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Association between dietary live microbe intake and emphysema prevalence: evidence from the National Health and Nutrition Examination Survey 2009-2018

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Abstract

Utilizing the National Health and Nutrition Examination Survey data from 2009 to 2018, this study examines the association between dietary live microbe consumption and emphysema prevalence in 24,174 participants. Dietary live microbe intake was classified into three categories: low, medium, and high. Adjusted logistic regression models demonstrated a significant inverse relationship between dietary live microbe intake and emphysema prevalence. Participants in the medium and high intake groups showed approximately 40% [odds ratio (OR)=0.595] and 60% (OR=0.378) reduced risk, respectively ($p<0.00001$). Subgroup analysis revealed a stronger protective effect in males, potentially linked to their higher oxidative stress and metabolic rates. These findings suggest that dietary live microbes may reduce emphysema risk by modulating immune responses and inflammation through the gut-lung axis. However, as this is a cross-sectional study, causality cannot be established, and further longitudinal research is required to validate these findings.

Key words*:* emphysema, dietary live microbes, NHANES.

Introduction

Emphysema is a chronic lung disease marked by alveolar wall destruction and reduced lung tissue elasticity, resulting in impaired gas exchange and worsening dyspnea [1]. As a critical subtype of Chronic Obstructive Pulmonary Disease (COPD), emphysema poses a significant global public health challenge. COPD ranks as the third leading cause of death globally, attributed to its complex pathogenesis involving prolonged smoking, environmental pollution, and genetic influences [2]. However, within the spectrum of COPD subtypes, emphysema has unique pathophysiological characteristics, characterized by localized alveolar destruction, loss of elastic recoil, and airway collapse. These features differentiate emphysema from other COPD subtypes such as chronic bronchitis.

In recent years, the concept of the gut-lung axis has gained attention, emphasizing the interaction between the gut microbiome and lung health [3,4]. The gut microbiota plays a crucial role in respiratory disease development by affecting systemic immune responses and inflammation [5,6]. Consumption of safe live microbes has been shown to interact with the mucosal surfaces of the digestive tract, modulating the immune system, reducing excessive inflammatory responses, enhancing gut function, and decreasing vulnerability to chronic diseases [7,8]. Considering the role of systemic inflammation and immune dysregulation in emphysema's development, investigating whether dietary live microbes can reduce emphysema prevalence through the gut-lung axis is highly relevant.

Presently, research specifically assessing the comprehensive effects of daily intake of safe live microbes on health outcomes is insufficient. Marco et al. proposed a classification system to define and assess dietary live microbe intake using NHANES [9]. Research indicates that consuming a diet rich in live microbes correlates with a reduced prevalence of COPD [10]. However, COPD is a highly heterogeneous disease comprising different subtypes, such as chronic bronchitis and emphysema.

While COPD has been extensively studied, the specific impact of dietary live microbe intake on emphysema remains unexplored. This study investigates the link between dietary live microbe consumption and emphysema using NHANES data from 2009 to 2018. By focusing on dietary live microbes, this study aims to deepen our understanding of their effects on alveolar structure and function, thereby clarifying their role in respiratory diseases.

Materials and Methods

Data source

This study utilized data from the National Health and Nutrition Examination Survey (NHANES), conducted by the National Center for Health Statistics (NCHS) to evaluate the health and nutritional status of U.S. populations. The project employs a complex, multi-stage

probability sampling strategy to create a nationally representative, non-institutionalized sample of U.S. citizens [11]. Participants first undergo home interviews to gather demographic, health, and socioeconomic information, which is then supplemented by laboratory tests and physical examinations conducted at mobile examination centers.The NHANES study procedures were approved by the NCHS Research Ethics Review Board, and all participants provided written informed consent. Details on the study design and data availability can be found at www.cdc.gov/nchs/nhanes/. This study followed the STROBE guidelines for cross-sectional studies [12].

Ethics statement

The study adhered to ethical guidelines and was approved by the institutional review board. All participants provided informed consent, guaranteeing their rights and confidentiality during the research. The NHANES study received approval from the National Research Ethics Committee on Health Statistics, and all participants provided informed consent. Following anonymization, the data from NHANES were made publicly available, permitting researchers to adapt it for research objectives. We followed research data guidelines, using it exclusively for statistical analysis and ensuring compliance with current standards and regulations. Throughout and following the data collection phase, the authors had no access to identifiable information of participants.

