

## Findings from a Pilot Study on the Intake of Prebiotics and the Health-Related Quality of Life in a Sample of Young Obese Women

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### Abstract

**Background:** The microbiome plays an important role in many physical and psychological health conditions. Administration of pre or probiotics leads to improvements in physiological and psychological symptoms, promoting a better health-related quality of life (HRQOL). The current understanding of HRQOL in people with intestinal problems and microbiome dysbiosis defines a twofold model with impairments which can be broadly reduced to psychosocial and gastrointestinal risk factors. Evidence exists that the microbiome also influences physiological conditions which could potentially lead to obesity.

Obese patients suffer from various abdominal complaints, such as abdominal pain, flatulence or changing stool behavior which can affect general well-being and adherence to dietary therapy. The aims of the current study are to explore the potential therapeutic effects of prebiotics on HRQOL in the context of a preliminary interventional study in obese women and to put the study findings into a conceptual framework of administration of pre and probiotics and HRQOL in obesity.

**Methods:** 26 obese women took a dietary supplement consisting of plasmolyzed herbal baker's yeast (Strath® Original) over a period of three weeks. Food intake was tracked via a smartphone app. HRQOL was assessed before and after the intervention using an adaption of the SF-12 questionnaire.

**Results:** Though not the primary goal of the study, data indicated changes in some aspects of HRQOL. Change scores and confidence intervals for six aspects of HRQOL were calculated and pre and post measurements were compared using a Wilcoxon Signed Rank Test. Results indicated a small but non-significant trend for improvements in satisfaction with health, general well-being and fatigue after meal intake. Coping with stress, satisfaction with social and occupational life slightly non-significant decreased after the intervention. As anticipated, participants did not lose weight.

**Conclusion:** Administration of a prebiotic dietary supplement in combination with nutrition- and exercise tracking leads to changes in the overall condition in obese individuals and to a higher problem awareness. The medical as well as psychological therapeutic potential of pre and probiotics should be put into the complex framework of obesity. More detailed and longer-term studies on the influence of pre and probiotics on obesity are needed.

**Keywords:** Microbiome; Prebiotics; Obesity; Health-Related Quality Of Life; Yeast Based Supplement

## Abbreviations

QOL: Quality of Life; HRQOL: Health-Related Quality of Life

## Introduction

Research on the microbiome and its changes through the intake of specific foods or pre- and probiotics has increased remarkably throughout the last two decades [1]. While the strains of non-pathogenic microorganisms of probiotics exert a positive influence on health and physiology when ingested, prebiotics, such as non-digestible food ingredients, stimulate the growth and/or activity of microorganisms in the bowel. In both ways, the main aim is the alteration and stimulation of the favorable population of the human microbiome, or to improve biodiversity. The state of the microbiome has been documented to have an influence on physical health conditions such as Crohn's Disease [2], irritable bowel syndrome [3], psoriasis and other skin related diseases [4,6], allergy problems [6], as well as arthritis and skeletal problems [7] or cancer [8,9]. It could furthermore be shown that altering the microbiome via external administration of specific strains of bacteria leads to improvements in certain diseases. For example, Bifidobacterium reduces abdominal pain in irritable bowel syndrome [10]. Further studies show the positive effects of administering single strains of probiotics or probiotic complexes in autoimmune arthritis [11], rheumatoid arthritis [12], or psoriasis [13]. Immunological effects were also demonstrated when taking dietary supplement consisting of plasmolyzed herbal baker's yeast [14,15]. Studies vary in methodological quality, definition, and severity of diseases analyzed, which still makes it difficult to suggest specific pro- or prebiotics to treat specific illnesses [16,17]. With regards to physiologic processes, probiotics seem to mainly affect certain inflammatory processes in the body, which is linked to a reduction of disease-specific somatic symptoms [18]. A second point of interest lies in the influence of the microbiome on the psychological state and even psychiatric disorders such as depression, anxiety [19] and chronic stress [20,21]. Several studies have shown a link between the composition of the microbiome and the presence and severity of depressive symptoms [19,22,23]. The interdependence between the brain-gut axis and the composition of the gut microbiome is of special interest, mostly regarding the functioning of the serotonergic system in the human body and problems resulting within this system, such as depression [24,25].

