BMC Nutrition

RESEARCH

Open Access

The diversity of factors influencing human digestive microbiota in healthy adults and their interaction: a scoping review

Begoña Pérez-Llano[1*], Celia Medrano Rodríguez[1] and Eduardo González Fraile[2]

Abstract

Background / objectives Human digestive microbiota is affected by a wide variety of different factors. The objective of this study was to perform a scoping review that gathers and updates the information available about factors that affect human digestive microbiota in healthy adults. It is also reviewed if other factors are considered and if some type of interaction between them is studied. We searched in MEDLINE, Web of Science, Scielo, PROSPERO, and Cochrane databases. Two authors independently reviewed study eligibility and data extraction. Articles were classified based on the main factor studied upon one of the following categories: diet, habits, environment, or chemical exposure.

Results The literature search provided a total of 73 studies that met the inclusion criteria. The presence of data about the influence of diet, habits, environment, and exposition to chemicals on digestive microbiota were registered. Analysis of the studies indicates that the assessment of risk factors is often focused on a specific aspect (diet, habits, environment, and chemicals) and the study of the interaction between factors is up to now not sufficiently investigated. In addition, there are some situations probably relevant to the human digestive microbiota that are not being assessed (snacking, intermittent fasting, type of sport practiced, living with pets or working with animals, type of transportation daily used, home cleaning habits, treatments with radiotherapy, immune suppressants, corticosteroids).

Conclusions Little is known about the impact of the combined interaction of factors related to diet, habits, environment, and chemical exposure on human digestive microbiota. Further studies are encouraged to evaluate more broadly the interactions between the risk factors that may influence the diversity of the human digestive microbiota. All of them are factors that affect our health every day. It would be a good practice for all or most of these factors to be considered in the anamnesis of patients whose microbiota status and the causes of their possible dysbiosis are to be analyzed.

Keywords Gut microbiota dysbiosis, Diet, Lifestyle, Environment, Chemicals

*Correspondence:
Begoña Pérez-Llano
begona.perez@unir.net
[1]Facultad de Ciencias de la Salud, Universidad Internacional de La Rioja S.A. (UNIR), Avenida de la Paz 137, Logroño 26006, Spain
[2]Instituto de Transferencia e Investigación (ITEI), Universidad Internacional de La Rioja (UNIR), Logroño, Spain

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Introduction

Knowledge about human microbiota has taken a growing interest in studies due to its impact on health. It has also been described that some factors, such as diet, consumption of prebiotics and probiotics, medication, living places, physical activity, socioeconomic status, alcohol and tobacco consumption, and stress, have an impact on the digestive microbiota [1–8]. In these studies, the data collection consists of microbiological and genetic analyses on feces or saliva. Several of them also use a questionnaire about habits and other circumstances of the participants that may impact the microbiota composition and diversity [8, 9].

Up to now, there are some details that have not been investigated that could be relevant to investigate. Working activity and place, living with pets and frequent contact with animals such as fish, chickens, or cows with their specific microbiota, are sources of microorganisms [10, 11]. To the best of our knowledge, these factors have not been included yet in research to study the human digestive microbiota.

We conducted a scoping review to compile the factors described in the literature that influence the human digestive microbiota. Our objective was to review these factors that have an impact on microbiota in healthy adults. Due to the influence of the digestive microbiota on health, a profound knowledge of the factors that influence the human microbiota and its interactions would pave the way for preventive health care.

Materials and methods

This scoping review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and meta-analyses (PRISMA) guidelines for Scoping Review (PRISMA-ScR) [12].

Eligibility criteria

Inclusion criteria

Original research articles included in the scoping review were studies involving healthy human adults older than 19 years describing factors that influence in digestive microbiota (including oral, gastric, or intestinal microbiota) leading to dysbiosis. We have classified these factors into four categories:

- DIET: characteristics of the diet, type of food consumed, nutritional supplements, pro and prebiotics, specific diets.
- CHEMICALS: commonly used drugs, antibiotics, vitamins, herbal products, herbicides, pesticides.
- ENVIRONMENT: rural or urban, type of accommodation, cohabiting family, work activity, workplace, pets, household cleaning, means of transportation frequently used.
- HABITS: sleep, physical activity, tobacco, alcohol, drugs.

We selected papers published from 1 January 1950 to 30 September 2023 in English or Spanish. We included any research articles (no design restriction), systematic reviews, or meta-analysis, with or without questionnaires. We did not include conference abstracts.

Exclusion criteria

Studies about menopause, gestation, and digestive diseases and their pathogeny, diagnosis, or treatment (intestinal inflammatory diseases, celiac disease, gastric or oral diseases, eating disorders, parasitic diseases, fecal transplant). We also excluded studies about any other diseases such as mental, nervous system, kidney, skin, eyes, respiratory system, liver, pancreas, blood, obesity, metabolic syndrome, diabetes, COVID, HIV, or cancer.

Literature search strategy

Bibliographic search was made in five scientific databases: Web of Science (WoS), PubMed, Scielo, Cochrane, and PROSPERO.

