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Possible metabolic interplay between quality of life and fecal microbiota in a presenior population: Preliminary results

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ABSTRACT

Objectives: The number of people aged ≥60 y is increasing worldwide, so establishing a relationship between lifestyle and health-associated factors, such as gut microbiota in an older population, is important. This study aimed to characterize the gut microbiota of a presenior population, and analyze the association between some bacteria and quality of life with the Short Form (SF) 36 questionnaire.
Methods: Participants were adult men and women ages 50 to 80 y (n = 74). In addition to the SF-36 questionnaire, fecal samples were collected in cryotubes, and 16S RNA gene sequencing was performed to characterize microbial features. Participants were classified into two groups according to SF-36 punctuation. Linear and logistic regression models were performed to assess the possible association between any bacterial bowl and SF-36 score. Receiver operating characteristics curves were fitted to define the relative diagnostic strength of different bacterial taxa for the correct determination of quality of life.
Results: A positive relationship was established between SF-36 score and *Actinobacteria* ($P = 0.0310$; $R = 0.2510$) compared with *Peptostreptococcaceae* ($P = 0.0259$; $R = -0.2589$), which increased with decreasing quality of life. Logistic regressions models and receiver operating characteristics curves showed that the relative abundance of *Actinobacteria* and *Peptostreptococcaceae* may be useful to predict quality of life in a presenior population (area under the curve: 0.71).
Conclusions: Quality of life may be associated with the relative abundance of certain bacteria, especially *Actinobacteria* and *Peptostreptococcaceae*, which may have a specific effect on certain markers and health care, which is important to improve quality of life in older populations.

Introduction

Quality of life (QoL) is defined, according to the World Health Organization (WHO), as "an individual's perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns" [1]. QoL is an important component of people's overall well-being, particularly in older adults. The correct measurement of health or the absence of disease is key to primary care and public health policies [2]. Indeed, self perception of health measured through questionnaires has been found to be a good predictor of morbidity and mortality [3,4].

There are several instruments to measure health-related QoL [5], such as the WHO QoL assessment [6], Nottingham Health Profile [7], and EuroQoL [8]. Probably, the most commonly used tool in the evaluation of clinical outcomes is the Short Form (SF) 36 health survey questionnaire [9], which is a self-administrated survey that provides direct quantitative information on an individual's health status [10], and incorporates both physical and mental dimensions of health

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through different items [11]. The questionnaire contains 36 items that measure health in eight domains: Physical functioning, physical role limitations, bodily pain, general health perceptions, vitality, social functioning, emotional role limitations, and mental health [12].

QoL may be influenced by numerous factors, such as familiar situation [13], chronic diseases [14], lifestyle factors [15], and putatively by the gut microbiota [16]. Actually, the presence or absence of noncommunicable diseases is associated with QoL [17]. Lifestyle modifications have shown improvements in specific QoL markers, such as reduced glycemic index and cardiovascular disease risk factors [18]. Gut microbiota involves a collection microorganisms along the gastrointestinal tract [19], and has been demonstrated to evolve across the life cycle [20]. An imbalance or dysbiosis in gut microbiota has been associated with many clinical and mental conditions, which are, to some extent, related to QoL life and wellbeing [21–23]; hence, there is increased interest in research in this field in the nursing scientific community [24].

Fecal microbiota is an adequate sample to study microbial composition, but testing can be carried out also on blood or saliva samples [25]. The characterization of intestinal microbiota has evolved over the years from traditional culture methods to shotgun or 16S rRNA sequencing, which is currently the most commonly used method [26,27]. The human microbiota is mostly composed of five phyla: *Firmicutes*, *Bacteroidetes*, *Actinobacteria*, and (to a lesser extent) *Proteobacteria*, and *Enterobacteriaceae* [28]. Moreover recent studies have shown a clear association between microbiota dysbiosis and some diseases, such as obesity [29], diabetes [30], autoimmune diseases [31], and neurodegenerative pathogenesis [32].