Study population

This study utilized NHANES data from 2009 to 2018. Among 49,693 eligible participants, 20,858 were under 20 years old. Emphysema status data was missing for 37 individuals, and dietary live microbe intake data was unavailable for 4,624 participants. The study ultimately included 24,172 women (Figure 1).

Live microbe intake

In the NHANES dataset, participants' dietary intake over two different 24-hour periods was recorded through face-to-face interviews and telephone follow-ups. The NCHS used USDA dietary nutrition data to accurately assess the energy and nutrient content of foods and beverages. A team of four experts, including Marco, assessed the live microbe content per gram in 9,388 foods across 48 subgroups within the NHANES database. These assessments were conducted using data from specialized literature, authoritative reviews, or inferred based on the known effects of food processing on microbial viability. Food microbial content was classified into three levels: low (<10^4 CFU/g), medium (10^4–10^7 CFU/g), and high (>10^7 CFU/g). Participants were categorized into three groups based on their dietary live

microbe intake: low (all foods classified as Lo), medium (at least one food classified as Med but none as Hi), and high (at least one food classified as Hi) [9,13]. In cases where inconsistencies arose during the evaluation of live microbe content, external consultation and discussion were utilized to resolve them.

Definition of emphysema

The main outcome assessed was the subject's history of emphysema. Emphysema data for selected cycles were gathered in participants' homes via a Computer-Assisted Personal Interviewing (CAPI) system by well-trained interviewers. Participants who answered "yes" to being asked if they had ever been told they had emphysema were classified as having the condition.

Covariates

Our study considered demographic variables such as age and racial categories, including Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, and other races. We examined BMI alongside the poverty-income ratio (PIR), classifying PIR into three categories: low income (<1.3), middle income (1.3-3.5), and high income (>3.5). For respiratory diseases, we accounted for asthma prevalence. Smoking status was documented by noting if participants had smoked a minimum of 100 cigarettes in their lifetime (yes/no). For drinking behavior, definitions varied by time period. In the 2009-2016 data, individuals consuming at least 12 alcoholic drinks annually and drinking at least once in the past year were classified as current drinkers. Former drinkers were identified as individuals who consumed at least 12 alcoholic drinks annually but reported no drinking in the past year. Participants who had fewer than 12 alcoholic drinks per year were defined as never drinkers. For the 2017-2018 data, participants were defined as current drinkers if they had consumed at least one alcoholic drink and reported a drinking frequency greater than 0 in the past twelve months. Participants who had consumed at least one type of alcohol but reported no drinking in the past twelve months were categorized as former drinkers, while those who had not consumed any alcohol were defined as never drinkers. We recorded diabetes and hypertension in the participants. Diabetes was determined through self-reported confirmation of a doctor's diagnosis, indicating that an individual has been informed by a physician of having diabetes. Hypertension was determined by a medical diagnosis, specifically being informed by a doctor of having the condition. For more information on variable measurements, visit the CDC's NHANES website at www.cdc.gov/nchs/nhanes/.

Statistical analysis

Data were analyzed using appropriate statistical methods to ensure accuracy and reliability. Descriptive statistics were calculated to summarize the data, and inferential statistics were employed to test hypotheses. Statistical significance was determined at a predefined alpha level. All analyses were conducted using specialized software to ensure precision and reproducibility. Continuous variables with a normal distribution are expressed as mean ± SD. We employed multiple linear regression to evaluate group differences and utilized the chi-square test to analyze categorical variables, presenting the results as percentages. Following STROBE guidelines, we developed three multivariate logistic regression models to examine the association between dietary microbe intake and emphysema prevalence.Model 1 remained unadjusted, Model 2 was adjusted for age and race/ethnicity, and Model 3 included all potential confounding factors. Subgroup analyses were performed considering age, gender, BMI, diabetes, hypertension, asthma, smoking, and drinking behaviors to better understand the link between dietary microbe intake and emphysema.Statistical evaluations were conducted using EmpowerStats and R, with $P < 0.05$ considered statistically significant.