After considering synonyms, keywords selected were: "Gastrointestinal microbiome", "Gastrointestinal or gut or enteric or intestine or stomach or oral or mouth", "Microbiome or microbiota or flora or microflora or bacteria", "Dysbiosis or dysymbiosis or dysbacteriosis". The final search strategy used was: ((Gastrointestinal OR gut OR intestine OR enteric OR stomach OR oral OR mouth) AND (microbiome OR microflora OR flora OR microbiota OR bacteria)) AND ((intestinal OR gut OR enteric) AND (dysbiosis OR dys-symbiosis OR dysbacteriosis)).

Eligibility assessment and data extraction

Literature search results were uploaded to the bibliography management tool Mendeley, and duplicates were removed. Screening by title and abstract was done by two trained review authors (BPL, CM) based on the inclusion and exclusion criteria. The full text of the selected references was retrieved, and BPL and CM screened them according to the selection criteria. The entire process was carried out independently and by blinding the reviewers. Disagreements were resolved by discussion and consensus.

Additional studies found by a non-systematic search that are relevant to the researchers have been included.

Data extraction included the following: First author, year of publication, number of participants, age, diet, habit, environment, chemical-related factors, and questionnaire item-descriptions.

Results

We retrieved a total of 2864 references. After eliminating duplicates (996) with the bibliographic tool Mendeley it remained 1868 references. 73 studies fulfilled the criteria for inclusion. The search strategy and selection of publications are shown in Fig. 1.

Of the total of 73 studies, 50 are research studies, and 22 are reviews or meta-analysis papers. Every research study found was classified into one of the following four categories of factors:

- DIET: 22 papers addressing probiotics, prebiotics, sweeteners, type of foods, ultra-processed food, specific diets (Mediterranean diet, vegan diet), fermented foods, plant-based food polyphenols, or protein supplements (Table 1).
- HABITS: 7 studies about sleep, physical activity, tobacco, alcohol, or drugs (Table 2).
- ENVIRONMENT: 11 articles regarding rural/urban environment, living near a mine, nursing homes, cohabiting family (partner, children, parents, grandparents), short hospitalization periods, long ocean voyages, or exposure to high altitudes (Table 3).
- CHEMICALS: 10 papers about antibiotics, methamphetamine, opioids, metformin, vitamin D, proton-pump inhibitors, herbicides, fungicides, titanium oxide nanoparticles, or herbal treatments (Table 4).

One study addressed two or more of these categories and was included in the discussion [59].

First, a review was made of the results related to the factors studied in every paper. In 41 of these research studies questionnaires were used. In Tables 1, 2, 3 and 4, questions of the questionnaires used in every study are split into the four categories mentioned (diet, habits, environment, and chemicals) and data from these four categories retrieved in every study were recorded.

Diet

Overall, diet was the most studied factor about its influence on digestive microbiota (43% of the papers included in the scoping review) (Table 1). As regards to probiotics,

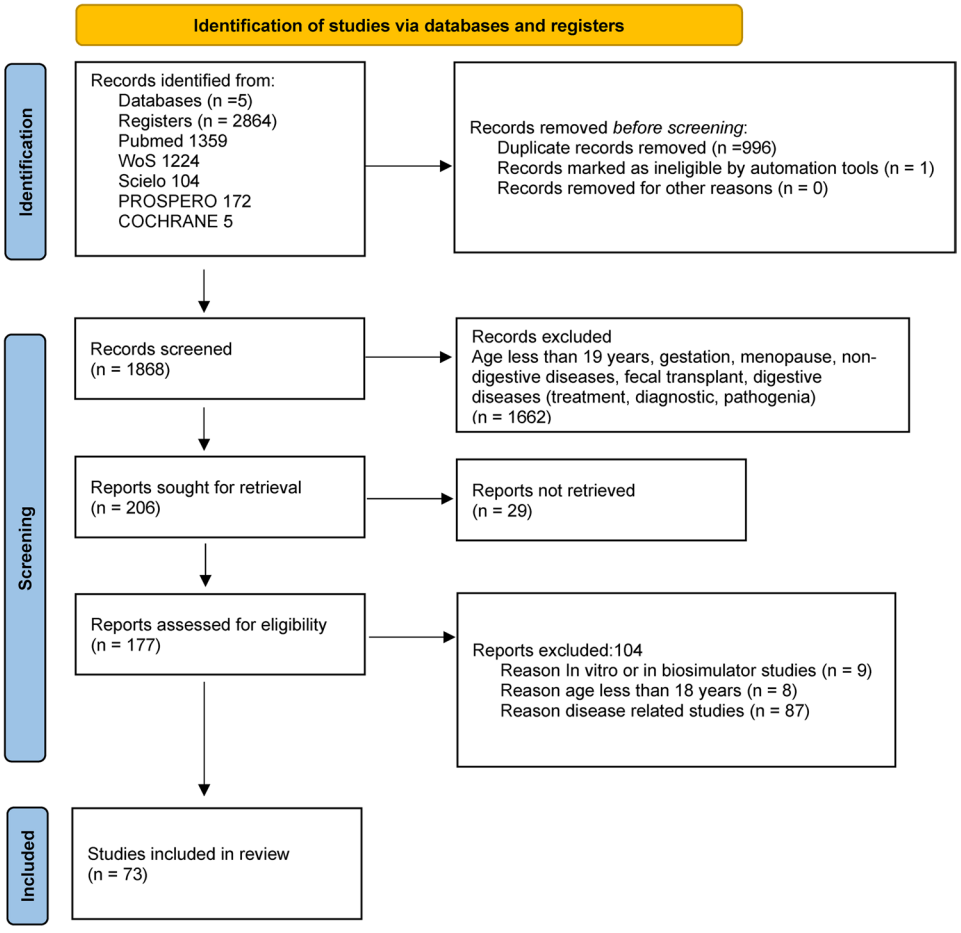

Fig. 1 PRISMA flow chart of the search, identification, and screening process of the scoping review about factors that affect human digestive microbiota in healthy adults

