

The use of *Lactobacillus plantarum* 299v (DSM 9843) in patients with cancers receiving home enteral nutrition – study protocol for a randomized, double-blind, and placebo-controlled trial

Kaźmierczak-Siedlecka Karolina (✉ leokadia@gumed.edu.pl)

Gdanski Uniwersytet Medyczny <https://orcid.org/0000-0002-0283-1436>

Marcin Folwarski

Gdanski Uniwersytet Medyczny

Karolina Skonieczna-Żydecka

Pomorski Uniwersytet Medyczny w Szczecinie

Jakub Ruszkowski

Gdanski Uniwersytet Medyczny

Wojciech Makarewicz

Gdanski Uniwersytet Medyczny

Study protocol

Keywords: Lactobacillus plantarum 299v, home enteral nutrition, cancer, nutritional status

Posted Date: February 17th, 2020

DOI: <https://doi.org/10.21203/rs.2.23667/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published at Nutrition Journal on September 11th, 2020.

See the published version at <https://doi.org/10.1186/s12937-020-00598-w>.

Abstract

Background

Nutritional treatment is one of the most important components of multidisciplinary anti-cancer therapy. Home enteral nutrition is considered a safe procedure, however, may be associated with the risk of side effects, such as nausea, vomiting, abdominal pain, and diarrhoea. It is uncertain whether diarrhoea is the result of the enteral formula or gut dysbiosis. One of the methods which may be used to alter the composition of gut microbiota is the administration of a probiotic strain. *Lactobacillus plantarum* 299v may be used as a supportive therapy in patients suffering from irritable bowel syndrome and *Clostridium difficile* infection. Therefore, the primary aim of this study is to determine the effect of *Lactobacillus plantarum* 299v on nutritional status of cancer patients receiving home enteral nutrition. The secondary aims are to evaluate the role of this probiotic strain in the improvement of tolerance of enteral formula and patients' quality of life.

Methods

Forty patients with cancer receiving home enteral nutrition will be enrolled in this clinical trial and randomized to receive one capsule of *Lactobacillus plantarum* 299v (Sanprobi IBS®) twice a day or placebo for 12 weeks in a double-blind manner. Laboratory tests (the level of albumin, total protein, transferrin, and total lymphocyte count), anthropometric parameters (body mass, the content of fat mass, muscle mass, and total body water), Nutritional Risk Screening (NRS 2002), tolerance of enteral nutrition as well as quality of life will be measured. Measurements will be obtained at the baseline and after 4 and 12 weeks of treatment.

Discussion

It is expected that the *Lactobacillus plantarum* 299v will provide beneficial effects, such as maintenance or improvement of nutritional status, enteral formula tolerance, and quality of life of cancer patients receiving home enteral nutrition.

Trial registration

ClinicalTrials.gov Identifier: NCT03940768

Background

The nutritional treatment is essential within the complexity of anti-cancer therapy. Appropriate nutritional support improves nutritional status, clinical outcomes, and as a consequence patients' quality of life [1]. Home enteral nutrition (HEN) is recommended for patients with an efficiently functioning alimentary tract who do not require hospital stay [2]. According to the Villar Taibo trial, almost 75% of patients qualified for HEN are malnourished [3]. Moreover, it is estimated that around half of patients with malignancies eventually develop cancer cachexia [4, 5]. HEN provides many benefits; however, it is associated with the

risk of developing adverse events, mainly diarrhoea, nausea, vomiting as well as abdominal pain [2]. Furthermore, it should be considered whether diarrhoea is the side effect of enteral feeding (for instance – the result of applying enteral formula too fast) or it is caused by alterations in the composition as well as the activity of gut microbiota. It should be emphasized that in patients with cancer gut dysbiosis described as qualitative and quantitative changes in gut microbiota may occur[6]. It was elegantly shown that there are at least several factors contributing to the development of gut dysbiosis among patients suffering from malignancies, namely infectious and anti-cancer agents, antibiotics and eating habits [6, 7].