Results

Baseline characteristics of participants

Based on specific inclusion and exclusion criteria, we analyzed data from 24,174 participants. As shown in Table 1, the mean age ranged from 49.3 to 64.6 years across the groups, with the emphysema group having a significantly higher mean age compared to the non-emphysema group ($p < 0.001$). Regarding race, the proportion of non-Hispanic Whites was highest in the emphysema group, while the proportions of other racial groups were relatively lower ($p < 0.001$). The emphysema group had a notably higher percentage of individuals lacking a high school diploma and a lower percentage of those with at least a high school education compared to the non-emphysema group. Additionally, the emphysema group exhibited a significantly lower mean poverty-income ratio (PIR), reflecting a lower socioeconomic status ($p < 0.001$). The BMI values were similar between the two groups, with no significant difference ($p = 0.405$). However, the emphysema group exhibited significantly higher prevalence rates of hypertension (62.0%) and diabetes (26.1%) compared to the non-emphysema group ($p < 0.001$). Smoking prevalence was also notably higher in the emphysema group compared to the non-emphysema group (91.0% vs. 42.6%, $p < 0.001$). Both the proportion of never drinkers and current drinkers were significantly lower in the emphysema group ($p < 0.001$). Asthma prevalence was significantly higher in the emphysema group than in the non-emphysema group (45.9% vs. 14.2%, $p < 0.001$).

Finally, the proportion of individuals with high dietary live microbe intake was significantly

lower in the emphysema group (37.2%) compared to the non-emphysema group (71.9%, $p < 0.001$).

Association between dietary live microbe intake and emphysema

Table 2 presents the logistic regression analysis results, highlighting the relationship between dietary live microbe consumption and emphysema prevalence. In Model 1, without adjusting for covariates, emphysema prevalence was notably reduced in the medium (OR = 0.622, 95% CI 0.504–0.769) and high (OR = 0.452, 95% CI 0.355–0.574, p = 0.00013) dietary live microbe intake groups compared to the low intake group. In Model 2, adjusting for age and race strengthened the association, with the odds ratio (OR) decreasing to 0.538 (95% CI 0.433–0.669) for the medium intake group and 0.378 (95% CI 0.295–0.485, $p < 0.00001$) for the high intake group. Model 3 included further adjustments for educational level, family income, BMI, chronic diseases (e.g., hypertension, diabetes), smoking, drinking, asthma, and other confounders.After adjustment, emphysema prevalence was significantly reduced in the medium (OR = 0.595, 95% CI 0.455–0.777) and high (OR = 0.378, 95% CI 0.295–0.485) dietary live microbe intake groups compared to the low intake group ($p < 0.00001$). The study reveals a significant association between increased dietary live microbe consumption and lower emphysema prevalence, independent of various potential confounders. The trend test consistently showed that higher dietary intake of live microbes was associated with a lower prevalence of emphysema in all models.

Subgroup analysis

Subgroup analyses were performed to assess the consistency of the relationship between dietary live microbe consumption and emphysema across various demographic groups, as presented in Table 3. Subgroup interaction tests considering age, gender, BMI, diabetes, hypertension, asthma, smoking, and drinking behavior identified significant effects in certain subgroups.In the gender subgroup analysis, a significant interaction was observed between dietary live microbe intake and emphysema (p = 0.0025), with men experiencing a stronger protective effect. High dietary intake of live microbes significantly reduced emphysema risk in men (OR = 0.490, 95% CI 0.344–0.697), with a weaker association observed in women. In various subgroups, including those defined by age, BMI, diabetes, and hypertension, higher intake of dietary live microbes was generally associated with a lower prevalence of emphysema. However, the interaction was not statistically significant, suggesting a consistent effect across these subgroups.

Discussion

Analysis of the NHANES database indicates a reduced prevalence of emphysema in individuals with higher dietary live microbe intake. Subgroup analysis revealed that gender might influence this association, with males showing a more significant protective effect. This study is the first to explore the link between dietary live microbe consumption and emphysema in American adults, suggesting that increased intake may offer a protective effect against the condition.