The number of people aged ≥60 y is increasing worldwide, and will continue to increase and more than double the older population in 2050 compared with 2019, especially in developed countries [33]. However, there is a lack of information on the lifestyle and health of older populations, which makes implementing interventions to improve the QoL of these people at risk of developing an unhealthy lifestyle difficult [34]. Therefore, information on the possible relationship between QoL and health are very scarce.

Although our knowledge of the gut microbiota accompanying disease is increasing, basic information of the microbiota composition in healthy individuals is still scant, and the relationship between gut microbiome and QoL needs to be explored further. The aim of this study was to characterize the intestinal microbiota of presenior adults, and specifically analyze the possible association between some bacteria richness and QoL with the SF-36 questionnaire to develop facility precision nursing and personalized health care.

Methods

Study population

A total of 74 participants met all the inclusion and exclusion criteria, and were recruited between January 2020 and September 2020 at the Center for Nutrition Research of the University of Navarra in Spain. Eligible participants were adult men and women ages 50 to 80 y with overweight grade II or obesity (body mass index [BMI] >27 kg/m^2) who met at least one of the following risk factors: Fasting glucose ≥100 to ≤125 mg/dL or type 2 diabetes [35], hypertension (systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or under antihypertensive medication) [36], low-density lipoprotein cholesterol (LDL-c) ≥160 mg/dL independent of lipid-lowering therapy [37], high-density lipoprotein cholesterol (HDL-c) cholesterol ≤40 mg/dL in men or ≤50 mg/dL in women [37], triacylglycerols (TG) ≥150 mg/dL independent of lipid-lowering therapy [37], waist circumference >95 cm in men or >82 cm in women [38] or sedentary behavior considering the American Heart Association recommendations of performing at least 150 min per wk of moderate-intensity aerobic activity or 75 min per wk of vigorous aerobic activity, or a combination of both, preferably spread throughout the week [39]. The exclusion criteria included BMI ≤27 kg/m^2 and ≥35 kg/m^2.

This study was retrospectively registered at ClinicalTrials.gov (identifier NCT04786925; registration date: March 5, 2021). The trial was approved by the research ethics committee of the University of Navarra (reference 2019/183). The research was performed in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). All participants provided written informed consent before being included in the trial.

Study design

The current research was a cross-sectional analysis of data from a larger randomized trial. Volunteers attended facilities at the Center for Nutrition Research of the University of Navarra in fasting conditions. Blood samples were drawn by venipuncture after an 8 to 10 h overnight fast. After 10 min of rest, blood pressure was assessed. Afterward, anthropometric measurements and body composition analyses were performed by a trained dietitian per validated procedures [40]. Stool and urine samples were also collected.

Participants were also asked to fill in different questionnaires on general health status (SF-36 Health Survey), Mediterranean diet adherence (14-Item Mediterranean Diet Assessment Tool), and physical activity (International Physical Activity Questionnaire). Study data were collected and processed using REDCap electronic data capture tools hosted at the Technical University of Madrid [41,42].

Anthropometrics, body composition, and blood pressure measurements

Body weight (kg) and height (cm) were measured without the participants wearing shoes and in light clothing and fasting conditions in the morning, using a calibrated scale and wall-mounted stadiometer, respectively [43]. Waist circumference (cm) was measured midway between the lowest rib and iliac crest using a measuring tape, and hip circumference (cm) was assessed at the widest lateral point of the hips [44]. Waist–hip ratio was calculated by dividing the waist circumference by the hip circumference. BMI was calculated as weight (kg) divided by the square of height (m) [45]. Body composition was determined with a bioimpedance analysis (TANITA SC-330 Scale; Tokyo, Japan), which is a method based on the measurement of the resistance and reactance of an alternating electrical current in the organism [46] per standardized protocols.

Blood pressure (mmHg) was measured with the use of an automatic sphygmomanometer (Intelli Sense. M6, OMRON Health care, Hoofddorp, the Netherlands) per the WHO criteria [47].

