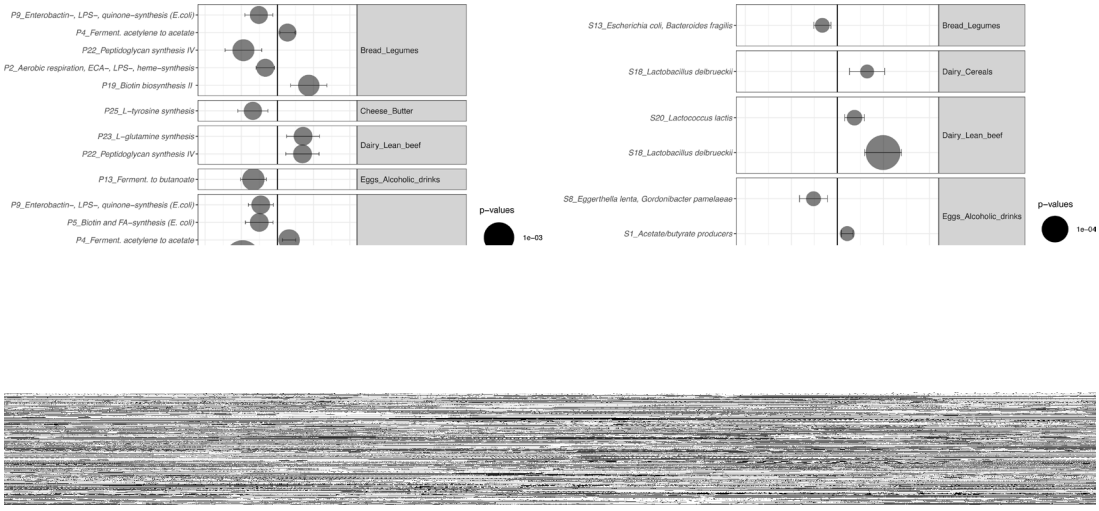

Figure 2 Consistent associations of dietary patterns with clusters of pathways (A) and species (B) in the cross-disease meta-analysis. Forest plot showing consistent results between dietary patterns and microbial clusters in a cross-disease meta-analysis of 1425 individuals spanning four cohorts (FDR_{Meta}<0.05, p-Cochran's-Q>0.05). Dots indicate pooled results of the meta-analysis; black lines indicate CIs. Dot size indicates the significance of the association (FDR-corrected p value). *X-axis* represents coefficients. Unsupervised hierarchical clustering was performed on dietary intake, species and pathway abundance, using squared Euclidean and Bray-Curtis distance. In each cohort, a multivariate linear model of food clusters versus microbial clusters was constructed, adding age, sex, sequencing depth and caloric intake as covariates. An inverse-variance meta-analysis was conducted on results obtained per cohort, followed by multiple testing correction and a Cochran's Q test. AA, amino acid; ECA, enterobacterial common antigen; FA, fatty acid; FDR, false discovery rate; ferment, fermentation; LPS,lipopolysaccharides; spp, species.

Clusters of breads, legumes, fish and nuts show a consistent negative association with several pro-inflammatory pathways

A food cluster comprising breads and legumes, and a cluster of fish and nuts, were negatively associated with groups of pathways involved in the synthesis of growth factors, endotoxins and cell wall components (P2, P9, P22, online supplemental table 4, figure 2A). Moreover, we observed a negative association between the fish and nuts cluster and pathways for the synthesis of L-tyrosine, L-phenylalanine, terpenoids, quinones and fatty acids, a profile predictive of *E. coli* (P25, P24, P20, P5, figure 2A). The bread and legumes cluster was associated with a lower abundance of an *E. coli*, *Bacteroides fragilis* and *Parabacteroides* cluster (S13: FDR=0.015, coef=−0.066, online supplemental table 5, figure 2B). Conversely, the cluster of breads and legumes, and the cluster of fish and nuts, were associated with a higher abundance of pathways involved in the synthesis of acetate and the urea cycle for detoxification of ammonium (P4, figure 2A).