Table 1 References that study diet-related factors and data collected in questionnaires (22 references)

First author Year of publication	Number of participants Age	Diet-related factors	Questionnaires with questions about:			
			Diet	Habits	Environment	Chemicals
De Preter et al. 2007 [13]	*N* = 20 21 ± 1 year old	Probiotics and prebiotics	-	-	-	-
Rampelli et al. 2013 [14]	*N* = 32 71–88 years old	Supplements with probiotics.	-	-	-	-
Reyes et al. 2016 [15]	*N* = 9 18 to 39 years old	Diet rich in unsaturated fatty acids and fiber	Food and drink frequency.	-	-	-
Odamaki et al. 2016 [16]	*N* = 33 20–50 years old	Yogurt with bifidobacteria and animal-based diet	Vegan or not vegan diet.	-	-	Routine use of medicine.
De Filippis et al. 2016 [17]	*N* = 153 18–60 years old	Mediterranean diet	Consumption of animal products, regular supplementation with prebiotics or probiotics	-	-	Drugs, antibiotics.
Elison et al. 2016 [18]	*N* = 100 18–60 years old	Supplementation with milk oligosaccharides	Consumption of probiotics.	-	-	Antibiotics, other medication in a regular basis.
Castro-Penalonga et al. 2017 [19]	*N* = 31 18–65 years old	Southern European Atlantic Diet (SEAD)	SEAD adherence history. Food Frequency Questionary with 113 items.	Physical activity, tobacco consumption, sleeping hours and the time to go to bed.	-	-
Alfa et al. 2018 [20]	*N* = 42 elder ≥ 70 years old *N* = 42 mid-age 30–50 years old	MS Prebiotic ® (resistant starch)	Consumption of probiotics, additional fibre supplements.	-	-	Antacids, antibiotics, other medication in a regular basis.
Moreno-Pérez et al. 2018 [21]	*N* = 12 Protein supplement 100 weeks; *N* = 12 control 18–45 years old	Long-term protein supplementation	Food frequency questionnaire with 93 food items. Use of nutritional supplements.	Smoking habits.	-	Medication.
Yuan et al. 2018 [22]	*N* = 12 27–46 years old	Green tea liquid	Frequency of consumption of foods commonly used in Chinese cuisine, general dietary behaviour and usual cooking methods.	Exercise, sleep habits.	Location change	Medication.
Dassi et al. 2018 [23]	*N* = 21 23 ± 1,23 years old	Commercial probiotics and non-probiotic yogurt	-	Oral care habits.	-	-.
Singh et al. 2020 [24]	*N* = 80 17–28 years old	Vitamin D supplementation	Dietary habits and supplementation.	Exposure to sunlight.	-	-
Ma et al. 2021 [25]	*N* = 307 healthy men 65–80 years old	Dietary fibre from cereals, fruits and vegetables	Food Frequency Questionnaire. Probiotic use.	Physical activity, Smoking habits.	-	Antibiotic use.
Márquez-Morales et al. 2021 [26]	*N* = 27 treated and *n* = 18 control 20–25 years old	Fermented food: aguamiel based beverage fermented with lactic acid bacteria	-		SISCO Academic Stress Questionnaire	-
Kiewiet et al. 2021 [27]	*N* = 11 inulin and *N* = 13 control groups. 55 to 88 years old	Chicory long-chain inulin (prebiotic)	Frequency of fibre-rich foods consumption (cereals, legumes, etc.).	-	-	-

Table 1 (continued)

First author Year of publication	Number of participants Age	Diet-related factors	Questionnaires with questions about:			
			Diet	Habits	Environment	Chemicals
Cuevas-Sierra et al. 2021 [28]	*N* = 359 40–50 years old	Ultra Processed Foods	Food frequency questionnaire validated in Spain that includes 137 food items. Adherence to Mediterranean Diet with a validated score.	Lifestyle characteristics, smoking status. Questionnaire to assess physical activity.	-	-
Serrano et al. 2021 [29]	*N* = 46 18–45 years old	Saccharin, lactisole (sweet taste receptor inhibitor), or saccharin with lactisole	-	-	-	-
Zhang et al. 2021 [30]	*N* = 42 ≥ 65 years old	Sesame seed snacks and plant-based smoothies	Diet designed by a dietician.	-	Residents in a living facility of a hospital.	-
Lacourt-Ventura et al. 2021 [31]	*N* = 80 adult female pre-menopausal 25 to 50 years old	Diet based heavily on beans (at least 3 servings per day) and dairy products.	Type of food, frequency of consumption.	Physical activity, smoking habits.	Educational level, income.	-
Wastyk et al. 2021 [32]	*N* = 36 ≥18 years old	Effects of a high fibre or fermented food diet.	-	International Physical Activity Questionnaire.	Health surveys (PROMIS): global health, fatigue, well-being index, cognition short form, perceiving stress scale.	-
Palmas et al. 2022 [33]	*N* = 17 centenarians, 29 nonagenarians, 46 healthy younger controls, *N* = 7 centenarians with their offspring.	Mediterranean Diet	Mediterranean Diet score. Coffee consumption.	Smoking status, alcohol. Physical activity scale for the elderly.	Mini mental state examination test.	-
Galena et al. 2022 [34]	*N* = 31 women 18 to 69 years old	Fermented vegetables	135-item food frequency questionnaire	-	-	-

