–303. Doi: [10.1007/s10534-005-3685-y](https://doi.org/10.1007/s10534-005-3685-y).
7. Stefanidou M, Maravelias C, Dona A, et al, 2006. Zinc: a multipurpose trace element. *Arch Toxicol.* 80(1), Pages 1-9. Doi: [10.1007/s00204-005-0009-5](https://doi.org/10.1007/s00204-005-0009-5).
8. Choi S, Liu X, Pan Z, 2018. Zinc deficiency and cellular oxidative stress: prognostic implications in cardiovascular diseases. *Acta Pharmacol Sin.* 39(7), Pages 1120–1132. Doi: <https://doi.org/10.1038/aps.2018.25>.
9. Asbaghi O, Sadeghian M, Fouladvand F, et al, 2020. Effects of zinc supplementation on lipid profile in patients with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials. *Nutr Metab Cardiovasc Dis.* 30(8):
10. Ranasinghe P, Wathurapatha WS, Ishara MH, et al, 2015. Effects of zinc supplementation on serum lipids: a systematic review and meta-analysis. *Nutr Metab.* 12, Pages 26. Doi: [10.1186/s12986-015-0023-4](https://doi.org/10.1186/s12986-015-0023-4).
11. Mihir Otia, Anvita Dubey, 2024. Antibiotics over usage: a vital contributor of antibiotic resistance. *International journal of therapeutic innovation, V 2 - I 2*, Pages 0130 – 0137. Doi: <https://doi.org/10.55522/ijti.V2I2.0030>.
12. Jafarnejad S, Mahboobi S, McFarland LV, et al, 2019. Meta-analysis: effects of zinc supplementation alone or with multi-nutrients, on glucose control and lipid levels in patients with type 2 diabetes. *Prev Nutr Food Sci.* 24(1), Pages 8–23. Doi: [10.3746/pnf.2019.24.1.8](https://doi.org/10.3746/pnf.2019.24.1.8).
13. Svane MS, Jørgensen NB, Bojsen-Møller KN, et al, 2016. Peptide YY and glucagon-like peptide-1 contribute to decreased food intake after Roux-en-Y gastric bypass surgery. *Int J Obes (Lond).* 40(11), Pages 1699-1706. Doi: <https://doi.org/10.1038/ijo.2016.121>.
14. Marzieh Daniali, Shekoufeh Nikfar, Mohammad Abdollahi, 2020. A brief overview on the use of probiotics to treat overweight and obese patients. *Expert Review of Endocrinology & Metabolism.* 15(1), Pages 1-4. Doi: <https://doi.org/10.1080/17446651.2020.1719068>.
15. Hartono Rudy, Aswita Amir, Agustian Ipa, et al, 2020. Zinc and Probiotic Combinations: Balancing Blood Sugar and Blood Fats in Children OBES and Bows. 2020. *Indian Journal of Public Health Research & Development.* Doi: [10.37506/ijphrd.v11i4.7743](https://doi.org/10.37506/ijphrd.v11i4.7743).
16. Mo SJ, Lee K, Hong HJ, et al, 2022. Effects of *Lactobacillus curvatus* HY7601 and *Lactobacillus plantarum* KY1032 on Overweight and the Gut Microbiota in Humans: Randomized, Double-Blinded, Placebo-Controlled Clinical Trial. *Nutrients.* 14(12), Pages 2484. Doi: <https://doi.org/10.3390/nu14122484>.
17. Hartono Rudy, Agustian Ipa, Aswita Amir, et al, 2021. Impact of zinc: Early prevention of obesity and fatty in children. *Obesity Medicine.* 21, Doi: <https://doi.org/10.1016/j.obmed.2020.100313>.
18. Saghaei M, 2004. Random allocation software for parallel group randomized trials. *BMC Med Res Methodol.* 4(26), Pages 1-6. Doi: [10.1186/1745-2875-4-26](https://doi.org/10.1186/1745-2875-4-26).
19. Dell RB, Holleran S, Ramakrishnan R, 2002. Sample size determination. *ILAR J.* 43(4), Pages 207-213. Doi: [10.1093/ilar.43.4.207](https://doi.org/10.1093/ilar.43.4.207).
20. Panahi Y, Khalili N, Sahebi E, et al, 2018. Effects of curcuminoids plus piperine on glycemic, hepatic and inflammatory biomarkers in patients with type 2 diabetes mellitus: a randomized double-blind placebo-controlled trial. *Drug Res.* 68(07), Pages 403–409. Doi: [10.1055/s-0044-101752](https://doi.org/10.1055/s-0044-101752).
21. Kim J, Ahn J, 2014. Effect of zinc supplementation on inflammatory markers and adipokines in young obese women. *Biol Trace Elem Res.* 157(2), Pages 101–106. Doi: [10.1007/s12011-013-9885-3](https://doi.org/10.1007/s12011-013-9885-3).

Pages

1260–71.