## Definition of QOL and HRQOL

Whereas the term quality of life (QOL) historically includes all aspects of life and general well-being, research since the mid '80s, especially in the medical field, has been more focused on impairment and resulting QOL in certain life and health domains which have emerged through a disease pattern [26]. This has led to measuring a narrower and more pointed range of life aspects and well-being referred to as HRQOL. Such a focus has an impact on the conceptualization and definition of HRQOL. In general, conceptual models rely on a multidimensional approach [27]. Earlier research on HRQOL lacked clear definitions of the dimensions measured and conceptual frameworks of QOL and HRQOL respectively. Newer research suggests four dimensions of health as being central in the definition of HRQOL [27]. Physical health covers disease symptoms and body sensations, mental health includes distress and diagnosable psychiatric disorders, social health is referred to as quantitative and qualitative aspects of social interactions and functional health covers physical functioning, self-care, mobility, and social role functioning. Disease or treatment-specific variables are often included additionally. Another proposal is given by Post [26]. The author suggests an integration of the PROMIS conceptual model into the definition of HRQOL [28]. This model aims to standardize self-reported health assessments. In its core definition, the PROMIS model operationalizes health in three dimensions: physical, mental, and social health. In conclusion, HRQOL should be conceptualized and measured in a multidimensional approach and newer definitions of HRQOL suggest at least a psycho-social dimension besides physical and mental health impairment.

## HRQOL and the microbiome

Studies regarding HRQOL and microbiome have mostly been conducted in disease-specific contexts. Alteration of a disease-specific QOL in pathologies linked to the microbiome was often realized by the application of various treatments such as probiotic intake [29,30],

pharmacotherapy [31], or psychological therapy [32]. A health-related measurement of quality of life in the context of gastrointestinal problems is often made in a sample of patients suffering from a specific disease by applying a standardized questionnaire such as the SF-36 [33] or the short form SF-12 [34], disease-specific instruments such as the IBS-QOL [35], the Nepean Dyspepsias Index [36] or sometimes only one-dimensional Likert scales [37]. Chang [37] proposes a conceptual model describing HRQOL in patients suffering from gastrointestinal problems with respect to psychosocial risk factors and gastrointestinal-related factors. According to this model, psychosocial risk factors comprised of adverse early life events, life stress, coping strategies, psychological conditioning, and social support. Gastrointestinal-related factors include extra-intestinal symptoms, sensitivity of the gastrointestinal tract, motility, infection, and inflammation. As such, this model has a twofold approach of definition to HRQOL, on both a psychosocial and physiological level, in patients with gastrointestinal problems. However, HRQOL and intake of probiotics are not limited to subjects with gastrointestinal and other pathological diseases. A study by Moreira-Rosario, *et al.* [38] [35] found that the intake of germ-enriched white bread had little changes in the microbiome and gastrointestinal functioning but reduced the subjective gastrointestinal discomfort in healthy subjects, especially in certain aspects of HRQOL (i.e. worries and concerns about gastrointestinal discomfort). In summary, the relatedness of HRQOL and gastrointestinal functioning to date should be considered an interaction between psychological and physiological processes. As such, intake and alteration of the microbiome via probiotics are seen to improve certain aspects and symptoms in the gastrointestinal tract, which further leads to an improvement of HRQOL. However, the psychosocial and psychological dimensions of HRQOL in gastrointestinal problems and treatment effects of pre- and probiotics on these dimensions have not yet been clearly differentiated.