Biochemical measurements

Blood samples were drawn from each participant after 8 to 10 overnight fasting, and processed (15 min; 3500 rpm; 5°C) at the Center for Nutrition Research facilities in the University of Navarra. The biochemical analyses included glucose (mg/dL), hemoglobin A1c (%), total cholesterol (TC, mg/dL), HDL-c (mg/dL), TG (mg/dL), uric acid (mg/dL), alanine aminotransferase (mg/dL) and aspartate aminotransferase (mg/dL) levels, which were measured by specific calorimetric assays in an automatic analyzer, Pentra C200 (Horiba ABX Diagnostics, Montpellier, France) with appropriate kits provided by the company. LDL-c levels were calculated using the Friedewald formula [48]: LDL-c = TC–HDL-c–TG/5.

Lifestyle and health assessments

The Mediterranean dietary pattern was determined according to a validated 14-point Mediterranean dietary score based on the consumption of nine food groups or nutrients (cereals, fruits and nuts, vegetables, legumes, fish, meat, dairy products, ratio of monounsaturated to saturated fatty acids, and alcohol). The final score ranged from 0 to 14, and a higher score indicated greater adherence to the Mediterranean diet and a score of ≥9 was considered as having good adherence to the Mediterranean diet [49].

Physical activity was assessed with the validated Spanish version of the International Physical Activity Questionnaire short form. The short form records activity of four intensity levels over the last 7 d: Vigorous-intensity activity, such as aerobics; moderate-intensity activity, such as leisure cycling; walking, and sitting [50]. Global health status was evaluated using the Spanish version of the SF-36 questionnaire [51]. Scores are transformed to range from 0 (worst possible health) to 100 (best possible health).

Fecal sample collection and metagenomic data

Fecal samples were collected in the cryotubes of OMNIgene.GUT kits from DNA Genotek (Ottawa, Ontario, Canada), a system of self collection and liquid stabilization of microbial DNA from feces per the supplier's standard guidelines [52]. Samples were immediately stored at -80°C for future analyses. Isolation of the DNA and bacterial DNA sequencing were carried out by the Center for Applied Medical Research (Pamplona, Spain). The sequencing of the bacterial 16S RNA gene was performed to characterize the phylogeny and taxonomy of the microbial samples per the protocol of the Illumina MiSeq equipment. Briefly, sequencing consists of two polymerase chain reaction (PCR) reactions, in which the V3 and V4 regions of the 16S rRNA gene were amplified, creating an amplicon of

approximately 460 base pairs. This process consists of two PCRs, and require the use of 16S-F and 16S-R specific primers (16S Amplicon PCR Forward Primer = 5 0 TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGCCTACGGGNGGCWGCAG; 16S Amplicon PCR Reverse Primer = 5 0 GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGGACTACHVGGGTATCTAATCC; Nextera XT DNA Index Kit FC-131–1002 Illumina; San Diego, CA).

The protocol followed for the first PCR was at 95°C for 3 min and 25 cycles of 95°C for 30 s, 55°C for 30 s, 72°C for 30 s, and 72°C for 5 min to later keep refrigerated at 4°C. After the cleansing process, 5 μl were taken from the first PCR sample to use for the second PCR. For the second PCR, the protocol followed was 95°C for 3 min and 8 cycles of 95°C for 30 s, 55°C for 30 s, 72°C for 30 s, and 72°C for 5 min to later keep refrigerated at 4°C. After each PCR, a cleansing process was carried out to clear the sample from primers. Then, the samples were loaded into the MiSeq equipment for sequencing and quantification. A code-based approach (barcoding) was used for the complete analysis of the gut microbiome using the operational taxonomic units (OTUs) grouping methods. Taxonomy was assigned using BLAST and HITdb, and sequences were filtered per the OTU LotuS quality criteria (version 1.58). The abundance matrices were filtered and then normalized at each level of classification: OTU, species, genus, family, order, class, and phylum.

Statistical analysis

The sample size was estimated according to the principal outcome, which a priori considered metabolic health score as the primary variable. This approach resulted in a sample size of 100 participants. This study is ancillary; thus, a post hoc analysis was performed to calculate the analytical power assuming an alpha value of 0.05 and effect size of 0.3 with the number of subjects (74), resulting in a statistical power >90%. In any case, types I and II errors cannot be discarded in this investigation.