Consumption of nuts, oily fish, fruit, vegetables and cereals is linked to a higher abundance of SCFA-producers

Also individually, these food items were related to several commensals capable of SCFA production (figure 3). For example, *Faecalibacterium prausnitzii* abundance was positively associated with consumption of fruits (FDR=0.005, coef=0.1), red wine (FDR=0.0003, coef=0.441) and oily fish (FDR=0.037, coef=1.695), but showed a negative association with high-sugar foods (soft drinks: FDR=0.028, coef= -0.131; sweets: FDR=0.039, coef= -0.669) (figure 3A). *Roseburia hominis* abundance was positively associated with nuts ($FDR=3.80\times10^{-05}$, coef=0.629), oily fish (FDR=0.0002, coef=1.057), vegetables (FDR=0.007, coef=0.079), legumes (FDR=0.029, coef=0.402), cereals (FDR=0.014, coef=0.485) and plant protein ($FDR=1.17\times10^{-05}$, coef=3.567) (figure 3B). These bacteria are known to have anti-inflammatory effects and provide protection of the intestinal mucosa through fermentation of fibre and pectins to acetate and butyrate.[13] Details of each taxon and pathway, including statistics for each cohort, as well as the meta-analysis, are provided in online supplemental tables 7 and 8.

Red wine is associated with a higher abundance of several acetate and butyrate producers but with a lower *Bifidobacterium* abundance

A cluster of acetate and butyrate producing species (S1) was positively associated with a cluster of different types of wine (FDR=0.002, coef=0.036, figure 2B). Specifically, red wine was linked to higher abundances of *Faecalibacterium prausnitzii*, *Eubacterium hallii*, *Ruminococcus obeum*, *Ruminococcus lactaris*, *Anaerostipes hadrus* and *Alistipes putredinis* (all FDR<0.05, p-Cochran's-Q>0.05, online supplemental table 7). Conversely, red wine intake showed a negative association with *Bifidobacterium* abundance, a SCFA-synthesising commensal (FDR=0.007, coef=−0.933).

Alcohol and sugar intake is associated with a higher abundance of quinone synthesis pathways

Consumption of spirits (pure grain-based alcohol) was associated with a higher abundance of quinone synthesis pathways, that we previously reported to be enriched in IBD (PWY-5840, PWY-5850, PWY-5860, PWY-5862, online supplemental table 8),[22] although after correcting for metformin use, this was not nominally significant anymore (FDR=0.094). Moreover, we observed a negative association of a pyruvate to propanoate fermentation pathway with total alcohol intake in energy-% (P108-PWY, FDR=0.0103, coef=−0.067). In contrast to alcohol and sugar, plant protein intake was negatively associated with quinone synthesis (PWY-5862, PWY-5896, online supplemental table 8, figure 4A).

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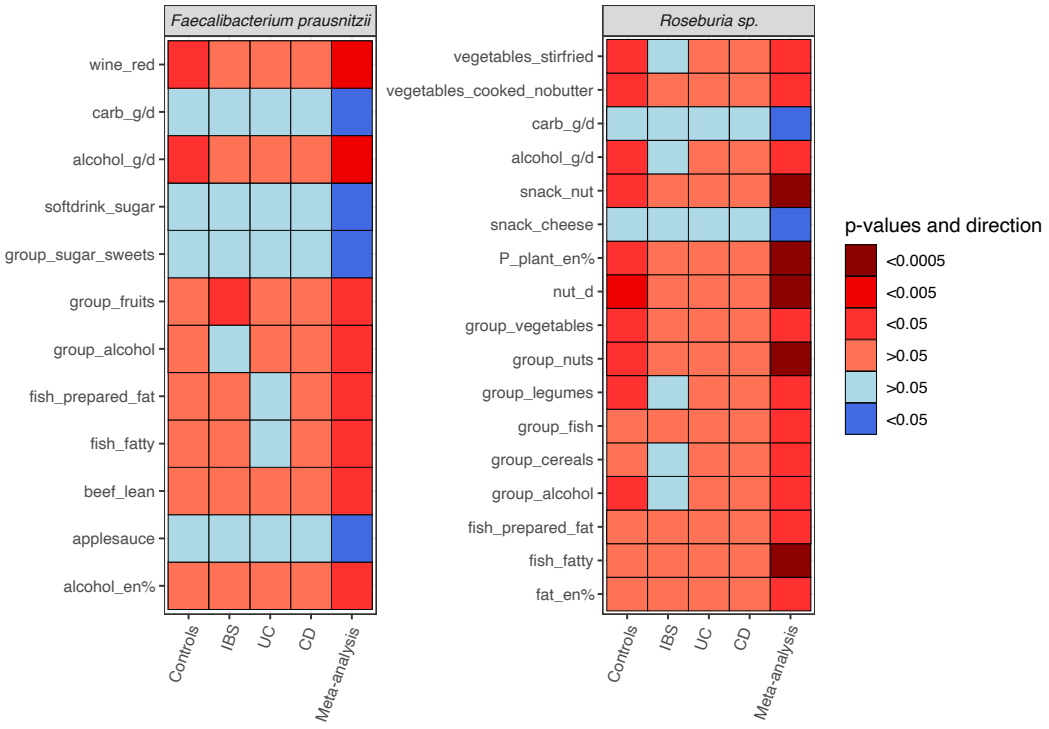