some studies with sample sizes less than 40 have been shown to influence digestive microbiota to prevent or treat some diseases, decrease dysbiosis due to age, help to maintain a normal microbiota in a meat-based diet or increase the diversity of the oral cavity microbiota [14, 16, 23, 60]. Fermented food has taken greater importance due to its relationship with positive microbiota changes, as increase of microbiota diversity and decrease markers of inflammation, and other effects such as reduction of academic stress and inflammatory markers [26, 32, 34].

The intake of dietary fiber with different prebiotics also influences digestive microbiota. A diet rich in fiber has caused increases in the levels of beneficial bacteria as *Bifidobacterium* and *Prevotella* and increases in short-chain fatty acids (SCFA) by means of increased microbiome-encoded glycan-degrading carbohydrate active enzymes (CAZymes) in studies with low (n = 9) and high (n = 153) sample sizes [15, 17, 61]. Supplementing with milk oligosaccharides has shown an induction of the growth of beneficial bifidobacteria (n = 42 to 100) [18, 20]. It has also been described that a greater intake of dietary fiber from cereals, fruits, and vegetables is associated with shifts in gut microbiome composition and a reduction of C-reactive protein (n = 307) [25]. Inulin consumption also modified the microbiota composition with higher microbial diversity in a small sample size trial (n = 24) [27]. Dietary addition of *L. casei*, *B. breve* and a prebiotic product, results in an improvement of intestinal physiologic traits (stool weight, fecal dry weight, total N fecal excretion) and an increase of total fecal bifidobacteria in a sample of 20 subjects [13].

Polyphenols also have been shown to affect the gut microbiota. Some of them have protective effects on the goblet cells of the intestinal mucosa and others have been shown to increase the counts of *Lactobacillus* and *Bifidobacterium* and improve gut and host health as is compiled in two review studies [62, 63]. The type of diet has also been related to gut microbiota status. High adherence to the Southern European Atlantic Diet produces a greater number of total bacteria, *Actinobacteria*, *Lactobacillus*, and *Bifidobacterium* genus in a sample of 31 subjects [19]. Significant correlations between bacterial

Table 2 References that study habits-related factors and data collected in questionnaires (7 references)

First author Year of publication	Number of participants Age	Habit-related factors	Questionnaires with questions about:			
			Diet	Habits	Environment	Chemicals
Estaki et al. 2016 [35]	*N* = 39 21–31 years old	Cardiorespiratory fitness level	24 h recall of food and supplements.	Physical activity readiness questionnaire.	-	-
Xu et al. 2017 [36]	*N* = 45 substance use disorders *N* = 48 healthy controls 19–46 years old	Heroine, ephedrine, and ice (methamphetamine)	-	-	-	-
Zhang et al. 2017 [37]	*N* = 11 24–49 years old	Sleep restriction	-	Circadian rhythm questionnaire and sleep disorders questionnaire.	-	-
Liu et al. 2020 [38]	*N* = 22 22–35 years old	Acute sleep-wake cycle shift.	Use of probiotics, prebiotics.	-	-	Use of antibiotics and antifungal 3 months before. No anti-inflammatory or antioxidant drugs.
Murugesan et al. 2020 [39]	*N* = 997 ≥ 18 years old	Smoking habits and coffee and tea consumption	Dietary habits.	Oral hygiene, smoking.	-	-
Lin et al. 2020 [40]	*N* = 116 22–75 years old	Consumption of alcohol and smoking habits	Probiotics.	Cigarette and alcohol consumption.	Marital status.	Use of antibiotics, PPI
Segovia Rodriguez et al. 2022 [8]	*N* = 507 mean age 19,8 ± 1,9	Consumption of alcohol	Food frequency questions.	Type of alcoholic beverage, the amount consumed, the time spent in each episode of drinking, physical activity.	-	-

taxa and Mediterranean Diet adherence were observed in 17 centenarians and 29 nonagenarians [33]. A meta-analysis of gut microbiota studies concludes that microbiota associated with Mediterranean diet was enriched with beneficial bacteria that induce anti-inflammatory status and reduce the risk of developing gut diseases [64]. Individual foods have also been shown to influence digestive microbiota. Green tea liquid consumed daily in a sample of 12 subjects decreased *Bacteroidetes* in feces and pathogenic bacteria in saliva [22]. A diet heavily based on beans and dairy products reduced gut diversity with less beneficial bacteria in a group of 80 healthy women [31]. A long-term protein supplementation in 12 cross-country runners caused a decrease in health-related taxa as *Roseburia*, *Blautia* and *Bifidobacterium longum* [21]. Nevertheless, natural plant extracts with polyphenols, prebiotics, probiotics, and regular physical exercise improved gut microbiota, reducing dysbiosis produced by High Protein Diet (HPD) as has been communicated in a critical review [65].