### Obesity, HRQOL, and the microbiome

Obesity has become one of the biggest health challenges in modern society with physiological, mental, and social health-related impairments. These challenges and impairments have been noted by different scholars and will not be dealt with comprehensively here (See Kolotkin, *et al.* 2002, 2017 [39,40]). Research on effects on QOL caused by obesity on physiological, mental, and social health has mostly dealt with the more specific HRQOL [40]. Obesity is described as a multifactorial illness with a wide range of physiological and psychological influencing factors and a reduction in HRQOL [41,42]. It has been documented that HRQOL is lower in individuals being overweight or obese and weight loss leads to an improvement of HRQOL [40,43,44]. Aspects of HRQOL in obesity include psychological impairment such as an augmentation of depressive symptoms due to dissatisfaction with weight and body image as well as lowered self-esteem [41,45-47]. Additionally, patients often reduce contacts, avoid visiting social events, and feel uncomfortable in general due to shame and lack of self-confidence. Regarding the psychological state and psychological functioning, depressive symptoms, anxiety, and dysfunctional emotion regulation are well-documented factors in the emergence and maintenance of obesity [48-50]. (42-45) and targeting those aspects leads to a reduction in weight [51,52]. Therefore, addressing the mental health in obese patients is of importance when attempting to influence or change HRQOL in said patients. Physiological impairments include chronic pain in the musculoskeletal system, gastrointestinal problems, blood-glucose fluctuations as well as cardiac and respiratory problems. Impairments in a patient's psychosocial life might include problems or challenges in public spaces where seats, beds, or toilets are too small or not firm enough, hindered access to buildings, or clothing that is not easily available. Individuals often face stigmatization such as fewer chances to be hired in jobs or at universities, lower wages, and fewer chances to get promoted in occupational life [53]. Obese people are viewed as less competent, lazy, and lacking in self-discipline [54]. Besides, those stigmatizations can lead to withdrawal from public life, which in turn leads to greater psychological distress and a reduction in HRQOL [55,56].

Studies on the microbiome in overweight or obese patients have suggested a connection between obesity and the composition of the microbiome [57-59]. The gut microbiome can have an influence on obesity either via energy extraction in the gut or via influencing metabolism throughout the body [60]. Studies could show that a high-fat diet alters the microbiome in mice, especially by changing the ratio of *Firmicutes/Bacteroides* bacteria [61] and lowering the numbers of *Bifidobacteria* in the gut microbiome [62] and that treating such conditions with pre- or probiotics leads to a reduction in obesity-associated inflammation processes and improved glucose tolerance [63,64].

Furthermore, the treatment of obese people with probiotics is documented to have an influence on weight loss and obesity-associated metabolic diseases such as diabetes or fatty liver [65,66]. It can, therefore, be claimed that targeting the microbiome in obese individuals with pre- or probiotics has potential in the multidimensional treatment of obesity. Treatment of obesity remains a complex and often long-lasting process and it has been documented that combined treatments (i.e. medical, psychological, and exercise) are more effective than a single treatment alone [67]. Moreover, relapse into old behavior and weight regain is common in conservative weight treatment as well as in the surgical treatment of obesity [68,69]. The psychological strain when experiencing weight regain and the loss of HRQOL is high [70]. The need for time- and cost-effective treatment options with a swift improvement of HRQOL in overweight and obese patients is demanding [71]. Therefore, medically treating obesity with the support of easy-to-administer products such as pre- or probiotics holds promising effects on a multitude of physiological, mental health- and psycho-social symptoms of these conditions. Looking at HRQOL in obesity taking the model of Chang [37], physical functioning could be supported and improved via weight loss and weight maintenance. Stress tolerance or mood could be enhanced, which might further lead to an augmentation of HRQOL on a psychosocial dimension. However, this model only takes into account the physiological and psychosocial dimensions of HRQOL concerning gastrointestinal problems and interventions. To our knowledge, a conceptual framework on the effects of pre- or probiotics on a three-dimensional definition of HRQOL in physiological, mental, and social health aspects in the treatment of obesity is still missing.

### Aim of the Study

The first aim of the current data analysis is to explore whether the intake of an herbal yeast product rich in  $\beta$ -glucan and  $\alpha$ -mannan leads to changes in HRQOL in a population of healthy young obese women. The second aim of this study is to develop a conceptual framework on the effects of the administration of prebiotics on HRQOL in a three-dimensional model with physiological, mental, and social health aspects in obese individuals.