The normality of the variables was first studied using a Shapiro–Wilk test. Data are expressed as a mean ± standard deviation or median ± interquartile ranges according to the normal distribution or not. Moreover, categorical variables are expressed as percentage using a X^2 test. The entire sample was categorized into two groups (above and below the median) according to the score obtained in the SF-36 questionnaire: Low (n = 37) and high (n = 37) QoL. A total of 74 participants were included for the comparative analyses.

Comparisons between two independent groups were performed using Student's *t* and Mann–Whitney U tests for normal and nonnormal distributions, respectively. Categorical variables were compared using a X^2 test. Simple or multivariable linear regression models were performed to predict whether any bacterial bowl is able to determine QoL. Multivariable adjusted logistic regression models were fitted to study the associations between being classified by the median in the high or low QoL group according to the SF-36 score with some bacteria. Correlations were assessed using Pearson's scatter plots for normal distribution.

Receiver operating characteristics curves were fitted to define the relative diagnostic strength of the different bacterial taxa for the correct determination of QoL. We used the area under the curve (AUC) to quantify accuracy. We interpreted an AUC between 0.90 and 0.80 as good, between 0.80 and 0.70 as fair, and between 0.70 and 0.60 as poor diagnostic tests. Alpha (mean of different species within subject) and beta (mean of different species between subjects) diversities were performed using MicrobiomeAnalyst [53] from phylum to genus. Richness (number of species in our population) was calculated with the number based on OTU counts. The software used for the statistical analysis was STATA, version 12.1 (StataCorp, College Station, TX).

Results

Participant characteristics

A flow chart of the participants in a CONSORT diagram is shown in Supplemental Figure 1. Baseline characteristics of the population divided according the median of the SF-36 score (83.0625) are shown in Table 1, including body composition, biochemical markers, and lifestyle factors. Age and SF-36 punctuation were significantly different between the groups, with the older group having poorer QoL and therefore a lower questionnaire score. Fat mass showed a marginal trend toward significance ($P = 0.0645$), and was lower in the higher QoL group. A close relationship was observed between fat mass and sex of the participants; therefore, a possible collinearity between the two variables could be attributed.

Table 1
Baseline characteristics of participants according to QoL categorized by Short Form 36 health survey median punctuation

