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Tu Junlan, Cai Xuehong, Wang Yifan, Ye Xiangyu, Yu Meijie, Yang Sheng, Yu Rongbin, Huang Peng

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Junlan Tu[1,△], Xuehong Cai[1,△], Yifan Wang[2,△], Xiangyu Ye[1], Meijie Yu[1], Sheng Yang[3], Rongbin Yu[1,✉], Peng Huang[1,✉]

[1]Department of Epidemiology, Center for Global Health, School of Public Health, National Vaccine Innovation Platform, Nanjing Medical University, Nanjing, Jiangsu 211166, China;
[2]Department of Infectious Disease, Jurong Hospital Affiliated to Jiangsu University, Jurong, Jiangsu 212400, China;
[3]Department of Biostatistics, Center for Global Health, School of Public Health, National Vaccine Innovation Platform, Nanjing Medical University, Nanjing, Jiangsu 211166, China.

Abstract

The current study used multivariable logistic regression analysis to investigate associations between the intake frequencies of 13 food groups (or four diet groups) and infectious diseases. The analysis included 487 849 participants from the UK Biobank, with 75 209 participants diagnosed with infectious diseases. Participants reporting the highest intake frequency of processed meat (odds ratio [OR] = 1.096 4, 95% confidence interval [CI]: 1.062 2–1.131 8) and red meat (OR = 1.089 5, 95% CI: 1.056 3–1.123 9) had a higher risk of infectious diseases, compared with those with the lowest intake frequency. Consuming fish 2.0–2.9 times (OR = 0.822 1, 95% CI: 0.795 5–0.849 6), cheese ≥ 5.0 times (OR = 0.882 2, 95% CI: 0.855 9–0.909 2), fruit 3.0–3.9 servings (OR = 0.886 7, 95% CI: 0.866 1–0.907 8), and vegetables 2.0–2.9 servings (OR = 0.937 2, 95% CI: 0.918 9–0.955 9) per week were associated with a lower risk of infection. Low meat-eaters (OR = 0.940 4, 95% CI: 0.924 3–0.956 7), fish-eaters (OR = 0.839 1, 95% CI: 0.788 7–0.891 9), and vegetarians (OR = 0.915 4, 95% CI: 0.856 1–0.977 8) had a lower risk of infectious diseases, compared with regular meat-eaters. The mediation analysis revealed that glycosylated hemoglobin, white blood cell count, and body mass index served as the mediators in the associations between diet and infectious diseases. The current study indicates that the intake frequency of food groups is a risk factor for infectious diseases, and fish-eaters have a lower risk of infection.

Keywords: infectious diseases, diet, food groups, UK Biobank, mediation analysis

Introduction

Infectious diseases are a global threat that contributes to excess morbidity and mortality annually, with a persistent potential for unpredictable pandemics, leading to a severe burden of diseases[1–2]. Particularly, the emerging infectious coronavirus disease 2019 (COVID-19), which has been rampant over the past three years, served as a lesson to countries worldwide and forced us to refocus our attention on infectious diseases[3]. Therefore, it is of public health importance to investigate the pathways or factors that may prevent infectious diseases.

Infectious diseases are generally caused by

△These authors contributed equally to this work.

✉Corresponding authors: Rongbin Yu and Peng Huang, Department of Epidemiology, Center for Global Health, School of Public Health, Nanjing Medical University, Nanjing, Jiangsu 211166, China. E-mails: rongbinyu@njmu.edu.cn (Yu) and huangpeng@njmu.edu.cn (Huang).

microorganisms, yet exposure to the pathogens is a necessary but insufficient condition for infectious diseases[4]. The pandemic of infectious diseases is influenced by natural and social factors, with the social factors being notably more significant[5–6]. Diet, as a crucial lifestyle factor, plays a role in the occurrence and epidemic of diseases, and a high number of disability-adjusted life years have been reported to be attributable to dietary risk factors[7]. To date, research on the associations between diet and diseases has predominantly focused on non-communicable diseases, such as cancers, cardio-vascular diseases, metabolic diseases, and obesity[8–11]. Numerous studies have demonstrated that diet is a crucial risk factor in non-communicable diseases. However, studies investigating the associations between diet and infectious diseases remain insufficient, and previous studies have only focused on a single infection[12–13]. Therefore, it is necessary and essential to conduct a prospective study with a large sample size to investigate the association between diet and the incidence of various infectious diseases.

Studies have demonstrated a strong association between diet and body metabolism. The types and quantities of food consumed regularly may significantly affect the metabolism, such as blood lipids and glycemic indices, including triglycerides (TG) and glycosylated hemoglobin (HbA1c)[14–15]. While studies have illuminated the critical role of body metabolism in various diseases, its involvement in the associations between diet and infectious diseases remains uninvestigated[16–17]. Furthermore, a balanced diet profoundly influences nutritional status of the body, and maintaining optimal nutrition may prevent numerous diseases and promote overall health[18–19]. Therefore, identifying indicators, such as body mass index (BMI), body fat percentage (BFP), and waist-to-hip ratio (WHR), that reflect the body's nutritional status, and investigating their roles in the associations between diet and infectious diseases may facilitate the prevention of infectious diseases. In addition, the immune level may also affect susceptibility to infectious diseases and their outcomes, so immune-related indicators, such as white blood cell count (WBC), should also be taken into consideration[20].

The United Kingdom (UK) Biobank is a large-scale research resource that contains lifestyle and health information from over 500 000 UK participants[21]. The UK Biobank recruitment center collected dietary information from participants, including the intake frequencies of main foods or food groups using the UK Biobank short food-frequency touchscreen questionnaire. Additionally, disease information was obtained through hospital diagnostic records. These initial conditions provide a unique opportunity to investigate hypotheses about diet and infectious diseases in the UK.

Here, we used data from the UK Biobank to evaluate the associations between infectious diseases (common subgroups: respiratory infectious diseases, digestive infectious diseases, and blood or sexually transmitted infectious diseases) and the consumption of various food groups. Subsequently, we conducted a series of subgroup analyses to assess these associations across sex and ethnic subpopulations. In addition, we assessed the associations of four common diets with infectious diseases and investigated the mediation effects of potential intermediate variables.

Subjects and methods

Study population

The UK Biobank is a large-scale research resource that contains half a million UK participants aged 40–70 years, recruited from 22 assessment centers between 2006 and 2010[22]. The UK Biobank has the ethical approval from the North West Multi-center Research Ethics Committee. Informed consent was obtained from each subject or their legal guardians. We used data collected up to March 26, 2021. There were 502 462 participants in this time period, and we excluded the individuals with a mismatch between genetic and social sex, as well as those who were redacted, thus lacking a corresponding ID in the UK Biobank, following the established protocols[5,23]. As a result, 487 849 participants in the UK Biobank were retained for subsequent analyses (***Fig. 1***).

Assessment of dietary intakes

The participants included in the UK Biobank were invited to complete a touchscreen questionnaire at the local assessment centers. This touchscreen questionnaire included 29 questions about diet, most of which were about the intake frequencies of main foods or food groups, including processed meat, poultry, beef, mutton, pork, oily fish, non-oily fish, cooked vegetables, raw vegetables, fresh fruit, dried fruit, cheese, bread, cereals, tea, water, and alcohol. This questionnaire required the participants to report their average intake of each type of food over the last year. In the current study, we combined two or three foods of the same kind into one food group and then grouped participants into four categories according to the distribution of data following the reported
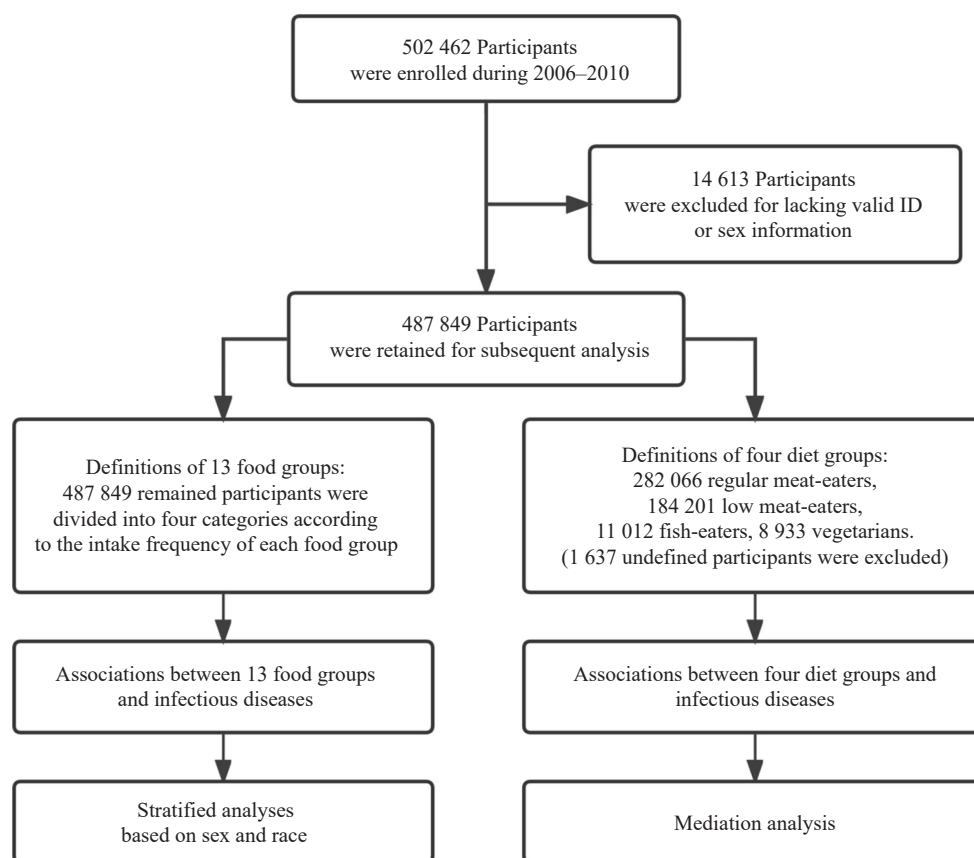
Fig. 1 **The flow diagram of participant selection in the UK Biobank.**

