Research Square

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The Effects of Dietary Nutrients and Physical Activity on Charlson Comorbidity Index Using Zero-Inflated Negative Binomial Regression Model: NHANES 2013–2014

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Abstract

Background: In recent years, chronic medical conditions have gradually became the dominant cause of death and disability, which combined with the increasing life expectancy, leading to multimorbidity became an increasingly serious global public health challenge. However, most existing studies have focused on the coexistence of specific diseases or relatively few diseases. Given one person may have various diseases at the same time, we applied Charlson Comorbidity Index (CCI) to synthetically evaluate one's 10-year mortality. In this study, we explored the effects of nutrients and physical activity on one's 10-year mortality using National Health and Nutrition Examination Survey (NHANES) 2013-2014 data.

Methods: The study sample consists of one continuous cycle (2013–2014) of NHANES, and 4386 eligible subjects were included in the study. We utilized zero-inflated negative binomial (ZINB) regression to investigate the effects in nutrients and physical activity on CCI by adjusting seven baseline covariates (age, gender, race, education, income, smoking and drinking).

Results: In Part 1 of the model, taking an extra gram of niacin resulted in 1.621 times of CCI versus eating less (RR=1.621, p=0.016). Conversely, lutein and zeaxanthin have a negative correlation with CCI (RR=0.974, p=0.031). Besides, sedentary time was also concerned significantly with CCI (RR=1.035, p=0.005). Moreover, those who do not have vigorous work activity would be more likely to have higher CCI than those who have (RR=1.275, P=0.045). In Part 2 of the model, those who do not have vigorous recreational activity have 0.541 times of taking CCI scored zero versus those who have (OR=0.541, p=0.004), and those who do not have moderate recreational activity have 0.708 times of taking CCI equals zero versus those who have (OR=0.708, p=0.017).

Conclusions: With the increasing intakes of niacin, participants were more likely to suffer from chronic diseases. However, lutein and zeaxanthin might have beneficial impact on individuals' health and decrease mortality. In the respect of physical activity, the death rate among people who have higher sedentary time and do not have vigorous work activity will be more likely to increase. In addition, persons do not have vigorous or moderate physical activity have the risk of death compared with those who have.

Background

Multimorbidity, usually refers to that one person is attacked by at least two chronic disease[1], has been linked to reduced quality of life, and dramatically increases death rates and health care costs[2]. In recent years, chronic medical conditions have gradually became the dominant cause of death and disability,

which combined with the increasing life expectancy, leading to multimorbidity became an increasingly serious global public health challenge[3, 4]. As a chronic disease, the death rate of diabetes increased by 32.1% between 2005 and 2015, while the death rate of diabetic nephropathy increased by 39.5% during the same period[5]. Increasing evidences show that diabetic patients will be more likely to suffer from one or more microvascular complications, including cardiovascular diseases, peripheral neuropathy, blindness, kidney diseases, and so on[6]. Moreover, researches indicated that hypertension, heart failure and diabetes were the most common comorbidities of chronic obstructive pulmonary disease, importantly, the incidence of patients with at least one comorbidity was 84.5%[7].

However, most existing studies have focused on the coexistence of specific diseases or relatively few diseases, such as diabetes, cardiovascular diseases cancer, rather than various chronic diseases affecting one person. Moreover, several studies have indicated that social determinants play an important part in pathological changes of the disease and were regarded as the direct cause of some chronic diseases, such as Type 2 diabetes, cardiovascular disease, cancers, infectious diseases and so on[8, 9] which includes income, education, occupation, lifestyles, government programs and many other elements that affect the health of individuals[10]. It has been demonstrated that nutrients and lifestyle changes can improve hypertension status[11, 12]. In addition, recent evidence suggests that smoking and drinking is associated with increased risk of cancers and other chronic diseases [13–15]. What is more, some large-scale population-based studies have indicated that serum folate concentration may be concerned with prostate cancer risk[16, 17]. Furthermore, patterns of dietary, intensity of physical activity and sedentary time play a crucial role in cardiovascular health[18].