	Entire population	Low QoL	High QoL	*P* value
n	74	37	37	
General characteristics				
Age, y	58.0 (54.0–62.0)	**59.0 (56.0–63.0)**	57.0 (53.5–60.5)	0.0323
Sex (women/men)	42/32	24/13	18/19	0.159
Body composition				
Weight, kg	86.6 (13.6)	84.7 (11.9)	88.5 (15.1)	0.2320
Body mass index, kg/m^2	31.1 (2.7)	31.5 (2.0)	30.8 (3.2)	0.2236
Waist circumference, cm	102.4 (10.3)	102.5 (8.0)	102.3 (12.2)	0.9412
Hip circumference, cm	110.8 (6.7)	111.4 (5.8)	110.2 (7.5)	0.4563
Fat mass, %	36.7 (31.0–42.9)	39.1 (33.9–42.9)	34.4 (29.0–41.4)	0.0645
Blood biochemical markers				
Systolic blood pressure, mmHg	130.8 (118.7–140.0)	129.0 (118.5–135.5)	134.3 (119.5–144.0)	0.1385
Diastolic blood pressure, mmHg	83.0 (78.6–90.0)	81.5 (78.0–88.0)	83.5 (79.5–91.5)	0.2723
Triacylglycerols, mg/dL	117.0 (79.0–158.0)	108.5 (78.5–152.0)	118.0 (80.0–170.0)	0.4974
Glucose, mg/dL	106.0 (99.4–111.2)	106.4 (102.1–112.0)	105.4 (97.5–111.2)	0.4974
Triacylglycerol glucose index, md/dL	8.7 (0.5)	8.7 (0.5)	8.7 (0.5)	0.7701
Insulin, U/mL	6.9 (4.7–11.2)	7.4 (4.9–11.1)	6.3 (4.6–11.3)	0.6117
Homeostatic model assessment-insulin resistance	1.9 (1.2–2.9)	2.1 (1.3–3.0)	1.7 (1.2–2.9)	0.5661
Hemoglobin A1C, %	5.5 (5.3–5.7)	5.5 (5.3–5.8)	5.5 (5.4–5.6)	0.8741
Uric acid, mg/dL	5.5 (4.7–6.4)	5.3 (4.7–6.1)	5.8 (4.8–6.8)	0.1747
Total cholesterol, mg/dL	235.2 (44.7)	232.1 (51.3)	238.1 (37.6)	0.5719
Low-density lipoprotein cholesterol, mg/dL	156.3 (38.5)	154.3 (45.1)	158.3 (31.4)	0.6596
High-density lipoprotein cholesterol, mg/dL	50.9 (42.3–61.4)	52.2 (46.7–59.9)	49.8 (40.8–61.9)	0.6590
Alanine transaminase, U/L	23.3 (17.8–35.9)	24.9 (16.8–37.7)	23.1 (20.1–34.0)	0.9340
Aspartate transaminase, U/L	21.7 (19.3–27.4)	22.2 (19.7–28.1)	21.5 (19.0–26.1)	0.3288
Gamma-glutamyl transferase, U/L	16.0 (9.0–29.0)	16.5 (10.5–29.0)	16.0 (8.0–29.0)	0.7363
Lifestyle factors				
Mediterranean diet adherence screener, points	8.4 (1.8)	8.2 (1.7)	8.6 (2.0)	0.4119
Physical activity, metabolic equivalents task units, min/wk	1639.5 (792–2772)	1452.0 (704–3168)	1662.0 (975–2415)	0.5235
Short Form 36 health survey, points	83.1 (74.7–89.0)	**74.7 (62.4–79.6)**	**89.0 (86.3–90.4)**	< **0.001**

QoL, quality of life 0
Variables are shown as mean (SD) or median (interquartile range) according to normal or nonnormal distribution. Categorical variables were compared using a X^2 test. Bold numbers indicate statistical significance.

Table 2
Relative abundance of different bacteria ($P > 0.1$) of participants according to QoL categorized by Short Form 36 health survey median punctuation

	Entire population			Men			Women		
	Low QoL	High QoL	*P* value	Low QoL	High QoL	*P* value	Low QoL	High QoL	*P* value
n	**37**	**37**		**13**	**19**		**24**	**18**	
Phylum									
*Actinobacteria**	6.2 (2.1)	6.6 (1.8)	0.3360	*5.7 (2.2)*	*6.9 (1.4)*	*0.0735*	6.4 (2.1)	6.3 (2.1)	0.8867
Family									
*Streptococcaceae**	6.4 (2.1)	7.0 (1.9)	0.1343	*5.9 (1.9)*	*6.8 (2.1)*	*0.0877*	6.7 (2.3)	7.2 (1.7)	0.3470
Genus									
Bacteroides	15.6 (0.8)	15.5 (0.8)	0.3173	*15.8 (0.8)*	*15.3 (0.8)*	*0.0951*	15.5 (0.8)	15.6 (0.8)	0.8588
*Coprococcus**	4.3 (1.0)	4.0 (0.9)	0.1400	3.9 (1.1)	3.9 (1.0)	0.9541	*4.4 (0.9)*	*4.1 (0.9)*	*0.0752*
*Faecalibacterium**	12.7 (0.9)	12.3 (1.2)	0.1055	12.4 (0.9)	12.5 (1.1)	0.5520	**12.9 (0.8)**	**12.1 (1.2)**	**0.0237**
*Lachnoclostridium**	10.8 (0.8)	10.5 (0.9)	0.1471	10.4 (0.8)	10.4 (1.0)	0.9708	*11.0 (0.7)*	*10.5 (0.8)*	*0.0888*
*Ruminococcus**	10.5 (1.5)	10.8 (1.8)	0.5356	10.6 (1.7)	10.3 (1.9)	0.6252	*10.5 (1.4)*	*11.3 (1.4)*	*0.0868*

QoL, quality of life.
Variables are shown as mean (SD). Bold numbers indicate $P < 0.05$. Italic numbers indicate $P < 0.1$.
*Normal-distribution variables.