study[24]. The cut-offs for the categories were chosen to ensure a reasonable and similar number of the participants in each group. For example, by combining beef, mutton, and pork into the "Red meat" food group, we then divided the participants into four categories: "< 1 time per week", "1.0–1.9 times per week", "2.0–2.9 times per week", and "≥ 3.0 times per week". In addition, oily fish and non-oily fish were combined into the "Fish" group; cooked vegetables and raw vegetables were combined into the "Vegetables" group; fresh fruit and dried fruit were combined into the "Fruit" group; processed meat and red meat were combined into the "Red and processed meat" group. We divided main foods or food groups into animal (including processed meat, poultry, red meat, red and processed meat, fish, and cheese) and other food groups (fruits, vegetables, bread, cereals, tea, water, and alcohol). The calculation methods and more details of the food groups are shown in *Supplementary Table 1* (available online).

Definition of outcome

In the current study, infectious diseases diagnosed after recruitment (the dietary survey) were defined according to diagnosis records in the UK Biobank, coded by the International Classification of Diseases, version 10 (ICD10) and version 9 (ICD9) (*Supplementary Table 2* [available online]). Referring to the coding terms, we identified a total of 75 209 (15.42%) cases of infectious disease. We further classified these into three subtypes of infectious diseases to investigate the association between dietary factors and common types of infectious diseases: (1) respiratory infectious diseases with 2 663 (3.54%) cases; (2) digestive infectious diseases (excluding food poisoning) with 18 678 (24.83%) cases; and (3) blood or sexually transmitted infectious diseases with 1 051 (1.40%) cases.

Definition of four diet groups

In the current study, we additionally categorized the participants into four common diet groups according to their reported consumption of meat and fish following the literature[25]: (1) regular meat-eaters (those who consumed meat including processed meat, red meat, and poultry more than five times a week); (2) low meat-eaters (those who consumed meat less than five times per week); (3) fish-eaters (those who consumed fish but never meat); and (4) vegetarians (those who never consumed any meat or fish). It should be noted that both regular meat-eaters and low meat-eaters may also have a habit of eating fish

(consuming fish more than zero times a week).

Statistical analysis

Continuous variables were presented as mean ± standard deviation or median (quartile) depending on the data distribution, and categorical variables were presented as counts (percentage). The baseline characteristics of the two groups were compared using the unpaired, 2-tailed Student's *t*-test or Wilcoxon test for continuous variables, and the χ^2 test was used for categorical variables.

Multivariable logistic regression was used to estimate associations between infectious diseases and reported intake of food or food groups. We treated sex, age, ethnicity, assessment center, activity, Townsend deprivation index (TDI), and education as covariates, and reported adjusted odds ratios (ORs) with 95% confidence intervals (CIs). Definitions of these covariates are listed in *Supplementary Table 3* (available online). Additionally, we treated the dietary exposures as the continuous trend variables in the multivariable logistic models to assess the linear trend.

We conducted a series of sensitivity analyses for infectious diseases. First, we excluded 55 318 participants who reported that they had made a major change to their diet in the past five years because of illness or preferred not to answer the question ("Have you made any major changes to your diet in the last five years?"), and re-analyzed the associations between infectious disease incidence and the consumption of food groups in the remaining 432 531 participants (adjusting for sex, age, ethnicity, assessment center, activity, TDI, and education). Second, we performed a stratified analysis by sex. To test the heterogeneity of the main associations by sex, we compared models with and without an interaction term for the main exposure (as a continuous trend variable) and sex, and evaluated the significance using the likelihood ratio test. Third, given that ethnicity may affect the associations, we assessed the associations between infectious diseases and the intake of food groups in four ethnic subgroups (*i.e.*, White, Asian or Asian British, Black or Black British, and Mixed or others).

We also performed a mediation analysis to estimate the proportion mediated by metabolic-related biomarkers (*e.g.*, TG, blood glucose, and HbA1c), immune-related indicator (WBC), nutritional status-related indicators (BMI, BFP, and WHR), and body fat distribution-related indicators (whole body fat mass, arm fat mass, leg fat mass, and trunk fat mass) for the associations between diet groups and infectious diseases. In conducting the mediation analysis, both

linear regression and logistic regression were used, and all regression analyses were adjusted for sex, age, ethnicity, assessment center, activity, TDI, and education.

All analyses were performed using R (version 4.1.2, R Foundation for Statistical Computing). *P* < 0.05 was considered statistically significant.

Results

Population characteristics

The current study included 487 849 participants from the UK Biobank. *Table 1* shows the baseline population characteristics. The mean age of these participants was 56.54 (± 8.09) years, with 223 312 (45.77%) men and 264 537 (54.23%) women.

There were 75 209 (15.42%) cases diagnosed with infectious diseases between 2006 and 2010, among whom 2 663 (3.54%) suffered from respiratory infectious diseases, 18 678 (24.83%) suffered from digestive infectious diseases, and 1 051 (1.40%) suffered from blood or sexually transmitted infectious diseases. Furthermore, there were additional infectious diseases that fell outside these three subgroups, such as bacterial infections. For infectious diseases, significant differences were observed in ethnicity, sex, age, TDI, BMI, income, education, working status, smoking status, and drinking status (all *P* < 0.000 1) between infected and non-infected individuals.

The participants' characteristics with the lowest and highest consumption of the 13 main food groups are shown in *Supplementary Table 4* (available online). The participants who consumed the highest amounts of red and processed meat tended to be current smokers and drinkers, and had a higher BMI than those who consumed the lowest amounts. However, those with the lowest intake of fruits and vegetables were more likely to be current smokers.

Associations between food groups and infectious diseases

The multivariable associations of the intake of animal and other foods with infectious diseases, adjusted for age, sex, ethnicity, assessment center, activity, TDI, and education, are shown in *Fig. 2* and *Fig. 3*, respectively. For animal foods, the participants with the highest reported intake frequency of processed meat (OR = 1.096 4, 95% CI: 1.062 2–1.131 8), poultry (OR = 1.034 0, 95% CI: 0.994 0–1.075 9), red meat (OR = 1.089 5, 95% CI: 1.056 3–1.123 9), and red and processed meat (OR = 1.073 8, 95% CI: 1.046 7–1.101 6) had a higher risk of infectious