Currently, several therapeutic methods, to modify gut microbiota are available, predominantly administration of prebiotics, probiotics, synbiotics, and faecal microbiota transplantation [8, 9]. Probiotic strain – *Lactobacillus plantarum* 299v (*L. plantarum* 299v) is able to reside the human colonic mucosa in vivo due to a specific mechanism of mannose adhesion [10, 11]. It should be emphasized that *L. plantarum* 299v demonstrates high tolerance to acidic and alkaline environment of the stomach and the duodenum, respectively. Therefore, this probiotic strain survives transit through the gastrointestinal tract to the colon, where it can modify gut microbiota [7, 10]. *L. plantarum* 299v provides anti-bacterial activity against potential pathogenic agents, such as *Listeria monocytogenes*, *Yersinia enterocolitica*, *Enterobacter cloacae*, *Enterococcus faecalis* and *Escherichia coli*. It increases transcription of the genes encoding mucins (MUC2 and MUC3) and their secretion from goblet cells [11]. *L. plantarum* 299v possesses immunomodulatory properties reducing the pro-inflammatory cytokine synthesis and increasing the IL-10 production and secretion. This probiotic strain plays a supportive role in the treatment of irritable bowel syndrome and *Clostridium difficile* infection [12–14]. Moreover, according to the Hoppe et al. trial, freeze-dried *L. plantarum* 299v increases the absorption of iron in young women [15]. There are limited data regarding the *L. plantarum* 299v and cancer therapy and no trials about its use in patients with cancer receiving home enteral nutrition. The present randomized, double-blind and placebo-controlled study hypothesizes that administration of *L. plantarum* 299v is able to nutritional status, enhance the enteral diet tolerance and quality of life of patients with cancers who receive HEN.

Hypothesis

Compared with a placebo, probiotic strain *Lactobacillus plantarum* 299v will improve enteral diet tolerance, nutritional status, and quality of life of patients with cancer who receive home enteral nutrition.

Specific Objective

The primary aim of the study is to determine the effect of *Lactobacillus plantarum* 299v on nutritional status of patients with cancer receiving home enteral nutrition. The secondary aims include the role of *Lactobacillus plantarum* 299v in the improvement of enteral diet tolerance and quality of life of patients with cancer receiving home enteral nutrition.

Methods

Study design

In this 12-week, single-centre, randomized, double-blind, and placebo-controlled study, 20 patients with cancers will be treated with probiotics and 20 patients will receive a placebo. The post-allocation clinical and laboratory assessment will be performed at weeks 0, 4, and 12 in all participants (Fig. 2). Patients in the probiotic- group will receive two capsules of Sanprobi IBS® containing 10^{10} CFU of *Lactobacillus plantarum* 299v for 12 weeks. Participants in the control group will receive placebo (two capsules daily) for 12 weeks. The participants will be recruited to this study by the nutritionist and the surgeon in Nutritional Counselling Centre Copernicus in Gdansk and Medical University of Gdansk (Department of Clinical Nutrition and Dietetics). The researches and participants will be blinded to the group assignment since the probiotic product and the placebo will be completely identical and indistinguishable from one another. The enrolment of participants is presented at Fig. 1.

Subjects

Inclusion criteria

Patients will be included if they meet all of the following criteria:

- Age ≥ 18 year
- The presence of cancer
- Artificial access to the gastrointestinal tract (naso-gastric tube, gastrostomy, percutaneous endoscopic gastrostomy, jejunostomy, percutaneous endoscopic gastrostomy with jejunostomy) – enteral feeding
- Qualify for home enteral nutrition
- written consent to take part in the study

Exclusion criteria

Patients will be excluded if they meet any of the following exclusion criteria:

- Qualify for home enteral nutrition, but suffering from another disease than cancer
- Patients requiring additional parenteral nutrition
- Not being able to visit the study centre

Allocation To Treatment, Randomization, And Blinding

At the beginning, the patients will have to sign an informed consent to participate in the study. After meeting all the inclusion criteria and obtaining a consent agreement, the participants will receive a unique number by the nutritionist. Each number will be allocated to particular intervention group. The eligible patients will be allocated to the treatment for 12 weeks with either to probiotic product or placebo.

Randomization will be performed by means of researchrandomizer.com software, typically used by clinical research associates. The randomization ratio will be 1:1. The researchers and participants will be blinded for treatment received by probiotic company. The patients will intake one capsule of study product (probiotic or placebo) in the morning after breakfast and one capsule in the evening after dinner. The participants who cannot swallow the capsule, will be instructed to mix the capsules' powder with 20 millilitres of water or saline and administer the solution through the enteral feeding access. The capsules (probiotic product as well as placebo) will be stored at refrigerator temperature.