Consumption of more than five servings per day of ultra-processed food produced in a cohort of 350 subjects a decrease in microbiota diversity [28]. Sesame seed snacks and plant-based smoothies produced a notable increase in endogenous antioxidants in plasma and an improvement in gut microbiota (n = 42) [30].

Pure saccharin supplementation did not alter gut microbial diversity (n = 46), while Vitamin D supplementation increased the overall diversity of gut microbiota in 80 healthy females with vitamin D deficiency [24, 29]. Food additives also affect gut microbiota composition. Some sweeteners and some emulsifiers may alter microbiota. A review of food preservatives indicates that these products increase the growth of proinflammatory bacteria, while anti-inflammatory bacteria decrease. Acidifiers can reduce coliform presence and increase lactic acid bacteria, and colorants can reduce microbiota diversity in vitro. Nevertheless, the long-term impact of food additives on gut microbiota needs to be examined [66].

Table 3 References that study environment-related factors and data collected in questionnaires (11 references)

First author Year of publication	Number of participants Age	Environment-related factors	Questionnaires with questions about:			
			Diet	Habits	Environment	Chemicals
Beghini et al. 2017 [41]	*N* = 1689 17–71 years old	Blastocystis in westernized and non-westernized individuals	-	-	-	-
Chen et al. 2017 [42]	*N* = 8 Ulcerous Colitis 53 ± 9.5 years (UC) and 8 healthy partners 42 ± 9.4 years	Healthy partners cohabiting with Ulcerous Colitis patients.	-	-	-	-
Cabral et al. 2017 [43]	*N* = 24 19–84 years old	Short-term hospitalization.	-	-	-	-
Fontana et al. 2019 [44]	*N* = 31 24–74 years old	Ethnicity and living regions	Diet (mediterranean, vegetarian, hyper or hypocaloric).	Alcohol and smoking habits.	-	-
Johnson 2020 [45]	*N* = 655 > 18 years old	Personality traits.	EPIC-Food Frequency questionnaire.		The 50 item International Personality Item Pool. State-trait anxiety inventory.	-
Shao and Zhu 2020 [46]	*N* = 40 (20 control in remote areas and 20 from mining area) 52 ± 10 (test) and 60 ± 7 (control) mean years old	Log-term exposure to metals in a mining and smelting area.	Dietary status.	Smoking status, drinking status.	Family history, year of residence.	Drug use within three months.
Haran et al. 2021 [47]	*N* = 166 nursing home residents ≥ 65 years old	Living location and hospital exposure. Medication and time spent in the nursing home.	Mini Nutritional Assessment tool.	Clinical Frailty Scale.	-	-
Zuo et al. 2022 [48]	*N* = 47,639 (Low altitude) and 26,335 (High altitude). Age 30–79	High altitude > 1500 m. Low altitude < 1500 m of living place	Diet. Vitamin D intake.	Physical activity. Alcohol, smoking status.	Education level.	-
Sun et al. 2022 [49]	*N* = 77 crew members, 20 to 35 years old Chinese male.	A 135-day sea expedition.	Overeating.	Poor sleep quality, insomnia.	Feeling lonely, depression.	-
Willis et al. 2022 [9]	*N* = 1648 13 to more than 60 years.	Members of the same family: twins, parents, brothers, grandparents, and grandchildren. Classmates.	Diet.	Hygiene, lifestyle.	-	-
Valles-Colomer et al. 2023 [50]	N= more than 9.700 human metagenomic datasets. < 1 to 85 years old	Detection of extensive bacterial strain sharing across individuals with known familiar relationships, from 20 different countries in five continents.	-	-	-	-

Habits

As shown in Table 2, there are different types of habits that influence digestive microbiota, such as physical activity, which has been shown to increase microbial diversity in 39 healthy participants [35]. The quality of sleep also influences the microbiota, although not in all circumstances. The microbiome of 11 subjects is resistant to changes after consecutive days of sleeping restriction [37]. However, an acute sleep-wake cycle shift of 2 to 4 h (22 subjects postpone their regular sleeping time for 2 to 4 h) affects the functional profiles of gut microbes and interactions among them [38]. Alcohol consumption, smoking or a combination of both cause gut microbiota dysbiosis in healthy men. Noteworthy, smoking alone causes more severe dysbiosis than drinking alone (n = 116) [40]. Furthermore, as was shown in a study with 997 subjects, smoking habits also modified oral microbiota diversity, and heavy episodic drinking is associated with a specific stool-type phenotype (Bristol stool scale) [39]. Consumption of heroin, ephedrine, and methamphetamine produced changes in the microbiota. Bacterial diversity was higher in 45 SUD (substance use disorders) subjects, and this increases with the length of substance abuse [36]. Intestinal colonization by oral bacteria has been demonstrated; therefore, oral hygiene becomes