Subjects with a low percentage of body fat mass were men, and women showed a higher percentage of fat mass.

Other lifestyle characteristics, such as adherence to the Mediterranean Diet or physical activity, as well as biochemical and body composition markers, were also analyzed. No statistically significant differences between the groups were found concerning the mentioned variables.

Analysis of associations between bacterial taxa and quality-of-life groups

A lack of association was found between alpha and beta diversities when considering the entire population. The relative abundance of different bacteria was categorized in the general population by median SF-36 score and separately by sex (Table 2), showing bacteria with $P < 0.1$. A difference that tends toward significance can be observed in some bacteria when comparing the low and high QoL groups. The abundance of the *Faecalibacterium* genus in women was higher in the lower QoL group ($P = 0.0237$).

Pearson's correlation scatter plots show how the relative abundance of *Actinobacteria* increases as the total SF-36 score is higher (Fig. 1A). However, *Peptostreptococcaceae* evidenced a negative association, increasing the concentration of this family when the QoL of participants decreased (Fig. 1B). Both genera, *Intestinibacter* (Fig. 1C) and *Lachnospira* (Fig. 1D), also demonstrated a significant negative association with QoL, indicating that their abundance decreased proportionally to a higher score on the QoL questionnaire.

To achieve the study purpose and evaluate the possible association between some bacteria and QoL, the bacterial phylum and families that presented an association with SF-36 score in previous analyses (*Actinobacteria* phylum and *Peptostreptococcaceae* family) were chosen to further construct the linear regression models.

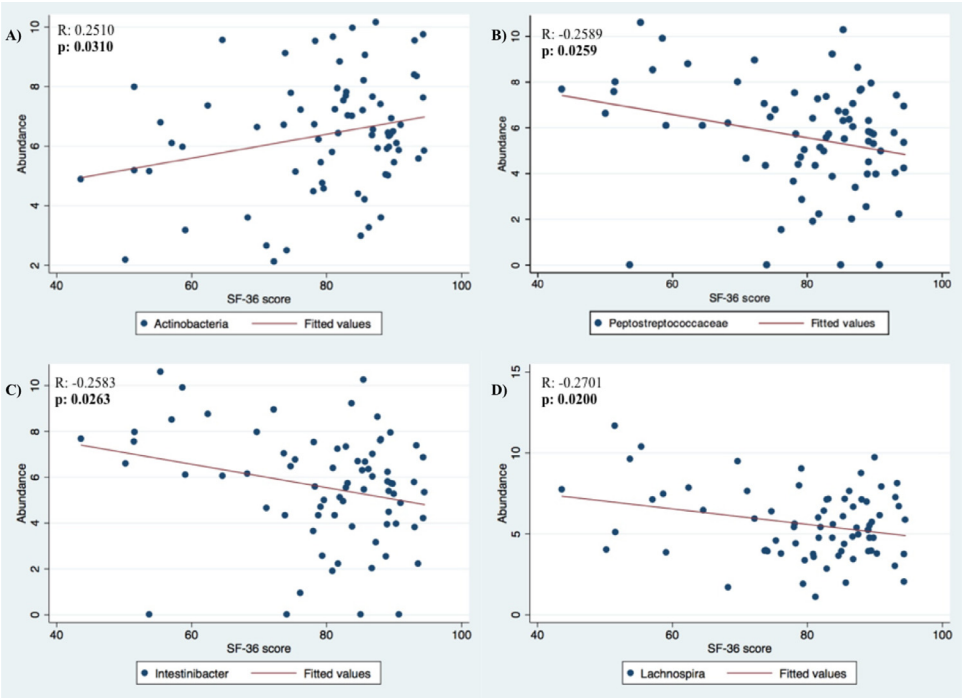

Fig. 1. Scatter plot showing Pearson's correlations of (A) *Actinobacteria*, (B) *Peptostreptococcaceae*, (C) *Intestinibacter*, and (D) *Lachnospira* with total quality-of-life score Bold numbers indicate statistical significance.