Table 1 **Population characteristics of participants from the UK Biobank**

Variables	Description		All (*N*=487 849)	*P*
	Non-infection (*n*=412 640)	Infection (*n*=75 209)		
Age [years, *n* (%)]				<0.000 1
<45	45 274 (10.97)	4 899 (6.51)	50 173 (10.28)	
45–49	57 503 (13.94)	6 528 (8.68)	64 031 (13.13)	
50–54	65 006 (15.75)	9 006 (11.97)	74 012 (15.17)	
55–59	75 759 (18.36)	12 346 (16.42)	88 105 (18.06)	
60–64	97 720 (23.68)	20 473 (27.22)	118 193 (24.23)	
≥65	71 378 (17.30)	21 957 (29.20)	93 335 (19.13)	
Male [*n* (%)]	186 190 (45.12)	37 122 (49.36)	223 312 (45.77)	<0.000 1
White ethnicity or race [*n* (%)]	389 308 (94.35)	70 433 (93.65)	459 741 (94.24)	<0.000 1
TDI [median (quartile)]	−2.22 (−3.67, 0.35)	−1.66 (−3.39, 1.50)	−2.15 (−3.65, 0.53)	<0.000 1
BMI [kg/m², *n* (%)]				<0.000 1
<18.5	9 637 (2.34)	1 731 (2.32)	11 368 (2.34)	
18.5≤BMI<25	130 642 (31.76)	18 731 (25.14)	149 373 (30.74)	
25≤BMI<30	176 513 (42.91)	30 241 (40.59)	206 754 (42.55)	
≥30	94 571 (22.99)	23 808 (31.95)	118 379 (24.37)	
Income [£, *n* (%)]				<0.000 1
<18 000	20 674 (5.83)	1 848 (2.99)	22 522 (5.41)	
18 000–30 999	76 325 (21.53)	8 310 (13.44)	84 635 (20.33)	
31 000–51 999	94 991 (26.80)	13 524 (21.88)	108 515 (26.07)	
52 000–100 000	88 934 (25.09)	16 982 (27.47)	105 916 (25.44)	
>100 000	73 561 (20.75)	21 159 (34.22)	94 720 (22.75)	
Education [*n* (%)]				<0.000 1
Less than high school	63 501 (15.57)	19 724 (26.70)	83 225 (17.28)	
High school or equivalent	157 572 (38.65)	28 889 (39.11)	186 461 (38.72)	
College or above	186 640 (45.78)	25 258 (34.19)	211 898 (44.00)	
Employment [*n* (%)]	379 689 (92.47)	65 507 (87.64)	445 196 (91.72)	<0.000 1
Adequate exercise [*n* (%)]	96 251 (20.20)	16 197 (3.40)	112 448 (23.60)	<0.000 1
Smoking status [*n* (%)]				<0.000 1
Never	231 346 (56.32)	34 365 (46.07)	265 711 (54.75)	
Previous	139 230 (33.90)	29 182 (39.13)	168 412 (34.70)	
Current	40 185 (9.78)	11 038 (14.80)	51 223 (10.55)	
Drinking status [*n* (%)]				<0.000 1
Never	17 168 (4.17)	4 378 (5.84)	21 546 (4.43)	
Previous	12 963 (3.15)	4 537 (6.06)	17 500 (3.59)	
Current	381 591 (92.68)	65 981 (88.10)	447 572 (91.98)	

The categorical variables are presented as counts (percentage) and compared with the χ^2 test between the two groups. The sum of the number of participants in all categories is not equal to the total number because of the missing data. Abbreviation: TDI, Townsend deprivation index.

diseases than those with the lowest intake frequency. Meanwhile, moderate consumption of red and processed meat (2.0–2.9 times per week; OR = 0.948 9, 95% CI: 0.923 9–0.974 7) reduced the incidence of infectious diseases, compared with those with the lowest consumption. For fish, participants with a higher reported intake frequency had a lower risk of infectious diseases, with all the three ORs less than
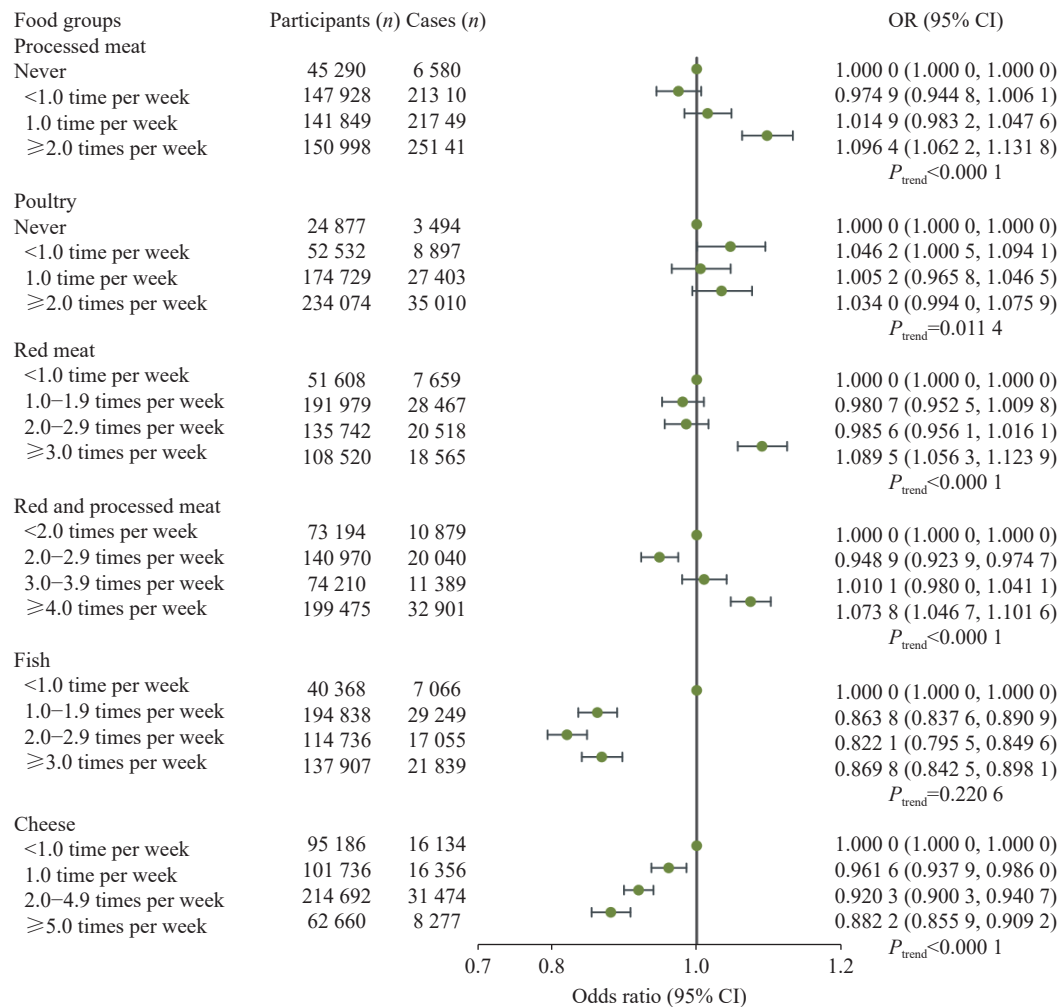
Food groups	Participants (*n*)	Cases (*n*)	OR (95% CI)
Processed meat			
Never	45 290	6 580	1.000 0 (1.000 0, 1.000 0)
<1.0 time per week	147 928	213 10	0.974 9 (0.944 8, 1.006 1)
1.0 time per week	141 849	217 49	1.014 9 (0.983 2, 1.047 6)
≥2.0 times per week	150 998	251 41	1.096 4 (1.062 2, 1.131 8)
			$P_{trend} < 0.000\,1$
Poultry			
Never	24 877	3 494	1.000 0 (1.000 0, 1.000 0)
<1.0 time per week	52 532	8 897	1.046 2 (1.000 5, 1.094 1)
1.0 time per week	174 729	27 403	1.005 2 (0.965 8, 1.046 5)
≥2.0 times per week	234 074	35 010	1.034 0 (0.994 0, 1.075 9)
			$P_{trend} = 0.011\,4$
Red meat			
<1.0 time per week	51 608	7 659	1.000 0 (1.000 0, 1.000 0)
1.0−1.9 times per week	191 979	28 467	0.980 7 (0.952 5, 1.009 8)
2.0−2.9 times per week	135 742	20 518	0.985 6 (0.956 1, 1.016 1)
≥3.0 times per week	108 520	18 565	1.089 5 (1.056 3, 1.123 9)
			$P_{trend} < 0.000\,1$
Red and processed meat			
<2.0 times per week	73 194	10 879	1.000 0 (1.000 0, 1.000 0)
2.0−2.9 times per week	140 970	20 040	0.948 9 (0.923 9, 0.974 7)
3.0−3.9 times per week	74 210	11 389	1.010 1 (0.980 0, 1.041 1)
≥4.0 times per week	199 475	32 901	1.073 8 (1.046 7, 1.101 6)
			$P_{trend} < 0.000\,1$
Fish			
<1.0 time per week	40 368	7 066	1.000 0 (1.000 0, 1.000 0)
1.0−1.9 times per week	194 838	29 249	0.863 8 (0.837 6, 0.890 9)
2.0−2.9 times per week	114 736	17 055	0.822 1 (0.795 5, 0.849 6)
≥3.0 times per week	137 907	21 839	0.869 8 (0.842 5, 0.898 1)
			$P_{trend} = 0.220\,6$
Cheese			
<1.0 time per week	95 186	16 134	1.000 0 (1.000 0, 1.000 0)
1.0 time per week	101 736	16 356	0.961 6 (0.937 9, 0.986 0)
2.0−4.9 times per week	214 692	31 474	0.920 3 (0.900 3, 0.940 7)
≥5.0 times per week	62 660	8 277	0.882 2 (0.855 9, 0.909 2)
			$P_{trend} < 0.000\,1$

Odds ratio (95% CI): 0.7 0.8 1.0 1.2

Fig. 2 Odds ratio (95% confidence interval) for the associations between animal food intake and infectious diseases in the UK Biobank. Multivariable logistic regression analysis was used and adjusted for age, sex, ethnicity, assessment center, activity, Townsend deprivation index, and education.

one. In addition, a higher frequency of cheese intake ($P_{trend} < 0.000\,1$) was associated with a lower risk of infectious diseases (*Fig. 2* and *Supplementary Table 5* [available online]).