Table 4 References that study chemicals-related factors and data collected in questionnaires (10 references)

First author Year of publication	Number of participants Age	Chemicals-related factors	Questionnaires with questions about:			
			Diet	Habits	Environment	Chemicals
Rogers and Aronoff 2016 [51]	*N* = 155 19 to 88 years old	Non-Steroidal Anti-inflammatory Drugs in community residents	Diet.	-	Demographics	Medical history and all medications in the past 30 days including herbal or vitamin/mineral supplements.
Imhann et al. 2016 [52]	*N* = 1815 26–65 years old	Proton Pump Inhibitors in healthy subjects and patients with gastrointestinal disease.	-	-	-	Current medication use.
Kabbani et al. 2017 [53]	*N* = 49 18–65 years old	*S. boulardii* effects with antibiotic treatment	-	Smoking. Gastrointestinal Symptom Raring Scale.	-	Antibacterial therapy
Cabral et al. 2017 [43]	*N* = 24 12 with antibiotic: 19–68 years 12 control: 45–84 years	Short term hospitalization and Azithromycin.	-	-	-	Antibiotic or immunosuppressive therapy within the six months prior to admission.
Elbere et al. 2018 [54]	*N* = 18 18–33 years old	Metformin in healthy volunteers	2-day food record before and 7-day food record during trial.	-	-	-
Hojo et al. 2018 [55]	*N* = 20 60 ± 12 years old	Proton pump inhibitors.	-	Smoking Alcohol consumption		
Burdet et al. 2019 [56]	*N* = 22 18 years old	Moxifloxacin	-	-	-	-
Cruz-Lebrón et al. 2021 [57]	*N* = 62; 28 non-opioid users (26–62 years old) and 34 methadone treated individuals (32–58 years old)	Methadone and *Akkermansia muciniphila*	-	-	-	Self-reported length of methadone treatment, other medications.
Haran et al. 2021 [47]	*N* = 166 ≥ 65 years old.	Polypharmacy in nursing home older adults.	Mini Nutritional Assessment tool.	Clinical Frailty Scale.	-	-
Anthony et al. 2022 [58]	*N* = 20; Healthy volunteers. 21–60 years old	Antibiotics	Diet.	-	-	Medications.

more important [39, 67]. In fact, the salivary microbiome was affected by denture use [39].

Environment

The environment is also an important factor to study in this context (Table 3). References retrieved have shown different sources of influence on gut microbiota. *Blastocystis*, a component of gut microbiota, has shown in a sample of 1689 subjects a higher prevalence in non-westernized individuals [41]. Differences in gut microbiota composition were found in 31 individuals with the same ethnicity but coming from different Italian regions [44]. Medication and time spent in the nursing home contributed to microbiota dysbiosis more than age and frailty. The microbiota of 166 residents who had lived in the nursing home for more than 1 year were enriched in inflammatory and pathogenic species and reduced in anti-inflammatory and symbiotic species [47].

Nevertheless, it has been described that short-term hospitalization in 24 patients did not impact the richness or structure of the salivary microbiome [43].

Indoor spaces often harbor unique microbial communities as was presented in a review about indoor environments. Indoor air in residences contained a greater number of bacteria than outdoor air. Differences in the microbiome in settled dust in two buildings were greater than differences between seasons. Bacterial communities on surfaces in offices were different between cities, and the microbiota in a home were identifiable by family. Humans are also major sources of bacteria in indoor air [68].

As for the quality of the environment, long-term exposure to metals in residents near a mining and smelting area (n = 20) or in remote areas (n = 20) produced different profiles of gut microbiota. These effects were higher in men because of mining and smelting activity [46]. In this review, it is under discussion whether air pollution due to emissions from factories, chimneys, or livestock also affects gut microbiota since it may be trapped in the food. Some studies showed that gut microbiota metabolized the inorganic arsenic into toxic metabolites. Currently, there are some chemicals and pesticides that are considered microbiota-disrupting chemicals [69]. The living altitude also influences the microbiota composition, which was enriched in *Prevotella* and *Bacteroidetes* in subjects living in high altitudes (> 1500 m, n = 26335) while *Faecalibacterium* and *Blautia* were increased in the low altitude group (< 1500 m, n = 47639) [48].

Microbiota diversity can also change due to traveling. Sun et al., (2022) reported that a 135-day sea expedition produced "seafaring syndrome" in 55 out of 77 crew members with abnormal defecation, frequent insomnia, poor sleeping quality, and overeating. Noteworthy, a significant correlation between the gut microbiome perturbation and this syndrome was found [49].

Cohabitation with other people also influences digestive microbiota. Microbial dysbiosis might be caused in eight healthy partners cohabiting with Ulcerative Colitis patients. A study about the relationship between the composition of the microbiota and human personality in 655 adults has evidenced that anxiety and stress are related to reduced microbiome diversity [42, 45]. People with larger social networks tend to have a more diverse microbiome. Cohabiting time affected strain sharing more than age or genetics, as it has been evidenced in a study with more than 9700 human metagenomes [50]. A high similarity in the oral microbiota composition was found between members of the same family, higher between twins, parents, or brothers, and less or none between grandparents and grandchildren in a sample of 1648 subjects. There was also a similarity between classmates [9].