Intervention group

The intervention group will be administered a Sanprobi IBS® capsule twice a day for 12 weeks. Each capsule contains 10^{10} CFU of *Lactobacillus plantarum* 299v. The intervention capsules will be produced and packed by Sanprobi company (Sanprobi IBS® Sanprobi Sp. z o.o., Sp. k., Szczecin, Poland; producer of capsules – Institute Rosell-Lallemand, Montreal, Canada; LP299v owner of probiotic strain – Probi AB, Lund, Sweden).

Control group

The control group will receive placebo capsules twice a day for 12 weeks. The placebo capsules, produced and packed by the same company as intervention capsules – Sanprobi, will not contain any microorganisms.. 1 capsule of placebo will contain 410 mg +/- 7.5%, potato starch – 403 mg, and 7 mg of magnesium stearate (magnesium salts of fatty acids).

Outcomes

Participant timeline

The timetable of follow-up visits and measurements is presented using The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) diagram at Fig. 2. Each of the participants will visit the study centre three times (at baseline, after 4 weeks, and after 12 weeks). During follow-up visits, patients will receive study products (probiotic or placebo depending on study groups). At baseline, 60 capsules for 30 days; after 4 weeks 120 capsules for next 60 days. If during this trial, any participant fails to continue the study protocol, the data will be collected and this information will be further noted in the publication.

Primary Outcome

The staff involved in the measurements will be blinded to the outcomes.

The primary outcome is the improvement in the nutritional status in a probiotic-receiving group in comparison to a placebo-receiving group. The nutritional status will be evaluated by means of anthropometric parameters, laboratory tests, and Nutritional Risk Screening 2002 (NRS 2002 tool).

Anthropometric parameters will be performed using:

<

- Analysis of body mass composition: fat mass, muscle mass, total body water.
- Body mass index.

Laboratory tests:

- The level of albumin, total protein, transferrin, and total lymphocyte count.

Nutritional Risk Screening 2002 tool

- This tool is divided into two parts. The first one estimates the nutritional status based on: unintentional weight loss over 1 to 3 months and food intake over 1 to 3 weeks. The second part regards the occurrence of diseases or types of treatment, which are related to increased daily calories intake (e.g. bone marrow transplant, treatment with radiotherapy or chemotherapy). Patients aged 70 and above, receive additional scoring point. This is a validated screening tool. Nutritional support should be provided if the NRS score is 3 and more.

Secondary Outcomes

- First secondary outcome is estimate the differences in tolerance of enteral diet in patients receiving placebo or probiotic supplements. The assessment will be based on own questionnaire including information such as number of stools, occurrence of nausea, vomiting, abdominal pain, and flatulence. The questionnaire will be filled every day for 12 weeks by patients and evaluated during follow-up visits after first 4 weeks and after next 8 weeks.
- Second secondary outcome evaluate the difference in quality of life of patients receiving placebo or probiotic supplements. To assess the patients' quality of life The World Health Organization Quality of Life-BREF (WHOQOL-BREF) questionnaire will be used. The questionnaire contains questions divided into 4 domains (environmental, psychological, somatic, social factors). The quality of life will be controlled at baseline, after 4 weeks, and after 12 weeks.

Blood sampling and preparation

The level of albumin, total protein, transferrin, and total lymphocyte count will be measured. The blood samples will be taken from a forearm vein by a nurse at the baseline, after 4 weeks, and next after 12 weeks. All blood samples will be taken in Counselling Nutritional Centre Copernicus in Gdansk and in the same day will be given to the laboratory to conduct the analysis.

Anthropometric parameters

The analysis of the composition of body mass (fat mass, muscle mass, total body water) will be conducted using a BIA analyser – Medical Jawon. It will be performed by a nutritionist in the Department

of Clinical Nutrition and Dietetics. The body mass index will be also calculated by the nutritionist.

NRS 2002 tool, tolerance of enteral nutrition, quality of life

NRS 2002 tool

- Assessment of nutritional status will be conducted by a nutritionist in the Department of Clinical Nutrition and Dietetics using NRS 2002 tool by the nutritionist three times (at baseline, after 4 weeks, and after 12 weeks). The content of the NRS 2002 tool is mentioned above.