Table 3
Linear regression models of quality of life based on the SF-36 score

	Quality of life (SF-36)		
	β	*P* value	R^2_{adj}
Model A		**0.0014**	0.1630
Sex	5.796	**0.031**	
Age	−0.519	**0.020**	
Actinobacteria	1.730	**0.013**	
Model B		**0.0004**	0.1927
Sex	6.854	**0.010**	
Age	−0.532	**0.015**	
Peptostreptococacceae	−1.671	**0.003**	
Model C		< **0.001**	0.2900
Sex	6.877	**0.006**	
Age	−0.608	**0.004**	
Actinobacteria	2.042	**0.002**	
Peptostreptococacceae	−1.898	< **0.001**	

SF-36, Short Form 36 health survey.
β represents changes in outcomes for increasing number of units of SF-36 punctuation in the entire population. Bold numbers indicate statistical significance ($P < 0.05$).

Linear regression models adjusted by sex and age were built because of the recognition of their influence on QoL (Table 3). Data revealed that the association of both bacterial taxa improved the adjusted R^2 value from 0.29. Additionally, logistic regressions and receiver operating characteristic curves, both adjusted by sex and age, were conducted to determine whether bacteria were able to predict QoL. AUCs were estimated as 0.68 for *Actinobacteria* and 0.67 for *Peptostreptococcaceae*. Interestingly, the multiple logistic regression including both *Actinobacteria* and *Peptostreptococcaceae* adjusted by sex and age significantly improved the model, reaching an AUC of 0.71 to predict QoL (Fig. 2).

Correlation with dimensions and domains of Short Form 36 questionnaire

Furthermore, *Actinobacteria* was significantly associated with the Mental Health Dimension ($P = 0.0217$; $R = 0.2666$) and mental health domain ($P = 0.0171$; $R = 0.2765$), and *Peptostreptococcaceae* was significantly correlated with the transition-of-health question ($P = 0.0018$; $R = -0.3322$), physical role limitation domain ($P = 0.0464$; $R = -0.2323$), Mental Health Dimension ($P = 0.0370$; $R = -0.2430$), emotional role limitation domain ($P = 0.0378$; $R = -0.2420$), and vitality domain ($P = 0.0288$; $R = -0.2543$; Table 4).

Discussion

In this study, we identified that the balance of gut microbiota is associated with a lower or higher QoL (with putative consequences on health) and nursing in a Spanish presenior population. Specifically, the abundance of two bacteria taxa, *Actinobacteria* phylum and *Peptostreptococcaceae* family, were found to be relevant to understand the interactions.

A lower QoL score was associated with younger age among cohort participants, so age was used as an adjusted variable as previously observed [54]. Moreover, Yamamoto et al. [55] found a negative association between age and physical dimension, and a positive association was established between age and mental health and role/social component score. QoL has been observed to decline steadily with age, especially in the physical dimension and physical role limitation [56]. QoL has been shown to depend on sex as well, in line with the results of our study, and male older adults reported better QoL than female older adults in 2020 studies [57,58]. However, other authors have shown an association with fat mass [59].

In this cohort, a similar association of QoL with fat mass content and sex was featured, showing that male participants presented with lower fat mass. Therefore, fat mas was not used as an adjustment variable because of potential collinearity. The lack of significant differences between the groups in biochemical, body composition, or lifestyle variables suggests that the observed changes are influenced by the QoL, sex (and therefore fat mass), and age of participants.

Interestingly, gut microbiota is directly related to the production of metabolites, identified as significant contributors to the symptoms of depression and anxiety [21,60]. Symptoms of impaired mental health status have been linked to gut microbiota, with sex as a biologic variable [61]. The results of this investigation showed that gut microbiota has a relationship with QoL, specifically *Actinobacteria* phylum and *Peptostreptococcaceae* family. In this study, we found a significant positive association of the mental components of the SF-36 questionnaire with the phylum *Actinobacteria*, indicating that the better the mental condition, the higher the abundance of this phylum. However, other research studies have reported increased *Actinobacteria* concentrations in patients with major depressive disorders [62] and bipolar disorder [63].