Figure 3 Dietary factors associated with *Faecalibacterium prausnitzii* (A) and *Roseburia* (B) relative abundance in the meta-analysis. Heatmap showing significant and consistent results of the cross-disease meta-analysis between individual foods and relative abundance of (A) *Faecalibacterium prausnitzii* and (B) *Roseburia* sp (FDR<0.05, p-Cochran's-Q>0.05). Dietary intake was assessed by Food Frequency Questionnaires. Energy adjustment was performed by the nutrient density method. For each food item, we constructed a multivariate linear model of the food intake versus taxa and pathways, adding age, sex and sequencing depth as covariates. Association analyses were performed per cohort, followed by an inverse-variance meta-analysis, multiple testing correction and a Cochran's Q test. carb; carbohydrates; CD, Crohn's disease; en-%, energy-per cent; FDR, false discovery rate; g/d, gram per day; IBS, irritable bowel syndrome; nut_d, nuts added to dinner; sp, species; UC, ulcerative colitis. Red, positive association; blue, negative association. Colour density indicates significance of the association (FDR-corrected p value).

Coffee intake is associated with a higher *Oscillibacter* abundance

Coffee consumption was significantly associated with *Oscillibacter* abundance (FDR=8.37×10^{-05}, coef=0.022), heterolactic fermentation and various glycolytic pathways (PWY-6969, FUC-RHAMCAT-PWY, P122-PWY, online supplemental tables 7 and 8).

Lactic acid bacteria and fermentation to butanediol are consistently associated with consumption of fermented dairy

Consumption of fermented dairy like buttermilk and yoghurt showed strong associations with lactic bacteria, as previously shown,[26] as well as with the fermentation of pyruvate to butanediol (P125-PWY) and peptidoglycan synthesis (PWY-6471) (online supplemental tables 7 and 8).

Plant-based food consumption is associated with higher synthesis and conversion of essential nutrients by the gut microbiota

Total intake of plant-derived protein was positively associated with pathways involved in the synthesis of SCFA (P108-PWY, P162-PWY), thiamin (PWY-6897), biotin (PWY-5005), flavin (PWY-6168), vitamin B6 (PWY0-845; PYRIDOXSYN-PWY) and L-ornithine (ARGININE-SYN4-PWY), and the degradation of sugar derivates (PWY-6531, HEXITOLDEGSUPER-PWY) (figure 4A). Participants consuming higher amounts of potatoes showed a higher abundance of starch degrading pathways (PWY-6731: FDR=0.038, coef=0.003).

Plant-derived and animal-derived foods and nutrients show inverse taxonomical associations

Already at the higher taxonomic levels we observed opposite relations of animal-based and plant-based foods and nutrients. While total intake of animal protein and fat was associated with a higher Firmicutes abundance, a negative association was found for plant protein and carbohydrate intake (FDR=1.30×10^{-05}, coef=3.646; FDR=0.042, coef=2.936; FDR=0.003, coef=−6.081; FDR=4.67×10^{-07}, coef=−1.735, respectively). Firmicutes-dominated communities have been observed in omnivores of the general population.[19] While plant protein and bread intake were consistently linked to a higher *Bifidobacterium* abundance (FDR=0.049, coef=4.982; FDR=0.004, coef=0.815, figure 4B), total fat and animal protein intake, cheese and fish were associated with a lower *Bifidobacterium* abundance (animal protein: FDR=1.30×10^{-05}, coef=−4.113), except for *Bifidobacterium dentium*. *Bifidobacterium dentium*, a dominant species of the upper gastrointestinal (GI) tract, showed a positive association with consumption of meat, animal protein and butter (FDR=0.001; FDR=0.048, FDR=1.91×10^{-05}).