Tolerance of enteral nutrition

- The tolerance of enteral nutrition will be evaluated by the nutritionist in the Department of Clinical Nutrition and Dietetics using own questionnaire. The content of the questionnaire is described in section – secondary outcomes. It will be checked at the baseline and after 4 weeks.

Quality of life

- Patients' quality of life will be assessed by the nutritionist in the Department of Clinical Nutrition and Dietetics with WHOQOL-BREF questionnaire. The content of WHOQOL is included in section – secondary outcomes. It will be assessed at the baseline, after 4 weeks, and after 12 weeks from baseline.

Adverse Outcomes

Patients are instructed to inform the researchers about any changing conditions during the trial. Furthermore, during follow-up visits the researchers will ask about adverse events which may be related to the intervention. If any adverse events occur it will be noted in report form and reported in publication.

Clinical trial registration

The study has been registered in ClinicalTrials.gov which is a database of privately and publicly funded clinical studies conducted around the world (ClinicalTrials.gov Identifier: NCT03940768).

Statistical analysis

When computing a priori sample size, we anticipated that the probiotic intervention will decrease the weight loss by 10% with an SD of around 15% for weight change. Calculating the mean weight loss in a 70kg men and assuming 1:1 allocation ratio and 80% statistical power we evaluated that the number of participants will be 36. Allowing for a withdrawal rate of 20% for the primary outcome we aim to randomly allocate 40 participants to receive either active product or placebo. The required sample size were evaluated using G-power analysis software.

The calculations will be carried out with the use of Statistica package by Dell Inc. The descriptive statistics will include averages, medians, standard deviations, maximum and minimum values. In order to

check the normality of distribution of populations subject to research, the W Shapiro-Wilk test will be applied. To check the homogeneity of variations of the groups compared, the Brown-Forsythe test will be applied. Then, depending on the type of data and shape of distributions compared, the U Mann-Whitney test, Student's t-test or a version of Student's t-test with independent variance estimation will be applied. Significance level will be 0,05.

Discussion

According to the best of our current knowledge, this is the first randomized, double-blind, and placebo-controlled trial, which is aimed to assess the role of *Lactobacillus plantarum* 299v in the improvement of nutritional status, tolerance of enteral nutrition, and quality of life of patients with cancers who receive home enteral nutrition

The beneficial effects of *Lactobacillus plantarum* 299v for several diseases have been demonstrated in many clinical trials [13, 14]. In Niedzielin et al. study [14] authors assessed the efficiency of *Lactobacillus plantarum* 299v in the treatment of irritable bowel syndrome. The participants were divided into two groups: first receiving probiotic (n=20) in dose 5×10^7 CFU/ml in dose of 200ml twice a day for 4 weeks and second consuming placebo (n=20). All the participants declared a resolution of abdominal pain and only 11 subjects from control group (p=0.0012). Moreover, the normalization of stool frequency was most often observed in probiotic group in comparison to placebo (p=0.17). The improvement of all symptoms of irritable bowel syndrome was noted in 95% subjects receiving probiotic and in 15% participants from control group (p<0.0001). Patients receiving home enteral nutrition often develop similar symptoms as patients with irritable bowel syndrome, such as nausea, vomiting, abdominal pain, and diarrhoea [2]. It should be emphasized that the enteral feeding provides many benefits for patients with cancer, mainly preventing mucosal atrophy, reducing endotoxins translocation, and preserving gut immunity [16]. The most common adverse event after administration of enteral formula is diarrhoea [2]. The pathogenesis of diarrhoea during enteral nutrition includes enteropathogenic infection, administration of antibiotics, as well as alterations of the physiologic response of the ascending colon where water is secreted into the lumen [17]. The frequency of diarrhoea varies, however it is estimated that diarrhoea affects patients in a wide range from 2% to even 95% [17]. It depends on the medical conditions and how diarrhoea is defined. The incidence of diarrhoea is increased in critically ill patients [18]. *Lactobacillus plantarum* 299v may be used as a prevention of *Clostridium difficile* infection. It was confirmed that routine use of *Lactobacillus plantarum* 299v may prevent *Clostridium difficile* infection during antibiotic therapy in patients receiving immunosuppressing agents and hospitalized in nephrological and transplantation wards. Furthermore, the results of Wullt et al. [19] study indicate that *Lactobacillus plantarum* 299v reduces the side effects of antibiotics on colonic fermentation in patients suffering from recurrent *Clostridium difficile*-associated diarrhoea. Probiotic strains may be used to prevent side effects of enteral nutrition, which was shown in Zhao et al. study [20]. This trial recruited 120 patients with gastric cancer who received enteral nutrition and probiotics for 7 days after the surgical procedure. The patients were divided into 3 groups: first received fiber-free nutrition formula (n=40), second consumed fiber-enriched nutrition formula (n=40), and third received fiber- and probiotics-enriched nutrition formula (n=40). Patients receiving probiotics-