Doi:

<https://doi.org/10.1016/j.numecd.2020.03.021>.

22. Kathleen Mahan L, Escott-Stump S, Raymond JL, et al, 2012. Krause's Food and the Nutrition Care Process. 13th ed. St. Louis: Elsevier Elsevier/Saunders.
23. Kriaucioniene V, Bagdonaviciene L, Rodríguez-Pérez C, et al, 2020. Associations between changes in health behaviors and body weight during the COVID-19 quarantine in Lithuania: the Lithuanian COVIDiet Study. *Nutrients*. 12(10), Pages 3119. Doi: 10.3390/nu12103119.
24. López-Sánchez GF, López-Bueno R, Gil-Salmerón A, et al, 2020. Comparison of physical activity levels in Spanish adults with chronic conditions before and during COVID-19 quarantine. *Eur J Public Health*. 31(1), Pages 161–6. Doi: <https://doi.org/10.1093/eurpub/ckaa159>.
25. Jayawardena R, Ranasinghe P, Galappathay P, et al, 2012. Effects of zinc supplementation on diabetes mellitus: a systematic review and meta-analysis. *Diabetol Metab Syndr*. 4(1), Pages 13. Doi: 10.1186/1758-5996-4-13.
26. Dieck Ht, Döring F, Fuchs D, et al, 2005. Transcriptome and proteome analysis identifies the pathways that increase hepatic lipid accumulation in zinc-deficient rats. *J Nutr*. 135(2), Pages 199–205. Doi: 10.1093/jn/135.2.199
27. Borgeraas H., L. K. Johnson, J. Skattebu, et al, 2018. Effects of probiotics on body weight, body mass index, fat mass and fat percentage in subjects with overweight or obesity, *Obesity Rev*. 19, Pages 219–232. Doi: 10.1111/obr.12626.
28. Kim G. B., S. H. Yi and B. H. Lee, 2004. Purification and Characterization of Three Different Types of Bile Salt Hydrolases from *Bifidobacterium* Strains, *J. Dairy Sci*. 87, Pages 258–266. Doi: [https://doi.org/10.3168/jds.S0022-0302\(04\)73164-1](https://doi.org/10.3168/jds.S0022-0302(04)73164-1)
29. Min-Tze, L., F. R. Dunshea, N. P. Shah, 2007. Effects of a symbiotic containing *Lactobacillus acidophilus* ATCC 4962 on plasma lipid profiles and morphology of erythrocytes in hypercholesterolaemic pigs on high- and low-fat diets, *Br. J. Nutr*. 98(4), Pages 736–744. Doi: 10.1017/S0007114507747803.
30. De Smet I., P. De Boever, and W. Verstraete, 1998. Cholesterol lowering in pigs through enhanced bacterial bile salt hydrolase activity, *Br. J. Nutr*. 79, Pages 185–194. DOI: 10.1079/BJN19980030
31. Fu J., M. J. Bonder, M. C. Cenit, et al, 2015. The Gut Microbiome Contributes to a Substantial Proportion of the Variation in Blood Lipids, *Circ. Res*. 117, Pages 817–824. 10.1161/CIRCRESAHA.115.306807
32. Barczynska R, Bandurska K, Slizewska K, et al, 2015. Intestinal Microbiota, Obesity and Prebiotics. *Pol J Microbiol*. 64(2), Pages 93-100.
33. Diamant M, Blaak EE, de Vos WM, 2011. Do nutrient-gut-microbiota interactions play a role in human obesity, insulin resistance, and type 2 diabetes? *Obes Rev*. 12(4), Pages 272-281. Doi: <https://doi.org/10.1111/j.1467-789X.2010.00797.x>.
34. Miglioranza Scavuzzi B, Miglioranza LH, Henrique FC, et al, 2015. The role of probiotics on each component of the metabolic syndrome and other cardiovascular risks. *Expert Opin Ther Targets*. 19(8), Pages 1127-1138. <https://doi.org/10.1517/14728222.2015.1028361>.
35. Rabiei S, Hedayati M, Rashidkhani B, et al, 2019. The effects of Synbiotic supplementation on body mass index, metabolic and inflammatory biomarkers, and appetite in patients with metabolic syndrome: *J Dietary Suppl*. 2019. 16(3), Pages 294-306. <https://doi.org/10.1080/19390211.2018.1455788>.
36. Mazloom K, Siddiqi I, Covasa M, 2019. Probiotics: how effective are they in the fight against obesity? *Nutrients*. 11(2), Pages 258. Doi: <https://doi.org/doi:10.3390/nu11020258>.
37. Zandbergen F, Van Dijk S, Müller M, et al, 2006. Fasting-induced adipose factor/angiopoietin-like protein 4: a potential target for dyslipidemia? *Future Lipidol*. 1(2), Pages 227-236. Doi: <https://doi.org/10.2217/17460875.1.2.227>.
38. Brown, A J S M, Goldsworthy A A. Barnes, et al, 2003. The Orphan G protein-coupled receptors GPR41 and GPR43 are activated by propionate and other short chain carboxylic acids, *J. Biol. Chem*. 278, Pages 11312–1131. Doi: 10.1074/jbc.M211609200.
39. Hadi A, Sepandi M, Marx W, et al, 2019. Clinical and psychological responses to synbiotic supplementation in obese or overweight adults: A randomized clinical trial. *Complement. Ther. Med*. 47, Pages 102216. Doi: 10.1016/j.ctim.2019.102216.
40. Sudha M.R.; Ahire, J, Jayanthi, N, et al, 2019. Effect of multi-strain probiotic (UB0316) in weight management in overweight/obese adults: A 12-week double-blind, randomized, placebo-controlled study. *Benef. Microbes*.10, Pages 855–866. Doi: 10.3920/BM2019.0052.
41. Minami J, Iwabuchi N, Tanaka M, et al, 2018. Effects of *Bifidobacterium breve* B-3 on body fat reductions in pre-obese adults: A randomized, double-blind, placebo-controlled trial. *Biosci. Microbiota Food Health*. 37(3), Pages 67–75. Doi: 10.12938/bmfh.18-001.
42. Kim J, Yun J.M, Kim, M.K, et al, 2018. *Lactobacillus gasseri* BNR17 supplementation reduces the visceral fat accumulation and waist circumference in obese adults: A randomized, double-blind, placebo-controlled trial. *J. Med. Food*. 21(5), Pages 454–461. Doi: 10.1089/jmf.2017.3937.
43. Turnbaugh, P.J, Hamady M.; Yatsunenko T, et al, 2009. A core gut microbiome in obese and lean twins. *Nature*. 457(7728), Pages 480–484. Doi: 10.1038/nature07540.
44. Mathur R, Barlow G.M, 2015. Obesity and the microbiome. *Expert Rev. Gastroenterol. Hepatol*. 9, Pages 1087–1099. Doi: <https://doi.org/10.1586/17474124.2015.1051029>.
45. Finotello F, Mastroianni E, Di Camillo B, 2018. Measuring the diversity of the human microbiota with targeted next-generation sequencing. *Brief. Bioinform*. 19(4) Pages 679–692. Doi: 10.1093/bib/bbw119.
46. Turnbaugh P J, Ley R E; Mahowald M A, et al, 2006. An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature*. 444(7122), Pages 1027–1031. Doi: 10.1038/nature05414.
47. De La Cuesta-Zuluaga, J, Corrales-Agudelo, V, Carmona J, et al. 2018. Body size phenotypes comprehensively assess cardiometabolic risk and refine the association between obesity and gut microbiota. *Int. J. Obes*. 42(3), Pages 424–432. Doi: 10.1038/ijo.2017.281.