Furthermore, we observed higher abundances of Erysipelotrichaceae, *Ruminococcus* species of the Blautia genus and *Streptococcus* species with animal protein, while the opposite direction was found for plant protein intake (online supplemental table 7, figure 4B).

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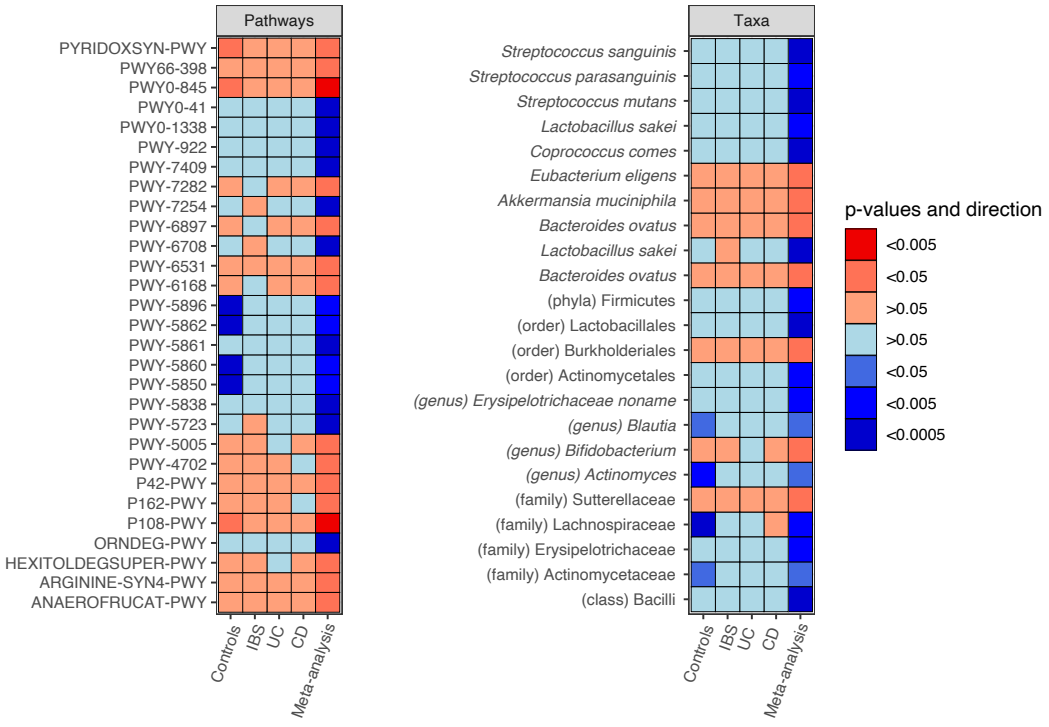

Figure 4 Microbial metabolic pathways (A) and taxa (B) associated with plant protein intake in the meta-analysis. Heatmap showing significant and consistent results of the cross-disease meta-analysis between plant protein intake and the relative abundance of (A) metabolic pathways and (B) taxonomical abundance of the gut microbiome (FDR<0.05, p-Cochran's-Q>0.05). Dietary intake was assessed by Food Frequency Questionnaires. For each food item, we constructed a multivariate linear model of the food intake versus taxa and pathways, adding age, sex and sequencing depth as covariates. Association analyses were performed per cohort, followed by an inverse-variance meta-analysis, multiple testing correction and a Cochran's Q test. CD, Crohn's disease; FDR, false discovery rate; IBS, irritable bowel syndrome; UC, ulcerative colitis. Red, positive association; blue, negative association. Colour density indicates significance of the association (FDR-corrected p value).