Among the microbiota studied to date, the gut microbiome remains the most extensively researched. The gut harbors an estimated bacterial load of around 10^14 bacteria [14], making it the most densely populated microbial site in the human body. Chronic lung diseases, such as asthma, COPD, and cystic fibrosis, have been shown to involve intestinal disease components, such as impaired gut barrier function or dysbiosis [15-17]. Research indicates that during the progression of various lung diseases, the gut microenvironment undergoes significant changes, including shifts in gut microbiome composition [18,19]. The gut-lung axis, acting as a bridge for systemic immune and metabolic regulation, provides a potential explanation for how dietary factors influence both gut microbiota and respiratory microbiome composition [20,21]. Modulating gut bacteria with probiotic supplements (specific live microbes) can enhance the gut barrier and improve systemic inflammation, serving as an effective treatment strategy for multiple diseases [22,23]. Studies have demonstrated that oral probiotic supplements can significantly alter the gut microbiome, shifting it toward a community enriched with short-chain fatty acid (SCFA)-producing and antioxidant-producing probiotics [24]. These changes may play a critical role in alleviating oxidative stress-induced lung inflammation. Compared to probiotic supplements, dietary sources of microbes often provide more enduring and stable health benefits. Fermented foods and other food types are rich sources of live microorganisms [9]. Fermented foods typically contain over 10^7 cells/g of live microbes, while raw, unpeeled fruits and vegetables contain 10^6-10^8 CFU/g [25,26]. In contrast, commercially sterile or pasteurized foods, such as refrigerated items like milk and deli meats, have microbial counts below 10^4 CFU/g [27,28]. These dietary sources often provide diverse microbial communities, which may contribute to more stable colonization and longer-lasting health benefits compared to isolated probiotic supplements [9,26,29]. Recent studies on fermented foods provide strong evidence supporting the health benefits of consuming live microbes [29-31]. Our findings align with this evidence, demonstrating that increased dietary intake of live microbes is associated with a reduced prevalence of emphysema.

The mechanisms by which high dietary live microbe intake may reduce emphysema prevalence include alterations in gut microbiota that impact lung immune responses via the

gut-lung axis [32,33]. A healthy and balanced gut microbiome facilitates the production of anti-inflammatory immune cells, such as regulatory T cells, thereby reducing inflammatory mediator release in the lungs [34]. In emphysema patients, inflammatory cells in the lungs and airways release pro-inflammatory cytokines and chemokines, causing structural damage to airway and alveolar walls. Dietary probiotics can promote anti-inflammatory cytokines, such as IL-10, while suppressing pro-inflammatory cytokines, like TNF-α and IL-6, effectively mitigating lung inflammation [35,36]. Additionally, certain fermented foods and specific probiotics may enhance the body's antioxidant capacity, reduce reactive oxygen species (ROS) production, and alleviate oxidative damage in lung tissue [36,37]. Together, these anti-inflammatory and antioxidant mechanisms may explain the observed protective effects of dietary live microbes on emphysema prevalence.

Notably, the negative correlation between live microbe intake and emphysema prevalence appeared more significant in men. This observation may be partially explained by gender differences in gut microbiota complexity and diversity, which can directly or indirectly influence sex steroid hormones and central gene activation [38-40]. Research indicates that testosterone and estrogen play crucial roles in shaping immune response patterns [41]. In this context, dietary live microbes may mitigate lung inflammation more effectively in men through immune system regulation. Men are widely recognized to have higher smoking rates than women, leading to a higher baseline risk for emphysema, which may amplify the observed protective effects of live microbes. Additionally, men experience higher oxidative stress levels [41-43], potentially enhancing the antioxidant benefits of dietary live microbes. The higher basal metabolic rate in men [44] may also influence the metabolism and activity of live microbes, though this mechanism requires further investigation. Overall, the exact pathways underlying these gender differences warrant more detailed research.

Research on the association between dietary live microbes and emphysema prevalence remains limited. This study addresses this gap by exploring the potential association in a large, representative U.S. cohort. Unlike prior studies focused solely on fermented foods or probiotics, our research examined a comprehensive daily diet incorporating live microbes. However, several limitations must be acknowledged. Being cross-sectional in nature, this study cannot establish causality. The observed association may be influenced by unmeasured confounders, such as genetic, environmental, or other unaccounted lifestyle factors. Furthermore, the dietary and lifestyle data were based on participants' self-reports, which could introduce recall or reporting biases, potentially impacting data accuracy.

Conclusions

Our study indicates that increased dietary live microbe intake is negatively associated with emphysema prevalence, suggesting a potential reduction in emphysema risk. These results highlight that dietary live microbes may have a protective effect in preventing or mitigating emphysema.

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Table 1. Basic characteristics of participants with and without emphysema.