When further determining the associations of different types of fish and red meat (as continuous variables) with infectious diseases, we found that the intake of oily fish was negatively correlated with infectious diseases (OR = 0.986 5, 95% CI: 0.978 8–0.994 3), while a higher intake of non-oily fish may be associated with a higher risk of infectious diseases (OR = 1.010 1, 95% CI: 1.001 4–1.018 8). Beef (OR = 1.034 7, 95% CI: 1.025 1–1.044 4), mutton (OR = 1.061 4, 95% CI: 1.046 5–1.076 5), and pork (OR = 1.058 0, 95% CI: 1.043 7–1.072 3) consumption were all positively associated with overall infection (*Supplementary Table 6* [available online]).

For other foods, participants with a higher intake of fruits and cereals ($P_{trend} < 0.000\,1$) had a lower risk of infectious diseases, compared with those with the lowest intake frequency (*Fig. 3*). For bread intake, compared with participants who consumed white bread, those who consumed brown bread (OR = 0.871 0, 95% CI: 0.847 4–0.895 2) and whole meal (or whole grain) bread (OR = 0.775 2, 95% CI: 0.760 2–0.790 5) had a lower risk of infectious diseases (*Supplementary Table 7* [available online]). For tea, those who drank 2.0–3.9 cups per day had a lower risk of infection (OR = 0.881 7, 95% CI: 0.862 4–0.901 3), compared with those with the lowest consumption. However, those drinking more than four glasses of water per day had a higher risk of infection than those drinking less than two glasses daily (OR = 1.144 4, 95% CI: 1.120 4–1.168 9). Interestingly, we found that consuming alcohol more frequently than once a week was negatively associated with infectious diseases, with the lowest risk at 3–4 times per week (OR = 0.685 8, 95% CI: 0.669 9–0.701 9) (*Supplementary Table 7*).
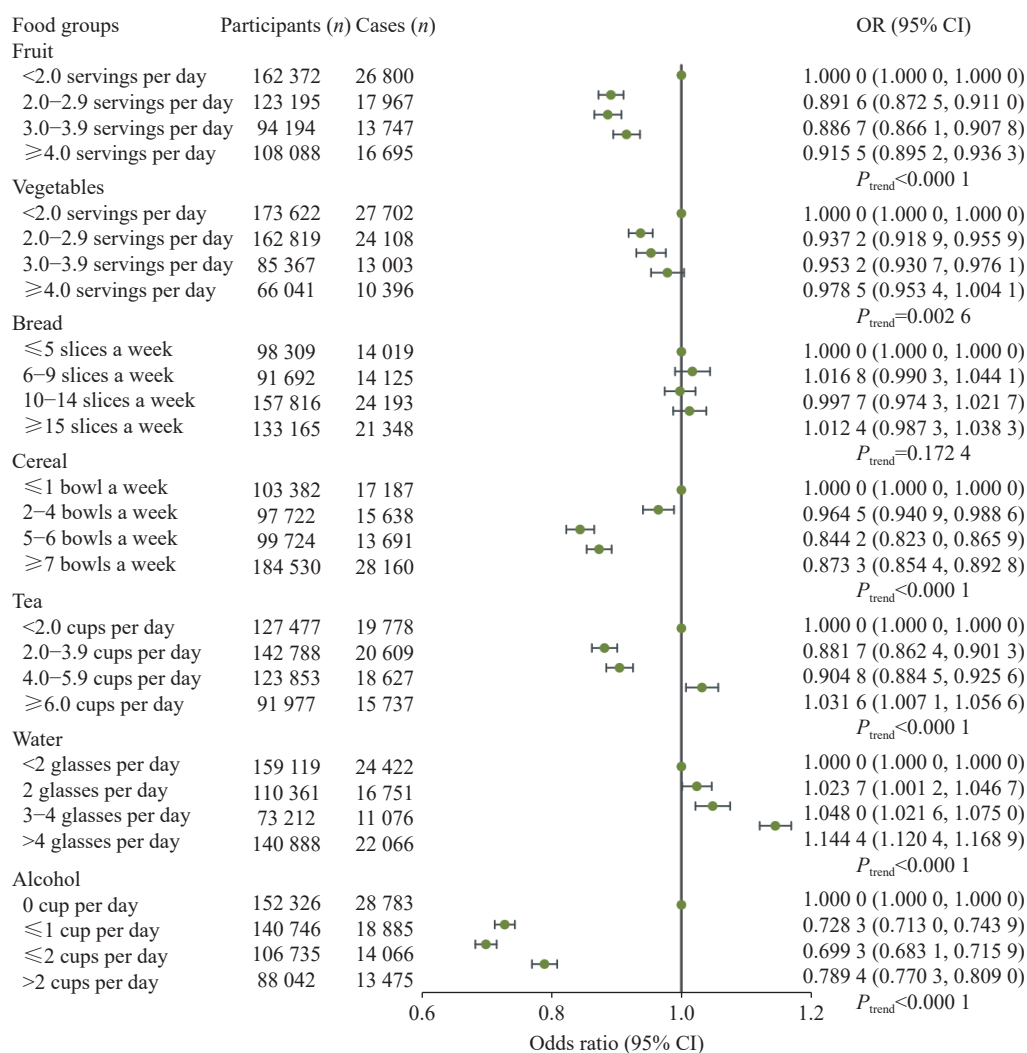
Food groups	Participants (*n*)	Cases (*n*)		OR (95% CI)
Fruit				
<2.0 servings per day	162 372	26 800		1.000 0 (1.000 0, 1.000 0)
2.0−2.9 servings per day	123 195	17 967		0.891 6 (0.872 5, 0.911 0)
3.0−3.9 servings per day	94 194	13 747		0.886 7 (0.866 1, 0.907 8)
≥4.0 servings per day	108 088	16 695		0.915 5 (0.895 2, 0.936 3)
				P_{trend}<0.000 1
Vegetables				
<2.0 servings per day	173 622	27 702		1.000 0 (1.000 0, 1.000 0)
2.0−2.9 servings per day	162 819	24 108		0.937 2 (0.918 9, 0.955 9)
3.0−3.9 servings per day	85 367	13 003		0.953 2 (0.930 7, 0.976 1)
≥4.0 servings per day	66 041	10 396		0.978 5 (0.953 4, 1.004 1)
				P_{trend}=0.002 6
Bread				
≤5 slices a week	98 309	14 019		1.000 0 (1.000 0, 1.000 0)
6−9 slices a week	91 692	14 125		1.016 8 (0.990 3, 1.044 1)
10−14 slices a week	157 816	24 193		0.997 7 (0.974 3, 1.021 7)
≥15 slices a week	133 165	21 348		1.012 4 (0.987 3, 1.038 3)
				P_{trend}=0.172 4
Cereal				
≤1 bowl a week	103 382	17 187		1.000 0 (1.000 0, 1.000 0)
2−4 bowls a week	97 722	15 638		0.964 5 (0.940 9, 0.988 6)
5−6 bowls a week	99 724	13 691		0.844 2 (0.823 0, 0.865 9)
≥7 bowls a week	184 530	28 160		0.873 3 (0.854 4, 0.892 8)
				P_{trend}<0.000 1
Tea				
<2.0 cups per day	127 477	19 778		1.000 0 (1.000 0, 1.000 0)
2.0−3.9 cups per day	142 788	20 609		0.881 7 (0.862 4, 0.901 3)
4.0−5.9 cups per day	123 853	18 627		0.904 8 (0.884 5, 0.925 6)
≥6.0 cups per day	91 977	15 737		1.031 6 (1.007 1, 1.056 6)
				P_{trend}<0.000 1
Water				
<2 glasses per day	159 119	24 422		1.000 0 (1.000 0, 1.000 0)
2 glasses per day	110 361	16 751		1.023 7 (1.001 2, 1.046 7)
3−4 glasses per day	73 212	11 076		1.048 0 (1.021 6, 1.075 0)
>4 glasses per day	140 888	22 066		1.144 4 (1.120 4, 1.168 9)
				P_{trend}<0.000 1
Alcohol				
0 cup per day	152 326	28 783		1.000 0 (1.000 0, 1.000 0)
≤1 cup per day	140 746	18 885		0.728 3 (0.713 0, 0.743 9)
≤2 cups per day	106 735	14 066		0.699 3 (0.683 1, 0.715 9)
>2 cups per day	88 042	13 475		0.789 4 (0.770 3, 0.809 0)
				P_{trend}<0.000 1

Odds ratio (95% CI) 0.6 0.8 1.0 1.2

Fig. 3 Odds ratio (95% confidence interval) for the associations of other foods with infectious diseases in the UK Biobank. These other foods included plant foods, staple foods, and drinks. Multivariable logistic regression analysis was used, and adjusted for age, sex, ethnicity, assessment center, activity, Townsend deprivation index, and education.