Fast food consumption is associated with higher abundances of *Blautia*, *Lachnospiraceae bacteria* and *Clostridium bolteae*

We observed significant positive associations between the consumption of fast food and savoury snacks and the abundance of *Blautia*, *Lachnospiraceae bacteria* and *Clostridium bolteae* in line with previous reports.[30] A fast food cluster consisting of meats, french fries, mayonnaise and soft drinks, showed a positive association with a cluster of *Clostridium bolteae*, *Coprobacillus* and *Lachnospiraceae bacteria* (1_4_56FAA and 2_1_58FAA) (FDR=0.040, coef=0.057, figure 2B). Moreover, the cluster of fast food showed a positive association with a *Ruminococcus gnavus* and *Lachnospiraceae bacterium 1_1_57FAA* cluster in IBS and HCs, which was not significant in CD and UC in the meta-analysis ($FDR_{HC}=4.99\times10^{-5}$, $FDR_{IBS}=3.22\times10^{-5}$, $FDR_{CD}=0.490$, $FDR_{UC}=0.761$, $FDR_{meta}=4.69\times10^{-6}$, $coef_{meta}=0.128$, p-Cochran's-Q=0.02). This finding reflects a difference in the effect size, with *Ruminococcus gnavus* being already enriched in CD and UC as compared with controls.[31] Moreover, fast food meals and savoury snacks were positively associated with *Parabacteroides johnsonii*, *Lactobacillus sakei*, *Lachnospiraceae bacterium 1_1_57FAA* and the *Ruminococcus* genus across all cohorts (online supplemental table 7).

Per cohort analysis also reveals disease-specific results

While the primary purpose of this study was to perform a meta-analysis across different conditions, heterogeneity tests and linear models performed separately per cohort also revealed disease-specific results for species that are enriched in IBD or IBS compared with controls[22 23] (online supplemental tables 4–8). We observed a positive association of the abundance of bile tolerant bacteria such as *Sutterella wadsworthensis*, *Bilophila*, *Bacteroides* and *Alistipes* spp. with the consumption of fast food or ready meals in CD, UC and IBS. This association was not statistically significant in the HC-group in which these taxa have a lower abundance, but showed the same directionality (coefficient) (online supplemental tables 7). In IBS, consumption of buttermilk, bread and cereals was associated with a lower abundance of hydrogen producing *Dorea* spp and with a higher *Bifidobacterium* abundance (all $FDR_{IBS}<0.05$). In UC, *Methanobacter smithii* abundance was positively associated with whole milk, butter, sauces, sweets and alcoholic drinks (all $FDR_{UC}<0.05$). In CD, *Bacteroides vulgatus* abundance was associated with milk, animal protein and fat intake ($FDR_{CD}=0.002$, coef =1.053; $FDR_{CD}=0.009$, coef =4.561, $FDR_{CD}=0.01$, coef =2.078).

Dietary patterns are associated with intestinal inflammatory markers

Lastly, we observed significant positive associations of Fcal with the cluster comprised of fast food ($FDR=4.14\times10^{-4}$, coef=0.242) and a cluster comprised of high-fat meat, potatoes and gravy (FDR=0.003, coef=0.218), that were consistent in the meta-analysis. By contrast, we saw a negative association of Fcal with the cluster comprised of fish and nuts (FDR=0.038, coef=−0.102) and of CgA with a cluster of breads and legumes (FDR=0.005, coef=−2.484) supporting the pro-inflammatory

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and anti-inflammatory role of the microbial features that were associated with these foods (online supplemental tables 6).

DISCUSSION

In this study we have shown how habitual dietary choices can impact the human gut ecosystem and its inflammatory potential by studying the relations between unsupervised dietary patterns, intestinal inflammatory markers and gut microbial composition and function across four cohorts. We identified significant associations that replicate across patients with Crohn's disease, ulcerative colitis, irritable bowel syndrome and the general population, implying a potential for microbiome-targeted dietary strategies to alleviate and prevent intestinal inflammation.