Chemicals

Chemicals have proven to be important factors that influence digestive microbiota (Table 4). Non-steroidal anti-inflammatory drugs (NSAID) provoke changes in gut microbiota in 155 adults. The bacterial population in the gastrointestinal tract reflects the combination of medications and varies with the type of NSAID that people take [51]. Proton Pump Inhibitors (PPI) have been associated with a decrease in microbiota diversity and an increase of *Lactobacilus*, *Steptococcus*, *Staphylococcus*, and *E.coli* in two studies with 1815 and 20 subjects respectively [52, 55]. Antibiotics are clearly an important factor that changes gut microbiota characteristics. Azithromycin alters the diversity of the salivary microbiome and delays the recovery of the diversity of gut microbiota after a treatment of 20 healthy volunteers [58]. Moxifloxacin reduced bacterial diversity in 22 adults, and it was not recovered until 16 to 21 days [56]. *S. boulardii* treatment can mitigate some antibiotic-induced microbiota changes (dysbiosis) in 49 healthy subjects [53]. Metformine reduces the gut microbiome diversity already after 24 h of administration (n = 18) [54]. Decreased diversity of Shanon and Chao indices was observed in 34 methadone-treated subjects in comparison with 28 non-opioid users [57]. Also, essential oils may be considered as a factor that influences the gut microbiome. In a pilot study with 19 subjects with intestinal dysbiosis, a component of these oils, geraniol, has been shown to increase butyrate-producer bacteria and improve intestinal dysbiosis [70].

Diet, chemicals, environment, and/or habits interaction

Summing up, diet, chemicals, environment, and habits have been described as influencing the digestive microbiota. Diet, sleep quality, medications, supplements, physical activity, and psychological status are considered possible causes of dysbiosis in the above-mentioned studies and in other review studies [59, 71, 72]. These factors are typically considered individually. However, it is also very important to study the interactions between factors on the microbiota quality. Boisseau et al. found that the microbiota of athletes is different from the rest of the population. Diets and treatments could be the origin of these differences. It is also known that exercise improves microbiota in sedentary people, but excessive practice does not improve microbiota and even worsens health. Nevertheless, there are no studies on humans that search for the interaction between diet and physical activity [6]. Also, a positive interaction was found between diet, physical exercise, and HPD. Natural plant extracts with polyphenols, prebiotics, probiotics, and regular physical exercise improved gut microbiota, reducing dysbiosis produced by HPD [65].

Discussion

Of the 73 articles that meet the inclusion criteria, the majority described the influence of diet, habits, chemicals, or environment independently affecting the gut microbiota. All the factors reviewed act together in people´s daily lives. Therefore, the existence of an interaction between them is something that should be considered. In fact, in almost all the studies analyzed, the questionnaires given to the participants contain questions about all or some of these factors.

In the group of 19 papers about diet influence (Table 1) data were collected about habits (12/19), environment (3/19), and chemicals (7/19). The 6 papers that analyze habits influence (Table 2) data were retrieved about diet (5/6), environment (1/6) and chemicals (2/6). In the 7 papers addressing the environmental factors (Table 3) data were recorded about diet (7/7), habits (7/7), and chemicals (1/7). The 8 papers regarding the chemical factors (Table 4) collected data about diet (5/8), habits (2/8) and environment (1/8).

Furthermore, there are some other situations related to these four types of factors that could be considered.

Diet

In addition to checking the consumption of foods whose influence on the microbiome has been evidenced, such as fermented foods [26, 32, 34], it would be interesting to investigate more about whether there is a difference between homemade and commercial fermentation meals since there are already many elaborate fermentation products on the market whose microorganism content is probably different from the homemade ones.

It would be also interesting to investigate the consumption of diets high in proteins or protein supplements and their duration, given that, in some cases, it can negatively influence the digestive microbiota [21]. UP foods should also be checked since high consumption has been seen to affect the diversity of the digestive microbiota [28]. Treatments with vitamin D are becoming more common in the population. Since this also influences the digestive microbiota [24], should be considered.

Furthermore, the influence of some nutritional habits, such as snacking, intermittent fasting, and the number of daily intakes were not investigated in relation to microbiota status. Herein, we suggest including snacking as another factor to be considered. Snacking behavior is a practice that can be done with different types of foods and therefore can contribute to improving diet but also to worsening it [72]. Other factors that may be suitable to include were intermittent fasting and the number of daily intakes. These are habits that may influence the function of the digestive tract at different rhythms and frequencies, and this may affect microbiota.

In relation to habits influence, it would be interesting to consider the influence of the type of sport practiced. Team sports and sports in contact with water must be possible sources of different microbiota. Furthermore, none of these studies considers body and hair hygiene, analyzing both frequency and time spent washing it. This may affect skin microbiota and, consequently, the digestive microbiota too.