Furthermore, we also evaluated the above associations in three common types of infectious disease subgroups and obtained results of digestive infectious diseases consistent with the main analysis in terms of the effects of processed meat, red meat, fish, cheese, fruit, vegetables, and alcohol consumption (*Supplementary Table 8* [available online]).

Sensitivity analysis

First of all, compared with those who had not changed their dietary habits in the past five years, the participants with dietary changes because of illness had a higher risk of infectious diseases (OR = 2.109, 95% CI: 2.061 2–2.157 7), which largely remained significant across three infectious disease subgroups (*Supplementary Table 9* [available online]). Therefore, we further reevaluated the associations

between these food groups and infectious diseases by excluding the participants who made a major dietary change because of illness in the past five years, and found that in terms of most food groups, the results derived from the retained 432 531 participants were largely similar to the main analysis (*Supplementary Table 5*).

Second, because one of the most common confounders in epidemiology, sex made a significant difference between infected and non-infected individuals, we conducted a stratified analysis by sex (*Table 2*). The results for processed meat, red meat, fish, fruit, tea, and alcohol in 223 312 males and 264 537 females were broadly consistent with the main analysis. However, there was heterogeneity by sex for the associations between infectious diseases and poultry ($P_{heterogeneity}$ = 0.016 8), red meat ($P_{heterogeneity}$ = 0.005 8), red and processed meat

Table 2 Associations between dietary factors and infectious diseases in men and women in the UK Biobank

Reported consumptions	Women (N=264 537)				Men (N=223 312)				$P_\text{heterogeneity by sex}$
	No	no	OR (95% CI)[a]	P	No	no	OR (95% CI)[a]	P	
Processed meat									
Never	33 246	4 699	1.0000 (Ref)		12 044	1 881	1.0000 (Ref)		
<1.0 time per week	100 385	13 897	0.9748 (0.9391, 1.0120)	0.1804	47 543	7 413	0.9864 (0.9308, 1.0457)	0.6445	
1.0 time per week	75 620	10 927	1.0047 (0.9665, 1.0446)	0.8125	66 229	10 822	1.0435 (0.9863, 1.1046)	0.1406	
≥2.0 times per week	54 385	8 363	1.0728 (1.0301, 1.1174)	0.0007	96 613	16 778	1.1341 (1.0734, 1.1989)	<0.0001	
			P_trend<0.0001				P_trend<0.0001		0.1615
Poultry									
Never	33 246	2 154	1.0000 (Ref)		8 621	1 340	1.0000 (Ref)		
<1.0 time per week	100 385	4 183	1.0289 (0.9704, 1.0913)	0.3412	25 317	4 714	1.0876 (1.0142, 1.1670)	0.0189	
1.0 time per week	75 620	13 352	0.9866 (0.9373, 1.0388)	0.6057	82 514	14 051	1.0525 (0.9869, 1.1233)	0.1212	
≥2.0 times per week	54 385	18 218	1.0249 (0.9748, 1.0781)	0.3380	105 984	16 792	1.0758 (1.0094, 1.1475)	0.0255	
			P_trend=0.0143				P_trend=0.0635		0.0168
Red meat									
<1.0 time per week	34 324	2 154	1.0000 (Ref)		17 284	2 802	1.0000 (Ref)		
1.0–1.9 times per week	107 793	4 183	0.9736 (0.9385, 1.0102)	0.1548	84 186	13 346	1.0080 (0.9609, 1.0578)	0.7446	
2.0–2.9 times per week	70 910	13 352	0.9785 (0.9410, 1.0176)	0.2762	64 832	10 433	1.0146 (0.9660, 1.0660)	0.5637	
≥3.0 times per week	51 510	18 218	1.0557 (1.0136, 1.0998)	0.0092	57 010	10 541	1.1427 (1.0880, 1.2006)	<0.0001	
			P_trend<0.0001				P_trend<0.0001		0.0058
Red and processed meat									
<2.0 times per week	51 828	7 435	1.0000 (Ref)		21 366	3 444	1.0000 (Ref)		
2.0–2.9 times per week	88 126	12 004	0.9459 (0.9154, 0.9775)	0.0009	52 844	8 036	0.9705 (0.9263, 1.0171)	0.2100	
3.0–3.9 times per week	42 290	6 152	1.0070 (0.9692, 1.0463)	0.7208	31 920	5 237	1.0359 (0.9851, 1.0894)	0.1694	
≥4.0 times per week	82 293	12 496	1.0441 (1.0105, 1.0789)	0.0098	117 182	20 405	1.1232 (1.0764, 1.1723)	<0.0001	
			P_trend<0.0001				P_trend<0.0001		0.0078
Fish									
<1.0 time per week	21 731	3 601	1.0000 (Ref)		18 637	3 465	1.0000 (Ref)		
1.0–1.9 times per week	101 708	14 274	0.8595 (0.8235, 0.8973)	<0.0001	93 130	14 975	0.8689 (0.8313, 0.9084)	<0.0001	
2.0–2.9 times per week	64 009	8 733	0.8052 (0.7694, 0.8429)	<0.0001	50 727	8 322	0.8421 (0.8031, 0.8832)	<0.0001	
≥3.0 times per week	77 089	11 479	0.8703 (0.8327, 0.9098)	<0.0001	60 818	10 360	0.8715 (0.8332, 0.9129)	<0.0001	
			P_trend=0.6259				P_trend=0.2869		0.0356

Table 2 Associations between dietary factors and infectious diseases in men and women in the UK Biobank (Continued)

Reported consumptions	Women (N=264 537)				Men (N=223 312)				$P_{\text{heterogeneity by sex}}$
	No	no	OR (95% CI)[a]	P	No	no	OR (95% CI)[a]	P	
Cheese									
<1.0 time per week	57 308	9 229	1.000 0 (Ref)		37 878	6 905	1.000 0 (Ref)		
1.0 time per week	56 721	8 558	0.955 8 (0.924 3, 0.988 4)	0.008 2	45 015	7 798	0.970 0 (0.934 1, 1.007 2)	0.112 7	
2.0–4.9 times per week	110 891	14 866	0.890 8 (0.864 8, 0.917 7)	<0.000 1	103 801	16 608	0.952 4 (0.921 7, 0.984 2)	0.003 6	
≥5.0 times per week	32 058	3 910	0.860 9 (0.825 3, 0.897 8)	<0.000 1	30 602	4 367	0.906 8 (0.868 0, 0.947 2)	<0.000 1	
			P_{trend}<0.000 1				P_{trend}<0.000 1		0.059 0
Fruit									
<2.0 servings per day	71 977	11 110	1.000 0 (Ref)		90 395	15 690	1.000 0 (Ref)		
2.0–2.9 servings per day	68 054	9 307	0.878 4 (0.851 4, 0.906 2)	<0.000 1	55 141	8 660	0.902 9 (0.876 1, 0.930 4)	<0.000 1	
3.0–3.9 servings per day	57 402	7 941	0.875 4 (0.847 3, 0.904 5)	<0.000 1	36 792	5 806	0.899 5 (0.869 0, 0.930 9)	<0.000 1	
≥4.0 servings per day	67 104	9 729	0.890 8 (0.863 3, 0.919 2)	<0.000 1	40 984	6 966	0.952 8 (0.922 2, 0.984 4)	0.003 7	
			P_{trend}<0.000 1				P_{trend}=0.000 2		0.002 1
Vegetables									
<2.0 servings per day	82 317	12 433	1.000 0 (Ref)		91 305	15 269	1.000 0 (Ref)		
2.0–2.9 servings per day	92 359	12 823	0.926 7 (0.901 2, 0.953 0)	<0.000 1	70 460	11 285	0.943 3 (0.917 3, 0.970 0)	<0.000 1	
3.0–3.9 servings per day	51 272	7 251	0.938 8 (0.908 6, 0.970 0)	0.000 2	34 095	5 752	0.962 0 (0.928 9, 0.996 1)	0.029 6	
≥4.0 servings per day	38 589	5 580	0.955 9 (0.922 1, 0.990 8)	0.013 8	27 452	4 816	0.995 1 (0.958 2, 1.033 1)	0.796 7	
			P_{trend}=0.001 5				P_{trend}=0.137 3		0.154 0
Bread									
≤5 slices a week	73 017	9 904	1.000 0 (Ref)		25 292	4 115	1.000 0 (Ref)		
6–9 slices a week	58 634	8 556	1.031 4 (0.998 4, 1.065 3)	0.062 1	33 058	5 569	0.993 0 (0.948 2, 1.039 9)	0.764 6	
10–14 slices a week	86 947	12 577	1.020 4 (0.990 6, 1.051 0)	0.181 8	70 869	11 616	0.963 5 (0.925 1, 1.003 7)	0.074 1	
≥15 slices a week	42 392	6 340	1.044 6 (1.008 2, 1.082 3)	0.015 9	90 773	15 008	0.978 6 (0.940 6, 1.018 3)	0.285 3	
			P_{trend}=0.003 4				P_{trend}=0.906 1		0.409 8
Cereal									
≤1 bowl a week	53 767	8 055	1.000 0 (Ref)		49 615	9 132	1.000 0 (Ref)		
2–4 bowls a week	52 989	7 949	0.987 8 (0.953 8, 1.023 0)	0.490 6	44 733	7 689	0.945 0 (0.912 4, 0.978 7)	0.001 6	
5–6 bowls a week	54 711	7 044	0.866 9 (0.836 4, 0.898 6)	<0.000 1	45 013	6 647	0.824 1 (0.794 7, 0.854 5)	<0.000 1	
≥7 bowls a week	101 946	14 785	0.914 8 (0.886 8, 0.943 6)	<0.000 1	82 584	13 375	0.837 2 (0.811 4, 0.863 8)	<0.000 1	
			P_{trend}<0.000 1				P_{trend}<0.000 1		0.074 1