We showed that dietary patterns comprising legumes, breads, fish and nuts are associated with a lower abundance of clusters of opportunistic bacteria, pathways for the synthesis of endotoxins and inflammatory markers in stool. Higher proportions of these bacteria and pathways have been implicated in IBD and colorectal cancer combined with inflammation through their metabolites such as LPS.[22 32] Conversely, we observed higher abundances of commensals such as *Roseburia, Faecalibacterium* and *Eubacterium* spp with the consumption of nuts, oily fish, fruits, vegetables, cereals and red wine across all cohorts. These bacteria are known for their anti-inflammatory effects in the intestine through fermentation of fibre to SCFAs.[13] A dietary pattern that is traditionally high in these foods is the Mediterranean diet which has been linked to a lower IBD-risk in retrospective studies.[33]

Accumulating literature demonstrates an anti-inflammatory role of polyphenol-rich foods such as coffee, tea, red wine and fruit. We observed a higher *Oscillibacter* abundance and a lower abundance of pro-inflammatory pathways with coffee consumption. Increases in *Oscillibacter* have been shown on administration of tea-phenols or berry-phenols at the expense of potentially pathogenic species in mice.[34] Moreover, we saw positive associations of red wine intake with several acetate and butyrate producers. Red wine polyphenols have been shown to increase *Faecalibacterium prausnitzii* and *Roseburia hominis* while reducing *E. coli* and *Enterobacter cloacae* abundance, C-reactive protein (CRP) and cholesterol levels in healthy and obese individuals.[35 36] In contrast, total alcohol intake and spirits were associated with pro-inflammatory pathways in our study. Alcohol-induced reduction of Bifidobacteria and higher endotoxin production has been suggested to increase intestinal inflammation in patients with GI cancers and liver disease.[37] Together, these findings support the earlier finding that moderate red wine intake is linked to higher microbial diversity, a parameter of gut health,[26 38] while also showing that alcohol is a limiting factor, especially in the context of intestinal inflammation. Red wine polyphenol extracts may have a role to potentiate SCFA-producers and to promote beneficial actions of probiotics through a host-microbe mutualism.[35 36]

We found a consistent association of plant protein intake with several fermentation pathways and the synthesis of anti-inflammatory nutrients and L-ornithine amino acid. Concordantly, a recent study in vegetarians showed an enrichment of pathways related to carbohydrate, amino acid, cofactor and vitamin metabolism.[39] Animal models have demonstrated that nutrients produced by microbial metabolism of plant polysaccharides downregulate the expression of pro-inflammatory cytokines,[40] suggesting an anti-inflammatory potential of plant-based diets through gut microbial metabolism.

We consistently observed inverse taxonomical associations of animal and plant foods across all cohorts. While animal protein intake was associated with lower *Bifidobacterium* abundance, the opposite direction was found for plant protein. A lower *Bifidobacterium* abundance has been observed in omnivores compared with vegans.[15 30] Here, we replicate this link also in patients with IBD and IBS, in whom Bifidobacteria are generally depleted. An intervention with glycated pea protein in mice has been shown to increase *Bifidobacterium* and *Lactobacillus* abundance at the expense of *Bacteroides fragilis* and *Clostridium perfringens*,[41] suggesting a specific role of plant protein besides other plant-derived nutrients to modulate the gut microbiome.

Animal protein dominated diets also tend to include higher amounts of saturated fats, which are impactful on the microbiome themselves.[5 42] We here observed a positive association of the total fat intake and meat consumption with species that are dominant in the upper GI tract and oral cavity, while the opposite direction was found for plant-derived foods. Higher colonisation of these bacteria in the intestine has been reported in IBD, liver cirrhosis, colon cancer[32 43] as well as several IMIDs such as arthritis and multiple sclerosis[2] and has been linked to high-fat diets.[30] Microbial carbohydrate fermentation normally creates a mildly acidic environment that inhibits overgrowth of these bacteria. A switch from a normal fat/carbohydrate ratio to a high-fat diet can impact the gut microbial composition and colonic pH. While there are many disease-related factors that influence the intestinal pH, our findings tentatively suggest that a high-fat omnivore diet affects the intestinal pH, further favouring colonisation of these bacteria in the intestine, as opposed to plant-dominated diets.

By contrast, fish showed consistent positive associations with *Roseburia hominis* and *Faecalibacterium prausnitzii* in our study. Fish is high in omega-3 polyunsaturated fatty acids (n-3 PUFA). Administration of n-3 PUFA in animal models has induced a decrease in pathobionts and pro-inflammatory metabolites and increased anti-inflammatory symbionts.[5] Conversely, high-fat diets rich in n-6 PUFAs have depleted SCFA-producers and increased CRP levels in humans.[42] These findings imply a role for optimised n-6/n-3 fatty acid ratios for gut microbiome targeted diets.