enriched nutrition formula had a lower risk of developing diarrhoea. However, the laboratory parameters assessing nutritional status did not differ significantly between groups [18]. The similar results were obtained by Xie et al. [21]. In this study including 140 patients with gastric cancer receiving enteral nutrition in combination with probiotics for 8 days, the decrease in the incidence of diarrhoea in the postoperative period and reduction of the of the pro-inflammatory cytokine level (IL-6, IL-8, and TNF- α) were reported. However, the laboratory parameters assessing nutritional status did not change [20]. Overall, the results of these abovementioned studies confirm that probiotic strains are effective in reducing the occurrence of diarrhoea. Since the periods of probiotics intake in these were short, it was not unexpected to not improve the nutritional status of patients. In our study, we decided to administer the probiotic strain *Lactobacillus plantarum* 299v in full dose (2 capsules per day) for 12 weeks, which allows us to expect changes in laboratory parameters (especially in cases of parameters with a long half-life, for instance in case of albumin).

Notwithstanding, diarrhoea can also be a result of gut dysbiosis caused by anti-cancer therapeutics or antibiotics (e.g. they can lead to pathogenic bacteria overgrowth) [18]. The administration of probiotic strains is one of the therapeutic methods used to restore gut microbiota [8]. *Lactobacillus plantarum* 299v—is highly tolerant to a wide range of pH and it can transit through the gastrointestinal tract causing the modification of gut microbiota composition [7,10]. Among others, due to above-mentioned properties, it may be used to alter gut microbiota and as a consequence contributes to the reduction of the incidence of diarrhoea. Furthermore, the administration of *Lactobacillus plantarum* 299v may improve patients' quality of life and enteral nutrition tolerance by the reduction of gastrointestinal side effects of multimodal anti-cancer therapy.

Abbreviations

HEN

home enteral nutrition

L. plantarum 299v

Lactobacillus plantarum 299v

NRS 2002

Nutritional Risk Screening 2002 tool

WHOQOL-BREF

World Health Organization Quality of Life-BREF

Declarations

Ethics approval and consent to participate

The study protocol has been approved by Independent Bioethics Committee for Scientific Research at Medical University of Gdańsk, Poland (the project identification code: 422/2016).

The participants will be informed about this study, potential benefits and risks. The consent agreement received from patients will be necessary to include them to the trial.

Consent for publication

Not applicable.

Availability of data and materials

It is only a study protocol, so the data are not available yet.

Competing interests

The company Sanprobi IBS® provided probiotics and placebo. They did not participate in study design or writing this study protocol. KSŽ received remuneration from Sanprobi; however, it has no relation with this article.

Funding

The company Sanprobi IBS® provided probiotics and placebo.

Author's contributions

KKS – the major contributor in writing this manuscript, study design; MF – study design and languages corrections; KSŽ – the major contributor in writing this manuscript; JR – writing manuscript and languages corrections; WM – study design and mentor.

Acknowledgments

No acknowledgments.

References

1. Gavazzi C, Colatruglio S; Valoriani F Mazzaferro V, Sabbatini A, Biffi R, et al. Impact of home enteral nutrition in malnourished patients with upper gastrointestinal cancer: A multicentre randomised clinical trial. *Eur J Cancer* 2016; 64:107–12.
2. Gramlich L, Hurt RT, Jin J, Mundi MS. Home Enteral Nutrition: Towards a Standard of Care. *Nutrients* 2018; 8: 1020.
3. Villar Taibo R, Martínez Olmos MÁ, Bellido Guerrero D, Casariego AV, Garcia RP, Sueiro AM, et al. Epidemiology of home enteral nutrition: an approximation to reality. *Nutr Hosp.* 2018; 3:511–8.
4. Dohono CL, Ryan AM, Reynolds JV. Cancer cachexia: mechanisms and clinical implications. *Gastroenterol Res Pract.* 2011; 601434.