Table 2   **Associations between dietary factors and infectious diseases in men and women in the UK Biobank** (Continued)

Reported consumptions	Women (*N*=264 537)				Men (*N*=223 312)				$P_{\text{heterogeneity by sex}}$
	No	*no*	OR (95% CI)[a]	*P*	*No*	*no*	OR (95% CI)[a]	*P*	
Tea									
<2.0 cups per day	69 331	10 129	1.000 0 (Ref)		58 146	9 649	1.000 0 (Ref)		
2.0–3.9 cups per day	77 238	10 449	0.890 4 (0.863 5, 0.918 1)	<0.000 1	65 550	10 160	0.868 8 (0.841 7, 0.896 9)	<0.000 1	
4.0–5.9 cups per day	68 141	9 597	0.923 7 (0.895 1, 0.953 1)	<0.000 1	55 712	9 030	0.879 8 (0.851 3, 0.909 2)	<0.000 1	
≥6.0 cups per day	48 901	7 680	1.035 9 (1.001 7, 1.071 2)	0.039 6	43 076	8 057	1.020 5 (0.986 0, 1.056 2)	0.246 3	
			P_{trend}<0.000 1				P_{trend}=0.000 2		0.545 6
Water									
<2 glasses per day	73 120	10 240	1.000 0 (Ref)		85 999	14 182	1.000 0 (Ref)		
2 glasses per day	58 517	8 246	1.023 0 (0.990 4, 1.056 7)	0.168 7	51 844	8 505	1.029 7 (0.998 6, 1.061 8)	0.060 9	
3–4 glasses per day	42 920	6 084	1.035 1 (0.998 9, 1.072 5)	0.057 6	30 292	4 992	1.072 1 (1.033 2, 1.112 3)	0.000 2	
>4 glasses per day	87 821	13 101	1.131 4 (1.098 6, 1.165 1)	<0.000 1	53 067	8 965	1.172 5 (1.136 6, 1.209 5)	<0.000 1	
			P_{trend}<0.000 1				P_{trend}<0.000 1		0.814 4
Alcohol									
0 cup per day	100 879	18 001	1.000 0 (Ref)		51 447	10 782	1.000 0 (Ref)		
≤1 cup per day	87 301	10 863	0.729 2 (0.709 6, 0.749 4)	<0.000 1	53 445	8 022	0.718 3 (0.694 2, 0.743 1)	<0.000 1	
≤2 cups per day	50 622	5 897	0.698 0 (0.675 3, 0.721 5)	<0.000 1	56 113	8 169	0.689 2 (0.666 3, 0.712 8)	<0.000 1	
>2 cups per day	25 735	3 326	0.789 9 (0.757 9, 0.823 1)	<0.000 1	62 307	10 149	0.777 2 (0.752 6, 0.802 5)	<0.000 1	
			P_{trend}<0.000 1				P_{trend}=0.970 4		0.616 0

[a]Adjusted for age, sex, ethnicity, assessment center, activity, Townsend deprivation index, and education. The unequal numbers of groups and each sex are because of the missing data.
Abbreviations: *No*, number of participants; *no*, number of cases; CI, confidence interval; OR, odds ratio.

($P_{heterogeneity}$ = 0.007 8), fish ($P_{heterogeneity}$ = 0.035 6), and fruits ($P_{heterogeneity}$ = 0.002 1). For example, in terms of poultry, there was a positive association observed in males (more than 2.0 times per week, OR = 1.075 8, 95% CI: 1.009 4–1.147 5) and no association in females (OR = 1.024 9, 95% CI: 0.974 8–1.078 1).

Third, considering that dietary habits vary across different races, we also estimated the associations between food groups and infectious diseases in different ethnicity or race, and found that the results for the white ethnicity or race were similar to the main analysis, while those for other ethnicities or races showed quite different results (*Supplementary Table 10* [available online]). These results added the evidence to the effects of food groups on the incidence of infectious diseases.

Associations of diet groups on infectious diseases and the mediators

The current study defined 282 066 regular meat-eaters, 184 201 low meat-eaters, 11 012 fish-eaters, and 8 933 vegetarians. Compared with regular meat eaters, low meat-eaters (OR = 0.940 4, 95% CI: 0.924 3–0.956 7), fish-eaters (OR = 0.839 1, 95% CI: 0.788 7–0.891 9), and vegetarians (OR = 0.915 4, 95% CI: 0.856 1–0.977 8) had a lower risk of infectious diseases (*Fig. 4* and *Supplementary Table 11* [available online]). For the three infectious disease subgroups, the protective effects of the low meat-

eaters and fish-eaters were only replicated in digestive infectious diseases.

In the mediation analysis, we disclosed the mediation effects of HbA1c and other indicators in the associations observed above. When the mediator was additionally adjusted, the associations were retained (*Table 3*). For low meat-eaters and fish-eaters, HbA1c mediated a proportion of 17.26% (95% CI: 13.42%–24.18%) and 12.75% (95% CI: 9.21%–21.41%); WBCs mediated a proportion of 24.14% (95% CI: 18.53%–34.1%) and 20.63% (95% CI: 14.37%–32.13%); while BMI mediated a proportion of 53.59% (95% CI: 41.18%–75.45%) and 44.87% (95% CI: 33.01%–73.12%) in these associations, respectively (*Fig. 5*, *Table 3*, and *Supplementary Table 12* [available online]). TG and indicators related to obesity and body fat distribution mediated the associations of low meat-eaters and fish-eaters (with regular meat-eaters as reference) on infectious diseases.

Discussion

In this large-scale contemporary study, we conducted comprehensive analyses to investigate the associations between diet and infectious diseases, and found that the consumption frequency of different food groups was associated with the risk of infection. A series of sensitivity analyses were performed to confirm the main results. Diet groups were also
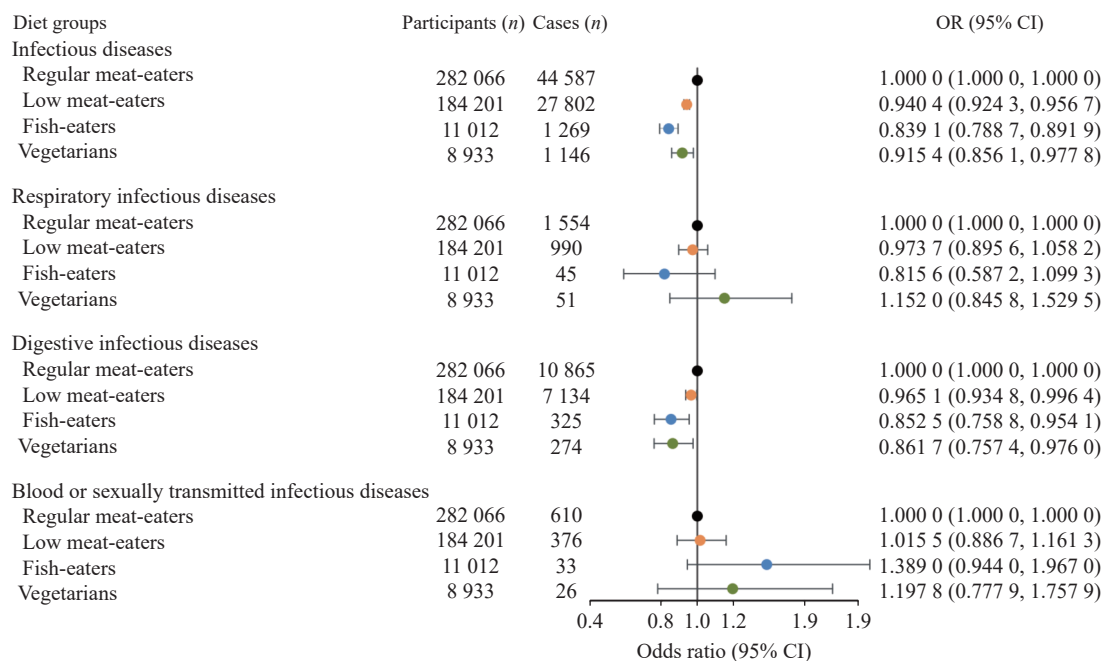
Diet groups	Participants (n)	Cases (n)	OR (95% CI)
Infectious diseases			
Regular meat-eaters	282 066	44 587	1.000 0 (1.000 0, 1.000 0)
Low meat-eaters	184 201	27 802	0.940 4 (0.924 3, 0.956 7)
Fish-eaters	11 012	1 269	0.839 1 (0.788 7, 0.891 9)
Vegetarians	8 933	1 146	0.915 4 (0.856 1, 0.977 8)
Respiratory infectious diseases			
Regular meat-eaters	282 066	1 554	1.000 0 (1.000 0, 1.000 0)
Low meat-eaters	184 201	990	0.973 7 (0.895 6, 1.058 2)
Fish-eaters	11 012	45	0.815 6 (0.587 2, 1.099 3)
Vegetarians	8 933	51	1.152 0 (0.845 8, 1.529 5)
Digestive infectious diseases			
Regular meat-eaters	282 066	10 865	1.000 0 (1.000 0, 1.000 0)
Low meat-eaters	184 201	7 134	0.965 1 (0.934 8, 0.996 4)
Fish-eaters	11 012	325	0.852 5 (0.758 8, 0.954 1)
Vegetarians	8 933	274	0.861 7 (0.757 4, 0.976 0)
Blood or sexually transmitted infectious diseases			
Regular meat-eaters	282 066	610	1.000 0 (1.000 0, 1.000 0)
Low meat-eaters	184 201	376	1.015 5 (0.886 7, 1.161 3)
Fish-eaters	11 012	33	1.389 0 (0.944 0, 1.967 0)
Vegetarians	8 933	26	1.197 8 (0.777 9, 1.757 9)