### Methodology

#### Study design and procedures

This study was carried out over 5 weeks (with a 2-week run-in phase) with a single-arm pre/post pilot intervention over 3 weeks with obese women in Switzerland. All study procedures were approved by the local institutional review board and are registered under ClinicalTrials.gov (NCT02694614) corresponding to the declaration of Helsinki.

#### Participants

We included 26 healthy adult women who speak German fluently and are Smartphone users (iOS or Android), capable of sending/receiving text messages and pictures. The inclusion criteria were gender (female), age (between  $\geq 25$  and  $\leq 35$  years), and BMI (between  $\geq 30$  and  $\leq 35$  kg/m<sup>2</sup>). Exclusion criteria were for pregnant or breast-feeding women, individuals with nutritional-therapy-dependent diseases and other diseases requiring continuous drug therapy, individuals who were on a diet during a 6-month period before the study; individuals who had taken medication for weight loss in the past or any person being enrolled in another weight-loss program at the time of the study. Subjects were invited to participate with flyers through the Center for Obesity and Metabolism Medicine Winterthur (Canton Zurich, Switzerland) via general practitioners, advertisements on the websites of the participating research institutions, local newspapers, Facebook and by word-of-mouth advertising. Interested persons received written and verbal information about the study. Before the interviewing and screening processes took place, informed consent for participation was obtained at least 24 h before. The researchers determined the eligibility of participants based on the inclusion and exclusion criteria.

### Treatment

During the first appointment following 4 to 8 weeks after the screening, the recruited women underwent a medical examination and food intake was monitored via a smartphone app (over the whole of intervention). At the second appointment the first stool sample collected at home one day before, blood investigation took place and received a dietary supplement as outlined below. Three weeks later, they handed in the second stool sample and were checked medically with another blood investigation again. Stool samples were then analyzed by shotgun sequencing (Core Biome, St. Paul, MN, USA). Additionally, paper and pencil questionnaires on HRQOL and stool quality were filled in by the participants at the beginning and the end of the intervention.

### Dietary supplement - treatment

Strath® liquid is a plasmolyzed herbal yeast preparation with over 60 vital substances (such as vitamins, minerals, enzymes, amino-acids, oligo-elements), which has been sold worldwide for almost 60 years (Bio-Strath® AG, Zurich, Switzerland). Ingredients: 83% plasmolyzed herbal yeast (type: *Saccharomyces cerevisiae* MEYEN), 9% malt extract, 5% orange syrup, 3% honey. In previous studies, a change in the gut microbiome was already detected after 2 - 7 days of nutritional intervention using Strath® [72,73]. A three-week intervention period was therefore considered sufficient to observe a significant change in the gut microbiome, changes in measures of stool quality and QOL. To be comparable to previous studies with Strath®, the standard dose was used as outlined on the package: 3 x 5 ml a day for the three weeks. Compliance was measured by assessing the quantity of dietary supplement remaining after three weeks of intervention.

### Oviva App - nutritional assessment/observation

A photo-based log for nutritional observations was used, first over the two-week run-in phase to review the average individual nutritional situation and afterward to guarantee a stable nutritional situation over the three-week supplemental period, also documenting estimation of calorie, fat, protein and carbohydrate intake and movement too.

### Measurement of health-related quality of life

Study participants were required to engage in a process where they rated the following points on a Likert scale from 1 (excellent/very satisfied/not tired) to 10 (bad/very dissatisfied/exhausted): their satisfaction with their state of health ("how would you describe your state of health?"), general well-being ("how is your well-being?"), fatigue after meal intake ("Are you tired after meal intake?"), coping with stress ("How well can you manage stressful situations?"), social situation ("How satisfied are you with your social situation?") and occupation ("How satisfied are you with your occupational situation?"). Items were taken and adapted from the German version of the SF-12, a short form of the SF-36 [74]. The SF-12 is a widely and commonly used questionnaire for the measurement of QOL [74]. It allows a sum score in three different dimensions, namely physical, mental, and social role functioning. In the present study, satisfaction with state of health, general well-being, and fatigue were used to measure physical functioning, satisfaction with coping with stress was used to measure mental-health functioning, and satisfaction with social situation and occupational situation were used to measure social-role functioning.