Characteristics	Overall	Emphysema		p
		No	Yes	
		N=23695	N=479	
Age(years)	49.6±17.633	49.297±17.596	64.574±12.188	<0.001
Race/ethnicity, n (%)				<0.001
Mexican American	3298 (14.47%)	3480 (14.687%)	18 (3.758%)	
Other Hispanic	2488 (10.29%)	2449 (10.336%)	39 (8.142%)	
Non-Hispanic White	9839 (40.7%)	9522 (40.186%)	317 (66.180%)	
Non-Hispanic Black	5292 (21.89%)	5225 (22.051%)	67 (13.987%)	
Other Race	3057 (12.65%)	3019 (12.741%)	38 (7.933%)	
Education level, n (%)				<0.001
Below high school	5454 (22.56%)	5281 (22.287%)	173 (36.117%)	
High school	5414 (22.4%)	5286 (22.309%)	128 (26.722%)	
Above high school	13306 (55.04%)	13128 (55.404%)	178 (37.161%)	
PIR	2.494±1.555	2.507±1.558	1.855±1.273	<0.001
BMI (kg/m2)	29.403±7.052	29.404±7.032	29.334±7.984	0.405
Hypertension, n (%)				<0.001
Yes	8905 (36.84%)	8608 (36.328%)	297 (62.004%)	
No	15269 (63.16%)	15087 (63.672%)	182 (37.996%)	
Diabetes, n (%)				<0.001
Yes	3251 (13.45%)	3126 (13.193%)	125 (26.096%)	
No	20316 (84.04%)	19989 (84.360%)	327 (68.267%)	
Borderline	607 (2.51%)	580 (2.448%)	27 (5.637%)	
Smoking behavior, n (%)				<0.001
Yes	10537 (43.59%)	10101 (42.629%)	436 (91.023%)	
No	13637 (56.41%)	13594 (57.371%)	43 (8.977%)	
Drinking behavior, n (%)				<0.001
Never drank	2730 (11.29%)	2704 (11.412%)	26 (5.428%)	
Used to drink	4137 (17.11%)	3966 (16.738%)	171 (35.699%)	
Be drinking	17307 (71.59%)	17025 (71.851%)	282 (58.873%)	
Asthma, n(%)				<0.001
Yes	3593 (14.86%)	3373 (14.235%)	220 (45.929%)	
No	20581 (85.14%)	20322 (85.765%)	259 (54.071%)	
Dietary live microbe group, n (%)				<0.001
Low	5135 (21.24%)	4978 (21.009%)	26 (5.428%)	
Medium	10494 (43.41%)	3966 (16.738%)	128 (26.722%)	
High	8545 (35.35%)	17025 (71.851%)	178 (37.161%)	

Mean±SD for continuous variables: the P value was calculated by the linear regression model (%) for categorical variables: the P value was calculated by the chi-square test. PIR, ratio of family income to poverty; BMI, body mass index.

Table 2. Association between dietary live microbe intake and emphysema.

Outcome	Model	Low dietary live microbes OR (95%CI)	Medium dietary live microbes OR (95%CI)	High dietary live microbes OR (95%CI)	p for trend
Emphysema	Model 1	1 (Reference)	0.622 (0.504, 0.769)	0.452 (0.355, 0.574)	0.00013
	Model 2	1 (Reference)	0.538 (0.433, 0.669)	0.378 (0.295, 0.485)	<0.00001
	Model 3	1 (Reference)	0.378 (0.295, 0.485)	0.595 (0.455, 0.777)	<0.00001

Model 1: no covariates were adjusted. Model 2: age, gender, race were adjusted. Model 3: age, gender, race, education level, PIR, BMI, hypertension, diabetes, smoking behavior, drinking behavior and asthma were adjusted. 95% CI, 95% confidence interval; PIR, ratio of family income to poverty; BMI, body mass index.

Table 3. Stratified analyses of the association between dietary live microbe intake and emphysema.