Odds ratio (95% CI): 0.4 0.8 1.0 1.2 1.9 1.9

Fig. 4 Associations of four diet groups with infectious diseases and three infectious disease subgroups. A multivariable logistic regression analysis was used, and adjusted for age, sex, ethnicity, assessment center, activity, Townsend deprivation index, and education.

Table 3 Mediation effects of diet groups on infectious diseases by potential variables in the UK Biobank

Mediators	Exposure	Effect with mediator adjusted (OR with 95% CI)[a]	Direct effect (OR with 95% CI)[a]	Mediation proportion (%) (95% CI)[a]	P
TG	Low meat-eaters *vs.* Ref.	0.950 2 (0.933 5, 0.967 1)	0.993 6 (0.991 4, 0.995 8)	14.19 (10.43, 20.61)	<0.000 1
	Fish-eaters *vs.* Ref.	0.861 1 (0.808 1, 0.916 8)	0.982 4 (0.975 4, 0.989 5)	7.92 (5.41, 12.68)	<0.000 1
Glucose	Low meat-eaters *vs.* Ref.	0.949 8 (0.932 4, 0.967 6)	0.993 6 (0.991 2, 0.995 8)	7.27 (5.21, 10.99)	<0.000 1
	Fish-eaters *vs.* Ref.	0.846 2 (0.791 3, 0.904 0)	0.980 4 (0.973 7, 0.987 9)	5.37 (3.63, 8.70)	<0.000 1
HbA1c	Low meat-eaters *vs.* Ref.	0.948 9 (0.932 2, 0.965 9)	0.993 5 (0.991 3, 0.995 7)	17.26 (13.42, 24.18)	<0.000 1
	Fish-eaters *vs.* Ref.	0.871 0 (0.817 1, 0.927 5)	0.983 6 (0.977 2, 0.990 7)	12.75 (9.21, 21.41)	<0.000 1
WBC	Low meat-eaters *vs.* Ref.	0.954 5 (0.937 9, 0.971 4)	0.994 2 (0.992 2, 0.996 4)	24.14 (18.53, 34.1)	<0.000 1
	Fish-eaters *vs.* Ref.	0.876 2 (0.822 5, 0.932 6)	0.984 3 (0.977 5, 0.991 3)	20.63 (14.37, 32.13)	<0.000 1
BMI	Low meat-eaters *vs.* Ref.	0.972 5 (0.955 7, 0.989 6)	0.996 5 (0.994 3, 0.998 7)	53.59 (41.18, 75.45)	<0.000 1
	Fish-eaters *vs.* Ref.	0.911 6 (0.856 1, 0.969 8)	0.989 3 (0.982 8, 0.996 7)	44.87 (33.01, 73.12)	<0.000 1
WHR	Low meat-eaters *vs.* Ref.	0.970 3 (0.953 6, 0.987 3)	0.996 3 (0.994 3, 0.998 4)	50.41 (39.72, 70.67)	<0.000 1
	Fish-eaters *vs.* Ref.	0.900 9 (0.846 3, 0.958 3)	0.987 7 (0.980 1, 0.995 1)	36.57 (25.73, 59.84)	<0.000 1
Body fat percentage	Low meat-eaters *vs.* Ref.	0.968 1 (0.951 2, 0.985 2)	0.996 0 (0.994 0, 0.998 1)	49.26 (38.37, 67.43)	<0.000 1
	Fish-eaters *vs.* Ref.	0.917 5 (0.861 3, 0.976 5)	0.989 9 (0.982 4, 0.997 1)	47.39 (33.09, 77.04)	<0.000 1
Whole body fat mass	Low meat-eaters *vs.* Ref.	0.971 7 (0.954 8, 0.989 0)	0.996 5 (0.994 3, 0.998 7)	53.45 (41.84, 76.09)	<0.000 1
	Fish-eaters *vs.* Ref.	0.919 1 (0.862 8, 0.978 3)	0.990 0 (0.983 2, 0.997 5)	46.87 (33.30, 77.84)	<0.000 1
Arms fat mass	Low meat-eaters *vs.* Ref.	0.964 5 (0.948 0, 0.981 4)	0.995 5 (0.993 3, 0.997 6)	39.69 (30.44, 55.78)	<0.000 1
	Fish-eaters *vs.* Ref.	0.893 2 (0.839 2, 0.949 9)	0.986 6 (0.979 5, 0.993 8)	31.54 (22.82, 51.12)	<0.000 1
Leg fat mass	Low meat-eaters *vs.* Ref.	0.961 4 (0.944 9, 0.978 2)	0.995 2 (0.993 1, 0.997 4)	34.99 (26.95, 51.17)	<0.000 1
	Fish-eaters *vs.* Ref.	0.887 9 (0.834 2, 0.944 2)	0.986 1 (0.979 3, 0.993 4)	28.44 (20.15, 47.18)	<0.000 1
Trunk fat mass	Low meat-eaters *vs.* Ref.	0.969 1 (0.952 2, 0.986 3)	0.996 1 (0.993 9, 0.998 2)	49.49 (38.15, 68.13)	<0.000 1
	Fish-eaters *vs.* Ref.	0.910 7 (0.855 0, 0.969 2)	0.989 3 (0.982 3, 0.995 9)	42.58 (30.17, 66.34)	<0.000 1

[a]Adjusted for age, sex, ethnicity, assessment center, activity, Townsend deprivation index, and education.
Abbreviations: CI, confidence interval; OR, odds ratio; TG, total cholesterol; WBC, white blood cells; BMI, body mass index; WHR, waist-to-hip ratio.

associated with the risk of infectious diseases, and HbA1c, WBC, and BMI may mediate the observed significant associations.