In the 7 papers addressing the environmental factors, other circumstances related to the environment could be considered. Living with pets may influence the human microbiota due to the interaction with their own specific microbiota. Domestic dogs share the house with the owners. Its microbiota has a taxonomic similarity with humans, much larger than mice or pig [73, 74]. Living or working with another type of animals may influence the human microbiota, too, due to their different specific microbiota. The microbiome of teleost fish, broiler chicken, and clam (*Agropecten ventricosus*) is different from the microbiome of mammals [10, 75, 76]. Cows are also a source of microorganisms such as *Firmicutes* and *Bacteroidetes* [11]. Not only microorganisms from pets but also parasites may alter gut conditions and contribute to intestinal dysbiosis [77, 78].

There are many professions developed in contact with animals and or with people with different microbiota composition, such as livestock, veterinary, fishing, agriculture, slaughterhouse, medicine, nursing, physiotherapy, nursing homes, public transport driver, police, prisons, schools, nurseries, masseuse, aesthetic centers (manicures, pedicures, tattoo artists, hairdressers), research laboratories with animal or biological material, zoos. We have not found any research about the influence of these kinds of environments on digestive microbiota, but they probably have some role in its variation. Moreover, the type of transportation daily used (individual, public) may also be an important source of variation of the microbiota taken from the environment.

Place of work may also be an influencing factor since different environments can harbor different microbiota: home, office, industry, field, ship, plane, educational center, and transports such as trucks and taxis. Home cleaning is a daily action that can also modify the home microbiome, and coexistence with domestic animals or working with them are also important data to collect in a questionnaire for microbiota research.

Pesticides also modify the microbiota of the animals. It has been described that long-term (lifelong) exposure to a low dose of a glyphosate herbicide (GBH-RUp) in drinking water led to significant changes in the intestinal microbiome composition in mice [79]. Daily contact with pesticides may be important for people working in aquaculture, poultry farming, and livestock farming.

Another possible source of variation in the human microbiota environment may be home cleaning habits. Cleaning of chicken sponges significantly affected its microbiome structure. The authors of this study visualize the role of kitchen sponges as microbial hot spots in building the environment with the capability to collect and spread bacteria [80]. The environment has a high microbial diversity. Sites like homes, offices, industry, and transport have very different physicochemical conditions. The role of the ambient microbiome in the skin and digestive microbiota is evident but not well understood nowadays [81].

Of the 8 papers regarding the chemical factors none of them consider some type of therapy that could also affect the digestive microbiome, such as radiotherapy [82]. There are also other treatments widely used as opioids [83], immune suppressants, corticosteroids, and anovulatory that should be considered.

Further studies are necessary to obtain more data about the interaction between these aforementioned factors to shed light on their implications for the quality of the digestive microbiota. Of all the articles reviewed, only one considers studying the interaction between factors. Boisseau et al. [6] reviewed the relationship between diet and physical activity and concluded that there are no studies on humans that search for the interaction between diet and physical activity. This can be extensive to the other factors. For example, it is possible that different changes in the microbiota of different individuals due to probiotic consumption could be due to differences in some other factor studied in this review related to habits, chemicals, environment, or some other traits of diet.

Limitations of this study: although the results of this scoping review incorporate studies with highly variable sample sizes (of the 50 research studies we have 22 studies about diet with sample sizes from 9 to 359 subjects, 7 studies about habits with sample sizes from 11 to 997 subjects, 11 studies about environment with sample sizes 16 to 1689 subjects (apart a metagenomic study with 9700 data and a study with 73974 data from people from high and low altitude) and 10 studies about chemicals with sample sizes from 18 to 1815 subjects) all the results presented have been statistically significant.

Because of the inclusion of systematic reviews and meta-analyses, the potential duplication of evidence was verified. Of the primary studies included in the reviews and meta-analysis cited in this Scoping Review, only were considered individually within the analysis one reference, about fiber effect [17], in two of the reviews: one about mediterranean diet [64] and one about lifestyle [72].

Conclusions

Summing up, diet, chemicals, environment, and habits have been described as influencing in the digestive microbiota. These factors are typically considered individually without considering the interactions between them. Furthermore, as shown in this review some cases that could influence human digestive microbiota are not yet studied. Not all the factors reviewed here have chronic effects on microbiota. The effect of antibiotic treatment is transient in most cases. But there are some factors that affect every day in our life as environment, social habits, diet habits, and some chemicals.

Further studies are necessary to obtain more data about the influence on the digestive microbiota of these aforementioned factors and about the interaction between them to shed light on their implications for the quality of the digestive microbiota.

Collecting data on all the factors mentioned here in a single investigation is not feasible since it would greatly complicate both data collection and processing. However, it would be a good practice for all or most of these factors to be considered in the anamnesis of patients whose microbiota status and the causes of their possible dysbiosis are to be analyzed.

Acknowledgements
Not applicable.

Authors' contributions
BPLL: Conceptualization, data curation, formal analysis, investigation, methodology, writing original draft and edition. CMR: Data curation, formal analysis, investigation, methodology, writing review and edition, validation. EGF: Formal analysis, methodology, supervision, validation, writing review.

Funding
The financial support for the publication of this paper is made by Universidad Internacional de La Rioja. The role of the sponsor of this review was restricted to providing economic support, and it were not involved in the study process, manuscript preparation, or submission.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 30 January 2025 / Accepted: 18 May 2026
Published online: 23 May 2026

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