5. Aoyagi T, Terracina KP, Raza A, Matsubara H, Takabe K, et al. Cancer cachexia, mechanism and treatment. *World J Gastroenterol Oncol*. 2015; 4:17-25.
6. D'Argenio V, Salvatore F. The role of the gut microbiome in the healthy adult status. *Clin Chim Acta*. 2015; 451: 97–102.
7. Banna GL, Torino F, Marletta F, Santagati M, Salemi R, Cannarozzo E, et al. *Lactobacillus rhamnosus* GG: An Overview to Explore the Rationale of Its Use in Cancer. *Front Pharmacol*. 2017; 8: 603.
8. Raman M, Ambalam P, Kondepudi K, Pithva S, Kothari C, Patel A, et al. Potential of probiotics, prebiotics and synbiotics for management of colorectal cancer. *Gut Microbes*. 2013; 3: 181–192.
9. Chen D, Wu J, Jin D, Wang B, Cao H. Fecal Microbiota Transplantation in Cancer Management: Current Status and Perspectives. *Int J Cancer*. 2019; 8: 2021-2031.
10. Johansson ML, Molin G, Jeppsson B, Nobaek S, Ahrné S, Bengmark S. Administration of different *Lactobacillus* strains in fermented oatmeal soup: in vivo colonization of human intestinal mucosa and effect on the indigenous flora. *Appl Environ Microbiol*. 1993; 59: 15–20.
11. Mack DR, Ahrne S, Hyde L, Wei S, Hollingsworth MA. Extracellular MUC3 mucin secretion follows adherence of *Lactobacillus* strains to intestinal epithelial cells in vitro. *Gut* 2003; 6: 827–33.
12. Dudzisz S, Kujawa-Szewieczek A, Kwiecień K, Więcek A, Adamczak M. *Lactobacillus plantarum* 299v reduces the incidence of *Clostridium difficile* infection in nephrology and transplantation ward-results of one year extended study. *Nutrients* 2018; 10: 1574.
13. Marlicz W, Zawada I, Starzyńska T. Irritable bowel syndrome—irritable bowel or irritable mind?. *Pol Merkur Lek Organ Pol Tow Lek*. 2012; 32: 64–9.
14. Niedzielin K, Kordecki H, Birkenfeld B. A controlled, double-blind, randomized study on the efficacy of *Lactobacillus plantarum* 299V in patients with irritable bowel syndrome. *Eur J Gastroenterol Hepatol*. 2001; 13: 1143–7.
15. Hoppe M, Önning G, Hulthén L. Freeze-dried *Lactobacillus plantarum* 299v increases iron absorption in young females—Double isotope sequential single-blind studies in menstruating women. *PLoS One*. 2017; 12: e0189141.
16. Zaman MK, Chin K, Rai V, Majid HA. Fiber and prebiotic supplementation in enteral nutrition: a systematic review and meta-analysis. *World J Gastroenterol*. 2015; 17: 5372-5381.
17. Whelan K. Enteral-tube-feeding diarrhoea: manipulating the colonic microbiota with probiotics and prebiotics. *Proc Nutr Soc*. 2007; 3: 299-306.
18. Wiesen P, Van Gossum A, Preiser JC. Diarrhoea in the critically ill. *Curr Opin Crit Care*. 2006; 12:149–154.
19. Dudzisz S, Kujawa-Szewieczek A, Kwiecień K, Więcek A, Adamczak M. *Lactobacillus plantarum* 299v reduces the incidence of *Clostridium difficile* infection in nephrology and transplantation ward-results of one year extended study. *Nutrients* 2018; 10: 1574.
20. Zhao R, Wang Y, Huang Y, Cui Y, Xia L, Rao Z, et al. Effects of fiber and probiotics on diarrhea associated with enteral nutrition in gastric cancer patients. *Medicine* 2017; 96:e8418.

21. Xie H, Lu Q, Wang H, Zhu X, Guan Z. Effects of probiotics combined with enteral nutrition on immune function and inflammatory response in postoperative patients with gastric cancer. *J Buon.* 2018; 23:678-683.