### Statistical analysis

Analyses were conducted using IBM SPSS Statistics for Macintosh, version 26.0 [75] and the level of significance was set at  $\alpha = 0.05$ . The final data set contained no missing data. A change score was calculated by subtracting the post-treatment measurement from pre-treatment measurement. 95% confidence intervals were calculated. Given the non-normal distribution of the change scores in the histograms and boxplots, a Wilcoxon Signed Rank Test was performed to assess the change scores of the HRQOL scales. The resulting six p-values were adjusted for multiple hypotheses testing using the Benjamini and Hochberg procedure.

**Results**

In the screening process, 60 obese women were checked and 32 could not be included, because after screening procedure they did not fulfill inclusion criteria and/or did not come to the first appointment. 2 more participants could not be included in the final analysis because the stool samples collected after the intervention were damaged during transportation to the laboratory. The baseline characteristics of participants included in the study are shown in table 1. The majority of the participants were single, had a higher educational status, and a middle-class income.

Age in years, mean SD	30.58 (+/- 2.8)
<b>Marital status, n (%)</b>	
Married	8 (30.8)
Single	18 (69.2)
<b>Educational status, n (%)</b>	
University/higher education	8 (30.8)
Apprenticeship	6 (23.1)
Vocational diploma	7 (26.9)
Higher School Certificate	5 (19.2)
<b>Mean Income (in CHF), n (%)</b>	
> 9000	7 (26.9)
6000 -9000	11 (42.4)
4500 - 6000	4 (15.4)
3000 - 4500	3 (11.5)
< 3000	1 (3.8)

**Table 1:** Demographics (N = 26).

No deviation from compliance in intake of dietary supplement was registered. The BMI did not change. Mean BMI before the intervention was 32.3 kg/m<sup>2</sup>, and 32.3 kg/m<sup>2</sup> after the three weeks of herbal yeast intake and continuous food monitoring (Change Score: 0.048 kg/m<sup>2</sup>, 95% CI from -0.131 to 0.227 kg/m<sup>2</sup>, p = 0.757). The main study findings are summarized in table 3, showing change scores and 95% confidence intervals of BMI and the ratings of HRQOL. After correction for multiple hypotheses testing, there was a small but non-significant improvement in satisfaction with state of health and general well-being, and a noteworthy marginally non-significant trend for improvement of fatigue after meal intake (Change Score: -0.962, 95% CI from -1.707 to -0.280, p = 0.096). Coping with stress did not change through the intervention, but data indicate a small decrease in the ability to cope with stress after the three weeks. Satisfaction with social situation and occupation both did not change significantly, but again data pointed towards a decrease of satisfaction in the respective scales.

	Baseline		Three Weeks	
	Mean	SD	Mean	SD
BMI (kg/m <sup>2</sup> )	32.28	1.92	32.33	2.00
Satisfaction with state of health	4.48	1.61	4.25	1.98
General well being	5.87	2.26	5.40	2.00
Fatigue after meal intake	5.60	1.72	4.63	2.23
Coping with stress	3.62	1.72	3.77	1.80
Satisfaction with social situation	2.90	1.89	3.31	1.95
Satisfaction with occupation	3.27	2.09	3.62	1.86

**Table 2:** Descriptives of weight and ratings on aspects of QOL before and after intake of dietary supplement.

**Note:** Lower mean of ratings indicate improvement.

	Change Score	95% CI (lower/upper)		p-value*
BMI (kg/m <sup>2</sup> )	0.048	-0.131	0.227	0.757
Satisfaction with state of health	-0.231	-0.873	0.411	0.384
General well-being	-0.462	-1.207	0.284	0.384
Fatigue after meal intake	-0.962	-1.707	-0.280	0.096
Coping with stress	0.154	-0.328	0.636	0.565
Satisfaction with social situation	0.404	-0.275	1.083	0.384
Satisfaction with occupation	0.346	-0.259	0.951	0.384

**Table 3:** Change Scores and 95% Confidence Intervals of Weight and Ratings on Aspects of QOL.

**Note:** A negative change score means improvement.

\*Corrected for six tests using the Benjamini and Hochberg procedure.