Finally, we have shown positive associations of fast food, processed meat, soft drinks and sugar with Fcal and the abundance of *Clostridium bolteae, Ruminococcus obeum, Ruminococcus gnavus* and *Blautia hydrogenotrophica*, Firmicutes that increase energy harvesting from the diet and are implicated in obesity and IMIDs.[2 44] Functional studies consistently demonstrated an impact of food processing on the gut microbiome, leading to gut permeability and intestinal inflammation through an increase in mucolytic bacteria like *Ruminococcus gnavus, Akkermansia muciniphila* and Proteobacteria, production of endotoxins and induction of TH17 cells.[5–11] Especially in the combination with a low fibre intake, these bacteria turn to the mucus layer, leading to an erosion of the gut barrier.[5] A high consumption of sugar and soft drinks combined with a low vegetable intake has already been linked to IBD.[7] We observed higher Fcal levels with the consumption of a high-sugar and high-fat diet, while the opposite was seen for plant-based foods. While this observation may not have a clinical benefit yet in the setting of IBS or HC with pre-clinical levels of Fcal, it implies a role for dietary strategies already at the public health level. Our findings suggest the gut microbiome as a link between diet and disease risk.

Our study has several limitations related to its cross-sectional nature and the complex interplay between diet and the gut

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Table 2 Overview of diet-gut microbiome associations consistent across cohorts in this study and their pro-inflammatory or anti-inflammatory role

Findings in this study			Supporting studies	
Taxa	Diet (↑)	Diet (↓)	Pro-inflammatory or anti-inflammatory role	References
Bifidobacterium spp	Plant protein, carbohydrates, bread, fruit	Protein, animal protein, fat, fish, savoury snacks, red wine, butter	SCFA synthesis (acetate); linked to dense mucosal barrier, reduced LPS levels and raised efficacy of cancer immunotherapy; depleted in IBD, IBS, obesity	13 15 22 35 41 51 52
Lactococcus lactis, Lactobacillus delbrueckii	Buttermilk, cluster of fermented dairy	No negative associations	SCFA and thiamine synthesis, anti-cancer activities	13 26 53
Eubacterium spp	Plant protein, cereals, fruit, red wine	Carbohydrates, non-alcoholic drinks, soft drinks	SCFA (butyrate) and phenolic acid synthesis; depleted in IBD	13 22 35
Roseburia spp	Fish, nuts, vegetables, plant protein, cereals, tea, legumes, vegetables, fruit	Total kcal, sugar, savoury snacks, meat, gravy, sweetened milk drinks	SCFA synthesis (butyrate) and anti-inflammatory effects; depleted in IBD	13 19 22 54
Faecalibacterium prausnitzii	Red wine, legumes, fruit, lean beef, fish, nuts, fat	Carbohydrates soft drinks, sweets, syrup	SCFA synthesis (butyrate) and anti-inflammatory effects; depleted in IBD	13 19 22 35 55
(phylum) Firmicutes and clusters of *Ruminococcus gnavus, Lachnospiraceae bacteria, Clostridium boltea*, *Coprobacillus*	Protein, animal protein, fat intake, cheese cluster of fast food and soft drinks	Plant protein, carbohydrates, bread	Enriched in obesity, increased energy harvesting capacity	19 44
Bacteroides fragilis	Cheese, custard	Cluster of breads and legumes	Opportunistic pathogen with increased abundance in IBD and colorectal cancer, raised LPS levels	22 32 41
Escherichia coli	No positive associations in the meta-analysis	Cluster of breads and legumes	Increased abundance in IBD and colorectal cancer, raised LPS levels	18 22 32
(family) Erysipelotrichaceae	Animal protein, soft drinks, syrup	Plant protein	Pro-inflammatory; associated with colorectal cancer, hypercholesterolaemia, and obesity.	56 57
Streptococcus spp	Protein, animal protein, fat, cheese, yoghurt drink, custard	Plant protein, nuts	Increased in IBD, alcoholism, liver cirrhosis, primary sclerosing cholangitis, colon cancer and IMIDs such as MS, ankylosing spondylitis and arthritis	2 22 32 43 58
Blautia spp	Animal protein, alcohol, meat, cheese, soft drinks, fast food pattern (*R. gnavus* cluster)	Plant protein, carbohydrates, fruit, bread	Increased in IBD, MS, ankylosing spondylitis and arthritis	2 22 42