Investigators have been unanimously concerned about the health effects of meat consumption[24,26]. Nowadays, people pay increasing attention to a balanced diet. The extensive consumption of meat may replace the consumption of other foods, such as vegetables, and result in changes to meal composition. In addition, Europeans have a habit of consuming raw meat like medium-rare steak, and the increased frequency of raw meat intake increases exposure to pathogens, contributing to the high risk of digestive infectious diseases[27]. These findings are consistent with the current study that the higher meat consumption may be associated with a higher risk of digestive infectious diseases. Furthermore, our results showed that moderate meat consumption reduced the risk of infection, and we suspect that the reason may be because of the fact that eating meat in small

amounts helps the body replenish nutrients like protein, lipids, and minerals[28]. Fish, as one of the most important sources of omega-3 polyunsaturated fatty acids, is associated with various health benefits. A meta-analysis of prospective cohort studies indicated that higher fish consumption might reduce all-cause mortality[29–30]. Our results showed that a higher intake of fish, especially oily fish, was associated with a lower risk of infectious diseases, providing further evidence that fish intake has health benefits. Cheese, a fresh or matured food obtained from the coagulation of milk, is rich in nutritional components, such as proteins, bioactive proteins, amino acids, minerals, and vitamins[31]. In the current study, we found that a higher frequency of cheese consumption was positively associated with a lower risk of infectious diseases, in both women and men. Consuming cheese more than five times a week may be recommended to reduce the infectious risk based on the current results. Nevertheless, this may also be
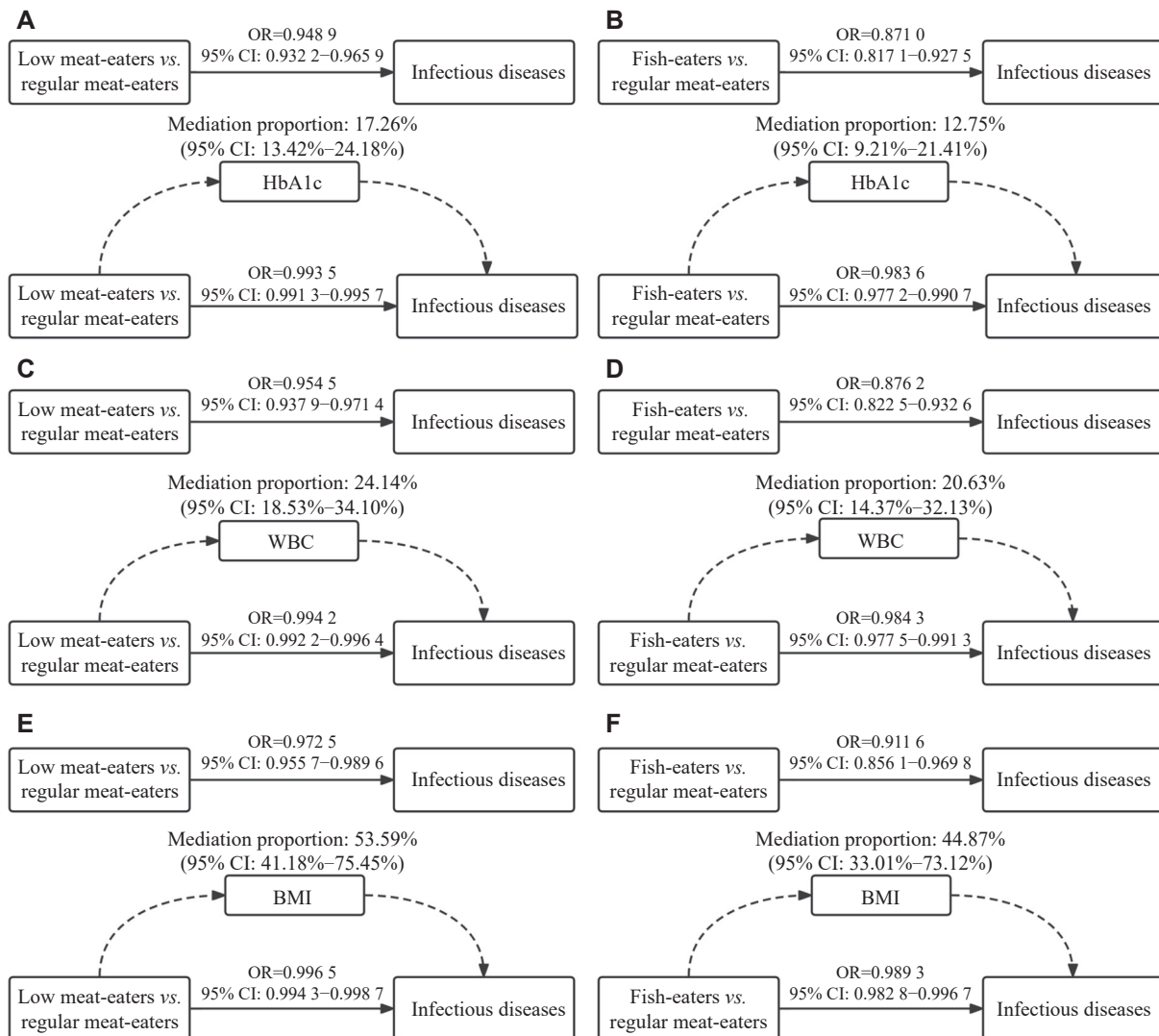
Fig. 5 **Results of mediation analysis.** Mediation effects of low meat-eaters and fish-eaters, compared with regular meat-eaters on infectious diseases by HbA1c (A and B), WBC (C and D), and BMI (E and F). Multivariable logistic regression analysis was used, and adjusted for age, sex, ethnicity, assessment center, activity, Townsend deprivation index, and education. Abbreviations: HbA1c, glycosylated hemoglobin; WBC, white blood cells; BMI, body mass index.

attributed to the common practice of consuming cheese with fresh foods.

Dietary guidelines worldwide recommend consuming more fruits and vegetables, which are rich in vitamins, minerals, dietary fiber, and a variety of phytochemicals to maintain health[32]. In the current study, we separately investigated the associations of fruits and vegetables with infectious diseases, and found that a daily intake of 3.0–3.9 servings of fruit and 2.0–2.9 servings of vegetables was associated with a lower risk of infectious diseases. These findings are consistent with a meta-analysis of 26 cohort studies, which found that five or more servings of fruits and vegetables per day were associated with less damage to health[33].

Bread and cereal are staple foods of Europeans. Whole grain bread offers advantages over other types of bread, which may be related to the ingredients, processing technology, and edible methods[34–35]. Tea, as a pleasant, popular, and socially accepted drink, is the richest source of a class of antioxidants called flavonoids and has the function of preventing intestinal flora infection and enhancing body immunity[36]. Combining the above evidence and our findings, moderate drinking of tea (2.0–3.9 cups daily) is worth advocating, but excessive tea intake increases disease risk, which may be related to the inhibition of essential trace elements.

An intriguing trend was observed in the current study, where individuals consuming more than four glasses of water per day exhibited a higher risk of infection than those consuming fewer than two glasses. Based on the literature, we posited the following potential reasons: although in developed

countries, there were millions of cases of waterborne infections each year[37–38]. Water intake is associated with the opportunity for exposure to pathogens in drinking water, where there may be over 500 types of waterborne pathogens. Despite strict management of drinking water quality being accessible in developed countries, it may not screen for fungi, algae, protozoa, and less significant bacteria, which leads to pathogens or organisms entering households through water as a medium of transmission. Additionally, the aging of drinking water treatment or distribution systems may also result in pathogen invasion[39–40]. Furthermore, areas with poor water quality often coincide with dense populations, lower economies, and other social factors, which may be associated with respiratory infections, sexually transmitted diseases, and other issues[38].

In general, after being ill, changing dietary habits is the common non-drug treatment to adjust the body status or prevent the disease progression; however, it may lead to a selection bias of participants[41]. The current study took this bias into consideration by excluding those participants who reported having made major changes in the past five years because of illness, and the results were consistent with those before the exclusion, indicating that the associations between diet and infectious diseases were valid.

We observed a sex-based heterogeneity in the associations of poultry, red meat, red and processed meat, fish, and fruit with infectious diseases. While these differences may not be clearly explained now, they indicate that the effect of sex on infectious diseases should not be ignored. There is evidence that the pathogen-induced immune responses are significantly influenced by the host's sex in many instances, and several genes have been observed to affect susceptibility to viruses, bacteria, parasites, fungi, and worms[42].

Ethnicity is another important social determinant of infectious diseases besides sex[43]. Our findings of the white ethnicity were aligned with the main results, while there were fewer associations in the Asian or African group. Such differences may be linked to genetic factors and immune responses, or it may have been difficult to detect those associations in a limited sample size.

Compared with the regular meat-eaters, the low meat-eaters, fish-eaters, and vegetarians had a lower risk of infectious diseases, suggesting that dietary preferences of meat and fish indeed influence the infection risk. Further analysis disclosed the mediation effects of nutritional status-related indicators such as BMI/BFP, metabolic-related indicators such as

HbA1c, and immune-related indicators such as WBC in the above-mentioned associations. According to the findings, we speculate that several aspects mentioned above may be potential factors or pathways influencing the risk of infectious diseases because of dietary influences. Among these mediators, the intermediate effect values of nutrition-related indicators are relatively significant. This suggests that it may be possible to reduce the risk of infectious diseases by adjusting the overall nutritional status of the population through the establishment of healthy dietary habits.

Nonetheless, the current study has several limitations. First, although we defined the dietary factors using the baseline survey data to help us confirm the intake of food groups, the eating habits of participants may change before suffering from infectious diseases, which may lead to inaccurately estimated associations between diet and infections. Second, the dietary data coming from the questionnaire was self-reported, which may have produced measurement errors and bias. Third, the current study focused on the frequency of food groups, and because of the lack of uniform standards for quantifying, the estimated associations between diet and infectious diseases may be biased. Fourth, because of variations in recurrence rates among different infectious diseases and the lack of practical significance in aggregating disease frequencies, the current study did not analyze the specific associations between diet and each infectious disease individually. However, future exploration and validation of such associations through alternative approaches, such as animal experiments, may be necessary.

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