### Discussion

A secondary goal of the study was to observe the impact which the intake of a microbiome-altering substance has on HRQOL, changes were noted in some areas related to HRQOL in the individuals treated with prebiotics. Parallel to these findings, further changes were noticed linked to the dietary behavior of the obese women who participated in the study concerned. Weight loss was not intended or expected as participants were not required to change their eating or dietary behaviors. Therefore, their weight did not change significantly over the three-weeks period. It is worth noting that ratings of health and general well-being did slightly improve, and data indicate that the participants felt less tired, but their ability to cope with stress diminished slightly and participants were altogether less satisfied with their social and occupational life.

Physical functioning in the part of the study where perceived health, general well-being, and fatigue were measured demonstrated the most important change in HRQOL through the intake of prebiotics in relation to weight and BMI. Participants also had changes in their blood pressure significantly as well as in their microbiome. The above-mentioned findings are not the primary focus of the trial and will therefore not be dealt with comprehensively here [76]. These findings are consistent with other studies showing an improvement of HRQOL through the intake of prebiotics(58). As stated in the model of Chang [37], HRQOL in patients with intestinal problems is not limited to disease of physiology-specific aspects, but further psychosocial aspects are present such as general stress in everyday life and coping mechanisms. Findings in this paper support the above-mentioned model by showing improvements through the intake of prebiotics on a physiological level: satisfaction with health and well-being, as well as a decrease in fatigue after meals. Interestingly, coping with stress diminished parallel to a reduction in satisfaction with social and occupational life. According to Grawe., *et al.* [77] a major step in a change process is known as “problem activation”, where patients encounter the formerly neglected problems more intensively and gain more emotional clarity regarding the nature of their problems. This usually goes hand in hand with an increase in negative emotions. In light of the above-mentioned findings, study participants might have better realized where psychological and personal needs in their social and occupational life were not satisfied adequately and therefore had more emotions (i.e. stress) to cope with over three weeks. This indicates that a short term intervention consisting of prebiotics in combination with logging of eating, drinking and exercise via digital photo tool OVIVA-App in obese women already leads to an increase in problem activation. Yet data indicate only a small effect through a short-term, single intervention of prebiotic intake alone. Furthermore, patients did not gain weight as in other studies, where patients had an increase in BMI when emotional clarity and problem activation occurred [51]. This leads to the assumption that patients perhaps became aware of unfulfilled needs through less physiological fatigue and therefore experienced more emotional clarity and stress. Moreover, our participants might have had better physiological support in coping with stress and other emotions that occurred during this clarification process. It remains challenging to determine to what extent the alteration of the microbiome through the intake of prebiotics alone

had an influence on these coping mechanisms. In a study exploring influence on stress through the microbiome, Bharwani, *et al.* [78] (60) documented the influence of neurological stress on the immune-responsibility of the microbiome in mice. When exposed to social stress the microbiome of the tested animals shifted towards less richness and diversity, especially in bacteria involved in the synthesis of neurotransmitter precursors and short-chain fatty acids. They also found that information processing in the nervous system was reduced due to these alterations. The researchers suggest that altering the microbiome could hold therapeutic effects related to stress and psychiatric illnesses. It is possible that subjects might experience an improvement in stress management, also regarding emotionally-triggered eating behavior and therefore had better stress resistance, whereas dissatisfaction in social- and occupational life became clearer. The current study showed improvements in ratings of satisfaction with health and general well-being through the intake of prebiotics, which, to some extent, is consistent with other studies that have found a reduction in worries about digestion or abdominal pain after wheat-germ intake [38]. Those aspects might further improve general stress management and improve coping with the requirements of everyday life.