On the other hand, *Peptostreptococcaceae* has been described as a nonbeneficial family for the host because of a decrease in concentration as the SF-36 total score increases. Thus, some authors have positively associated the increase of this family with anxiety symptoms [64]. However, Fei et al. [65] reported an enrichment in this bacterial family in participants with a lower total cardiometabolic risk.

The result of this research shows a positive relationship between *Actinobacteria* and QoL, and a negative association between *Peptostreptococcaceae* and SF-36 total score. Nevertheless, the effect of the gut microbiota on the QoL (measured by questionnaires) of a presenior population is not well evidenced yet in the literature, and further studies are needed.

Given the increasing prevalence of chronic diseases worldwide and the particular importance of mental health in recent years, both researchers and clinicians, as well as nursing staff, should be aware of all possible metabolic pathways associated with the

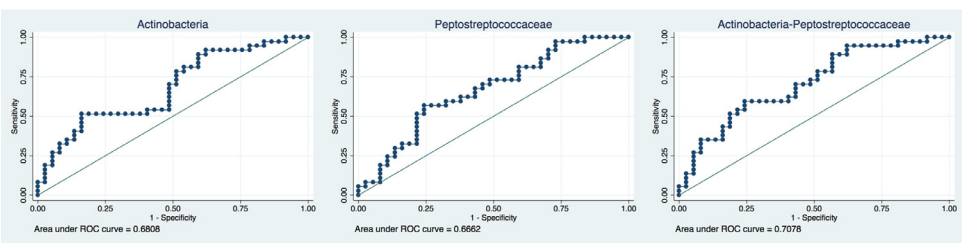

Fig. 2. Receiver operating characteristics curve analysis for three linear regression models of quality of life based on Short Form 36 punctuation

Table 4
Pearson correlation analysis of *Actinobacteria* and *Peptostreptococcaceae* taxa with different dimensions and domains of Short Form 36 health survey questionnaire

		Transition of health	Physical Health	Physical functioning	Physical role limitations	Bodily pain	General health perception	Mental Health	Emotional role limitation	Mental health	Vitality	Social functioning
Actinobacteria	R	0.1924	0.1669	0.1261	0.1205	0.1192	0.1941	0.2666	0.1562	0.2765	0.2063	0.1968
	P value	0.1005	0.1553	0.2843	0.3065	0.3118	0.0975	**0.0217**	0.1838	**0.0171**	0.0779	0.0929
Peptostreptococcaceae	R	−0.3322	−0.1744	−0.1525	−0.2323	−0.1585	0.0286	−0.2430	−0.2420	−0.1102	−0.2543	−0.1161
	P value	**0.0038**	0.1372	0.1946	**0.0464**	0.1773	0.8091	**0.0370**	**0.0378**	0.3500	**0.0288**	0.3245

Bold numbers indicate statistical significance ($P < 0.05$).

symptoms to consider each patient's risk of developing these diseases; thus, improving health-related QoL [61], which may have particular relevance to health care.

This study has some limitations. Variables were adjusted for possible confounders (age and sex), but other potential confounders may also have an influence. Our sample is relatively small, and the population cannot be completely representative of the general population because only subjects from Navarra, Spain were recruited. The lack of references in the literature on gut microbiota and QoL in senior populations may also make comparisons with other findings difficult. On the other hand, to the best of our knowledge, this is the first study evaluating the relation between QoL measured with the SF-36 questionnaire and gut microbiota in a Spanish population.

Conclusions

This research supports that QoL may be associated with the relative abundance of certain bacteria, especially the phylum *Actinobacteria* (beneficial) and the family *Peptostreptococcaceae* (detrimental). This investigation evidences that both age and sex may influence this association, as well as fat mass because of its collinearity with sex. We also suggest that *Actinobacteria* and *Peptostreptococcaceae* may have a more specific effect on certain markers of QoL. However, further research is needed to confirm these observations.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.nut.2022.111841.

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