48. Ferrarese R, Ceresola E, Preti A, et al, 2018. Probiotics, prebiotics and synbiotics for weight loss and metabolic syndrome in the microbiome era. *Eur. Rev. Med. Pharmacol. Sci.* 22(21), Pages 7588–7605. Doi: 10.26355/eurrev\_201811\_16301.
49. Cotillard A, Kennedy SP, Kong LC, et al, 2013, Dietary intervention impact on gut microbial gene richness. *Nature.* 500(7464), 585–588. Doi: 10.1038/nature12480.
50. Frost F, Storck LJ, Kacprowski T, et al, 2019. A structured weight loss program increases gut microbiota phylogenetic diversity and reduces levels of *Collinsella* in obese type 2 diabetics: A pilot study. *Plos One.* 14(7), Pages e0219489. Doi: 10.1371/journal.pone.0219489.
51. Heinsen FA, Fangmann D, Müller N, et al, 2016. The beneficial effects of a dietary weight loss intervention on human gut microbiome diversity and metabolism are not sustained during weight maintenance. *Obes Facts.* 9(6), Pages 379–391. Doi: 10.1159/000449506.
52. Seganfredo FB, Blume CA, Moehlecke M, et al, 2017. Weight loss interventions and gut microbiota change in overweight and obese patients: a systematic review. *Obes Rev.* 18(8), Pages 832–851. Doi: 10.1111/obr.12541.
53. Leeming ER, Johnson AJ, Spector TD, et al, 2019. Effect of diet on the gut microbiota: rethinking intervention duration. *Nutrients.* 11(12), Pages 2862. Doi: 10.3390/nu11122862.
54. Gerber GK, 2014. The dynamic microbiome. *FEBS Lett.* 588(22), Pages 4131–4139. Doi: 10.1016/j.febslet.2014.02.037
55. Sowah SA, Milanese A, Schübel R, et al, 2022. Calorie restriction improves metabolic state independently of gut microbiome composition: a randomized dietary intervention trial. *Genome Med.* 14(1), Pages 30. Doi: <https://doi.org/10.1186/s13073-022-01030-0>.