A special focus of the study lies in the administration of prebiotics in a population of obese women and the several positive changes which have emerged regarding the microbiome and HRQOL. This leads to assumptions about the possible influences of prebiotics in obesity. Based on these findings, an adaption of the HRQOL-model by Chang (2004) with respect to obesity and gastrointestinal functioning is suggested. However, in contrast to Chang (2004), the model proposed here divides HRQOL threefold, which includes a mental-health component, a physiological component, and a social-life component. The latter is not only included due to the high impact of everyday life that often comes with obesity but further implements the threefold definition of HRQOL(36; 61). Furthermore, an adaption of the definition of HRQOL by Chang (2004) is suggested, by including the presence or absence of impairment as the intake of prebiotics might lead to a reduction of specific obesity-related impairments and as such influences HRQOL, as the data within this study indicates.

A general model on the intake of pre and probiotics in an obese condition and effects of HRQOL in obesity is suggested. This general model proposes that, through the intake of prebiotics, several factors influencing obesity are altered in direct or indirect ways. Alterations happen on the nutritional level (intake of the prebiotics themselves) as well as in emotional state and in emotion regulation (via changes in neurotransmitter systems and signal processing in the nervous system) and the physiological functioning of the gut microbiome is altered (i.e. better digestion and alteration in chemical processes in the human body).

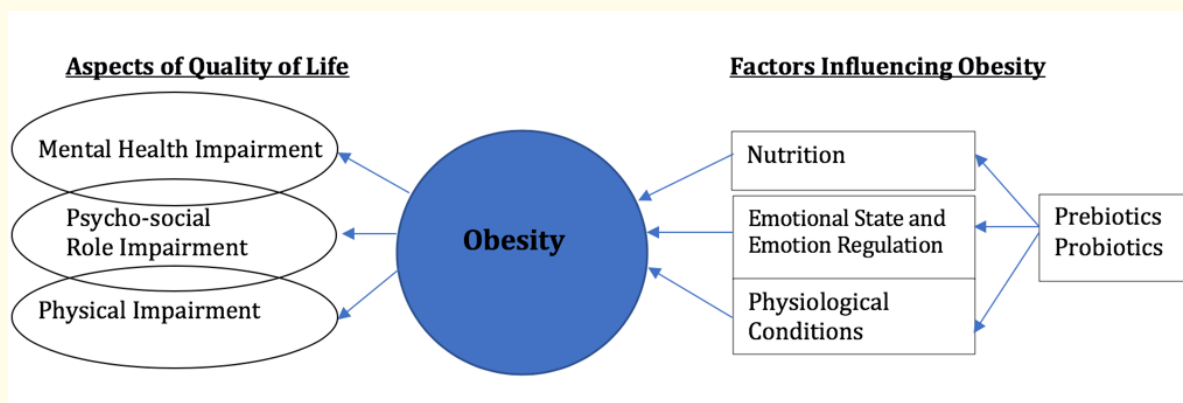


Figure 1: General model on intake of pre and probiotics and effects on HRQOL in an obese condition.

Influencing factors affecting obesity are not always fixed or consistent. The alteration of these influencing factors, in turn, affects aspects related to HRQOL of obese individuals on a physical, mental health, and psycho-social level (i.e. psychological state and function-