		OR (95% CI)	p for interaction
Stratified by age			
<40	Low	1 (Reference)	
<40	Medium	1.126 (0.359, 3.531)	
<40	High	0.818 (0.230, 2.912)	
Stratified by age			
40-60	Low	1(Reference)	0.6666
40-60	Medium	0.959 (0.624, 1.475)	
40-60	High	0.630 (0.377, 1.053)	
Stratified by age			
60	Low	1 (Reference)	
60	Medium	0.679 (0.513, 0.901)	
60	High	0.571 (0.412, 0.793)	
Stratified by gender			
Male	Low	1 (Reference)	
Male	Medium	0.531 (0.393, 0.718)	
Male	High	0.490 (0.344, 0.697)	0.0028
Stratified by gender			
Female	Low	1 (Reference)	
Female	Medium	1.229 (0.841, 1.796)	
Female	High	0.843 (0.550, 1.291)	
Stratified by BMI			
<30	Low	1 (Reference)	
<30	Medium	0.672 (0.501, 0.902)	
<30	High	0.600 (0.426, 0.846)	0.396
Stratified by BMI			
30	Low	1 (Reference)	
30	Medium	0.891 (0.611, 1.300)	
30	High	0.603 (0.392, 0.928)	
Stratified by diabetes			
Yes	Low	1 (Reference)	
Yes	Medium	0.804 (0.511, 1.265)	
Yes	High	0.553 (0.326, 0.937)	
Stratified by diabetes			
No	Low	1 (Reference)	0.9174
No	Medium	0.741 (0.560, 0.981)	
No	High	0.616 (0.444, 0.853)	
Stratified by diabetes			
Borderline	Low	1 (Reference)	
Borderline	Medium	0.586 (0.200, 1.717)	
Borderline	High	0.709 (0.202, 2.485)	
Stratified by hypertension			
Yes	Low	1 (Reference)	
Yes	Medium	0.728 (0.542, 0.977)	
Yes	High	0.517 (0.368, 0.727)	0.2759
Stratified by hypertension			
No	Low	1 (Reference)	
No	Medium	0.833 (0.573, 1.211)	
No	High	0.830 (0.537, 1.283)	
Stratified by asthma			
Yes	Low	1 (Reference)	
Yes	Medium	0.916 (0.639, 1.314)	
Yes	High	0.632 (0.417, 0.958)	0.3371
Stratified by asthma			
No	Low	1 (Reference)	
No	Medium	0.652 (0.483, 0.882)	
No	High	0.578 (0.407, 0.819)	
Stratified by smoking			
Yes	Low	1 (Reference)	
Yes	Medium	0.725 (0.570, 0.923)	
Yes	High	0.563 (0.424, 0.746)	0.2627
Stratified by smoking			
No	Low	1 (Reference)	
No	Medium	1.158 (0.494, 2.717)	
No	High	1.230 (0.485, 3.119)	
Stratified by drinking			
Never drank	Low	1 (Reference)	
Never drank	Medium	0.609 (0.218, 1.703)	
Never drank	High	0.449 (0.125, 1.607)	
Stratified by drinking			
Used to drink	Low	1 (Reference)	0.3407
Used to drink	Medium	0.573 (0.394, 0.835)	
Used to drink	High	0.431 (0.269, 0.689)	
Stratified by drinking			
Be drinking	Low	1 (Reference)	
Be drinking	Medium	0.896 (0.657, 1.221)	
Be drinking	High	0.731 (0.517, 1.033)	

In subgroup analyses stratified by age, gender, BMI, diabetes status, hypertension status and asthma, smoking behavior, drinking behavior. The model adjusted for covariates such as age, race, education level, PIR, BMI, hypertension, diabetes, smoking behavior, drinking behavior and asthma. But the model did not adjust for the stratification variables themselves.

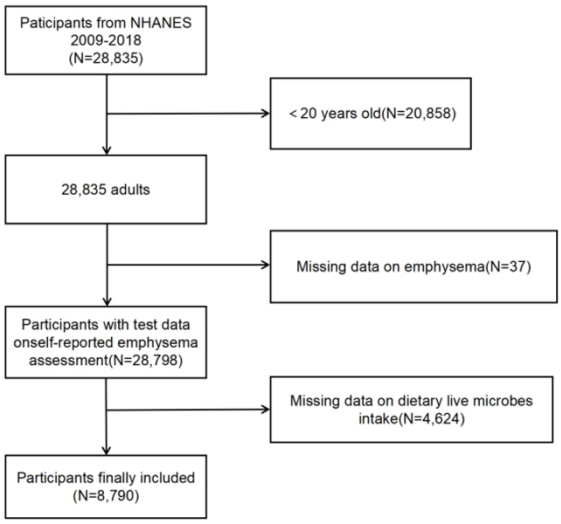

Figure 1. Flow chart of participants' selection.