Table

Due to technical limitations, Table 1 is provided in the Supplementary Files section.

Figures

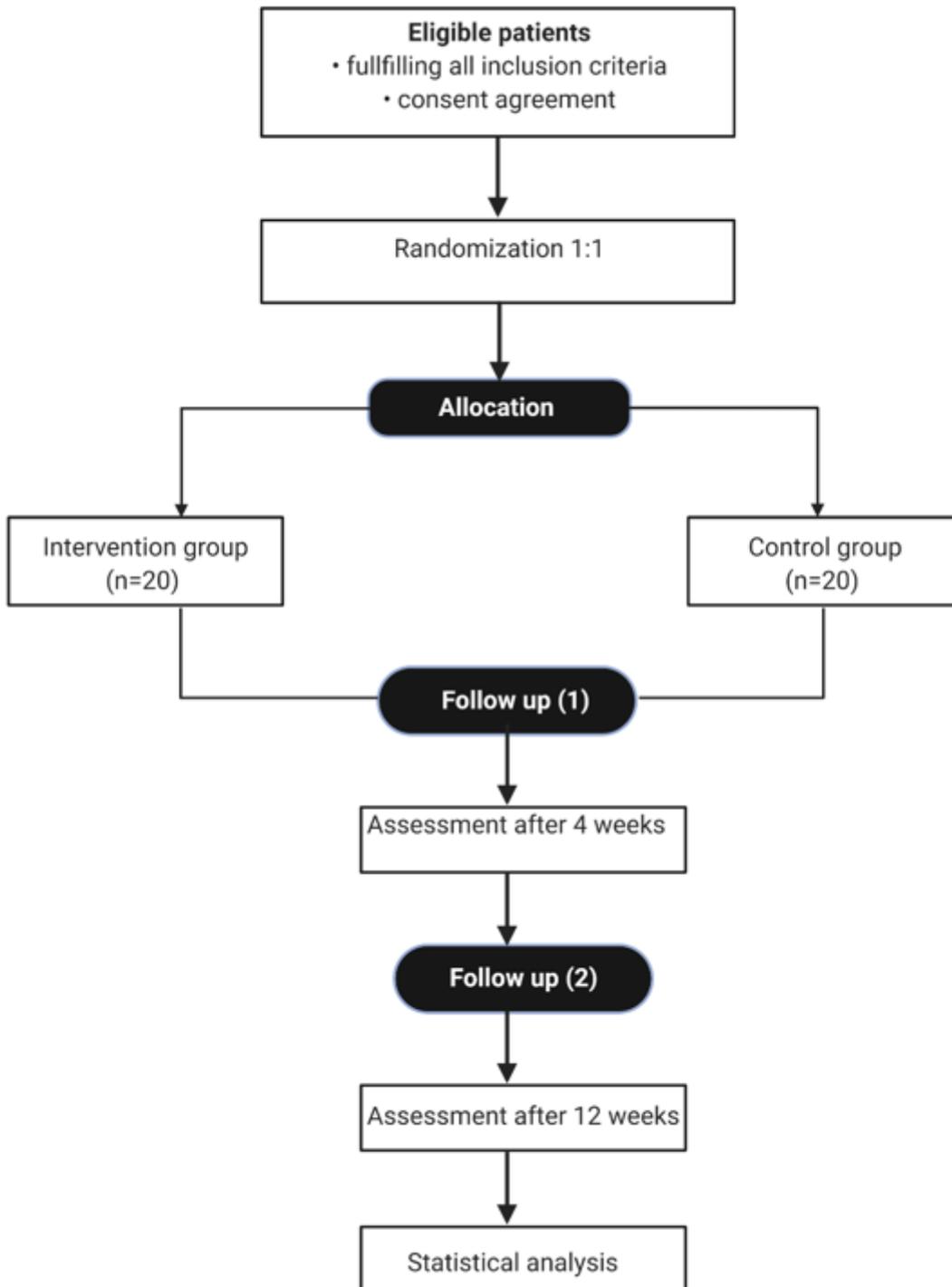


Figure 1

Participants flow diagram.

Supplementary Files

This is a list of supplementary files associated with this preprint. [Click to download.](#)

- [Table1.odt](#)