ing as well as in psychosocial role functioning). The model above proposes that, as a result of the alteration of influencing factors related to obesity via pre and probiotics, a reduction of impairment in mental-health, physiological, and psychosocial role aspects takes place. Mental-health impairment is reduced through the reduction of physiological stress levels, improved coping mechanisms on a physiological level, and a further improvement in cognitive functioning and management. This additionally leads to a reduction of stress-related psychological problems such as depression and anxiety disorders, which might enhance cognitive resources and stress-endurance capacity to cope with the strain present in everyday life, for example in occupational life. The positive impact on stress levels also leads to possible improvements in relation to stress-induced eating behavior. This might additionally help in behavioral changes and reduction of pathological eating habits which further leads to better weight reduction. Furthermore, by reducing their weight, obese individuals might become more self-confident due to a reduction of obesity-related shame. Physical impairment is reduced via a reduction of pain and discomfort related to digestion in the stomach/intestinal area. Moreover, the cardiac system is influenced by a reduction in blood pressure. This again leads to lower levels of physical impairment, which could in some cases be noticed by the individual. After a certain period of prebiotic intake and respective changes, individuals might re-establish social contacts and become more socially active in general. Through weight loss, obese individuals can get easier access to public spots areas such as toilets, seats in public transport or airplanes, and everyday products such as clothing and furniture. In summary, weight loss and reduction of pain, general physiological discomfort, shame, fear, depressive symptoms, and improvements in mental-health function all lead to more freedom for the individual. This all comes together with a renewed increase in activity in everyday life and social life with fewer limits and at the same time increased access to various areas in public life. Whereas treatment studies in obesity have comprehensively documented such outcomes through medical-, surgical-, psychological- and life-style-focusing interventions [67], specific studies on the application of pre- and probiotics are still lacking. The model suggested within this paper could be utilized to study the subject concerned in a more detailed and comprehensive manner and over a longer period. The influence of pre- and probiotics on mental health and physiological factors leading to obesity as well as the outcome in mental health-, psycho-social and physiological functioning of obese individuals needs to be verified in more detail. Nevertheless, the findings and general model suggested throughout this paper serve as a promising basis for the potential of prebiotics in the treatment of obesity.

### Study Limitations

The primary intention and focus of the study were not on the alteration of HRQOL, therefore HRQOL was not measured in a more detailed manner with regards to physiological, mental health, and psycho-social aspects. The study was exploratory in nature and thus the number of participants was kept to a minimum. Further studies could be conducted in more depth and in larger cohorts on those aspects and differentiation of HRQOL, e.g. measurements of bodily pain, regulation of emotion, more detailed coping with emotions and stress, anxiety, and depression. Furthermore, the participants did not exclusively receive prebiotics, but dietary intake was also monitored via smartphone app. Therefore, some of the changes in HRQOL might also result from the process of online dietary tracking when the participants were observed externally. This might have led to the perception of a more structured everyday life or more general attention towards everyday life on a personal level. Further studies could potentially focus on the comparison of these treatments, i.e. dietary or online treatment vs. prebiotics in a randomized, double-blind setting with a treatment and a control group. Additionally, the intervention lasted for only 3 weeks and it is, therefore, challenging to measure and/or predict the effects of prebiotics on HRQOL in the longer term. It would therefore also be beneficial if further studies measured the long-term effects of prebiotics on HRQOL.

### Conclusion

Administration of prebiotics is documented to have a positive influence on many microbiome-associated illnesses as well as psychological functioning through the alteration of inflammatory processes and the gut-brain axis. Treating such conditions with pre and probiotics leads in most cases to an augmentation in many aspects of HRQOL. As such, pre and probiotics hold potential in the treatment of obesity, not only by influencing its emergence on a nutritional, psychological, and physiological level, but also in leading to a reduction

of impairments in the obese individual, thus promoting the improvement of HRQOL. Administration of pre and probiotics in combination with other interventions such as the monitoring of nutritional and exercise status leads to a problem activation which can be further used in the therapeutic process of obesity. Studies on the therapeutic effects of pre and probiotics on obesity and its psychological aspects as well as HRQOL are currently still lacking. Further research should study those aspects in more detail and over a longer period, especially regarding weight loss, psychological functioning, and HRQOL. While not a primary goal of this particular exploratory study, data suggests that the intake of prebiotics has therapeutic potential in the psychological functioning and HRQOL in obesity. Therapeutic effects of pre and probiotics can emerge on the physiological level and reduce bodily fatigue, but treatment effects can also include improvement of mental health and emotion regulation capacity. It could, therefore, be argued that prebiotics hold a cost-effective therapeutic potential on all physiological and mental-health aspects of obesity and obesity-related impairment.

### Author Contributions

All authors were involved in the study design. R.M. was responsible for interviewing quality of life data and drafted the manuscript. S.M. led data collection and performed interpretation. S.C. was responsible for study monitoring. C.L. was responsible for the collection and interpretation of nutritional data. All other authors critically reviewed and revised versions of the manuscript. All authors read and approved the final manuscript.

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### Conflict of Interest

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