Diet (↑) positive relationship; Diet (↓) negative relationship.
IMIDs, immune-mediated inflammatory diseases; kcal, caloric intake; LPS, lipopolysaccharides; MS, multiple sclerosis; ref, reference; SCFA, short-chain fatty acid; spp, species.

microbiome. First, the cross-sectional nature of this study cannot identify causality in the observed associations. Second, while the use of whole shot-gun metagenomic sequencing allowed us to explore predicted metabolic profiles, further studies using faecal metabolomics and in vitro studies will be needed to confirm an increase or decrease in certain microbial functions and metabolites. Third, the time that is needed to elicit a lasting response of gut microbiota to dietary changes has not been well defined. Studies suggest that long-term habitual diet has a larger impact on a 'core' gut microbiome composition and function[17–19] while short-term interventions have temporary effects.[15 16 45] Longitudinal studies using high-resolution multi-omics data and dietary interventions with long-term follow-up will help us determine the time-dynamics of the gut microbiome in future, considering day-to-day variations and intestinal transit.[29]

CONCLUSIONS

Despite these limitations, we were able to derive dietary patterns that consistently correlate with groups of bacteria and functions known to infer mucosal protection and anti-inflammatory effects. We believe that the diet-microbiota associations that we described in this manuscript are robust: the results are consistent in the different cohorts and also remained significant after adjusting for additional cohort-specific factors such as medication usage. The findings suggest shared responses of the gut microbiota to the diet across patients with CD, UC, IBS and the general population that may be relevant to other disease contexts in which inflammation, gut microbial changes and nutrition are a common thread.[3 46] A decrease in the here identified bacteria and their anti-inflammatory functions has already been identified in numerous inflammatory diseases, including cancer, atherosclerosis, obesity, non-alcoholic steatohepatitis, liver cirrhosis and IBD.[3 4 22 32] Long-term diets enriched in legumes, vegetables, fruits and nuts; a higher intake of plant over animal foods with a preference for low-fat fermented dairy and fish; while avoiding strong alcoholic drinks, processed high-fat meat and soft drinks, have a potential to prevent intestinal inflammatory processes via the gut microbiome (table 2). Poor adherence to these principles has already been linked to an increased risk of IBD.[33 47 48] We provide support for the idea that the diet can be a significant complementary therapeutic strategy through the modulation of the gut microbiome.[3 49] For example, pre-clinical evidence shows that SCFA-producers such as *Bifidobacterium* species aid in invigorating a tumour specific T-cell response, raising the efficacy of cancer immunotherapy.[50] It can be speculated that consumption of plant-based diets increases the abundance of these gut microbiota, further augmenting treatment responses.

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Contributors RKW designed the study. LAB and AVV performed analyses. LAB wrote the manuscript. LAB, AVV, FI and RKW gathered during the study. RG and AK provided statistical advice. AVV, FI, VC, VP, CW, AK, MJECK, JF, GD, AZ and RKW were involved in data collection and preparation and critically reviewed the manuscript.

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Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval The study was approved by the Institutional Review Board (IRB) of the University Medical Center Groningen (1000IBD 2008.338; LifeLinesDEEP M12.113965).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All relevant data supporting the key findings of this study are available within the article and the supplementary files. Raw metagenomic sequencing reads and extended phenotypic data are available from the European Genome-phenome Archive data repository: 1000 IBD cohort [EGAD00001004194] and LifeLines Deep cohort [EGAD00001001991]. Codes used for generating the microbial profiles are publicly available at:[https://github.com/WeersmaLabIBD/Microbiome/blob/master/Protocol_metagenomic_pipeline.md]. All statistical analysis scripts are written in R and can be found here: https://github.com/WeersmaLabIBD/Microbiome/blob/master/Diet_Microbiome.md.

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