Given one person may have various diseases at the same time, we applied Charlson Comorbidity Index (CCI) to synthetically evaluate one's 10-year mortality[19]. In this study, we explored the effects of nutrients and physical activity on one's 10-year mortality using National Health and Nutrition Examination Survey (NHANES) 2013–2014 data. Different from other studies, we investigated the relationship by utilizing zero-inflated negative binomial (ZINB) regression, which could distinguish those who have risk of death and those who have no risk, and find its relative factors respectively[20].

Methods

Study population

The study sample consists of one continuous cycle (2013–2014) of NHANES, which used a stratified multistage probability cluster design to be representative of the civilian, noninstitutionalized U.S. population, conducted by the National Center for Health Statistics, under the Centers for Disease Control and Prevention[21]. A total of 10175 individuals participated in NHANES during 2013–2014, but 5769 adults who were 20 years of age or older were restricted to our study. We excluded participants who were pregnant or lactating (n = 104). Besides, adults with caloric intakes of <500 kcal or >5000 kcal per day were excluded(n = 60). Then, we excluded 1219 participants due to missing covariate information, leaving 4386 eligible subjects for the study. Study protocols for NHANES were approved by the National

Center for Health Statistics ethnics review board. All the participants signed the informed consent before participating in the study.

Assessment of sociodemographic and lifestyle characteristics

The study included a number of covariates evaluated as potential confounding factors, such as age (20–39; 40–59; 60 and above); gender (male, female); race/ethnicity (Hispanic, Non-Hispanic White, Non-Hispanic Black, Other Race); educational attainment (less than high school; high school, including general equivalent diploma; college or higher); income ($0-$24999, $25000-$54999, $55000-$74999, $75000 or above); smoking (yes, no); drinking(yes, no).

In addition, physical activity was also incorporated into the paper. The Physical Activity Questionnaire is based on the Global Physical Activity Questionnaire[22], and the questions were asked using the Computer-Assisted Personal Interview software. The main outcomes of physical activity were defined using the following questions: (1) Sedentary activity: “How much time do you usually spend sitting on a typical day?”; (2) Vigorous work activity: “Does your work involve vigorous-intensity activity that causes large increases in breathing or heart rate like carrying or lifting heavy loads, digging or construction work for at least 10 minutes continuously?” (yes, no); (3) Moderate work activity: “Does your work involve moderate-intensity activity that causes small increases in breathing or heart rate such as brisk walking or carrying light loads for at least 10 minutes continuously?” (yes, no); (4) Moderate recreational physical activity: “Do you do any moderate-intensity sports, fitness, or recreational activity that cause a small increase in breathing or heart rate such as brisk walking, bicycling, swimming, or volleyball for at least 10 minutes continuously?” (yes, no); (5) Vigorous recreational physical activity: “Do you do any vigorous-intensity sports, fitness, or recreational activity that cause large increases in breathing or heart rate like running or basketball for at least 10 minutes continuously?” (yes, no).

Assessment of dietary nutrients

NHANES subjects were asked for two averaged 24-h recalls of dietary intakes using the USDA’s Automated Multiple-Pass method[23]. The first dietary recall was conducted by trained dietary interviewers, they gathered detailed information on all the foods and beverages participants consumed in the past 24 hours, and a second recall was administered by telephone 3 to 10 days later. The total dietary nutrients taken through food and beverages are averaged over two days, nonetheless, if one did not complete the second dietary interview, only the first interview was used for. Dietary supplements were also evaluated by the information on the number of days they were taken and the amount that were taken in the past 30 days. What is more, the level of supplements intakes was measured by the average intakes of 30 days. Furthermore, total dietary nutrients intakes were evaluated by foods and supplements.

Response variable

Forty nine chronic diseases (including infectious diseases like hepatitis) were included in the study, which were diagnosed by questionnaire data. Diagnosed diseases were defined by positive responses to one or more questions such as: “Have you ever been told that you have the illness?” and “Are you now taking some pills to control your disease?”. The comprehensive health status of a participant was measured by the Carlson Comorbidity Index (CCI) [24], which was shown in *Additional file 1.* Derived from adding up the scores of forty nine diseases, CCI evaluates a participant’s severity of comorbidity and the mortality in 10 years.

Statistical analyses

CCI was supposed as an over-dispersed and zero-inflated count variable, so we utilized zero-inflated negative binomial (ZINB) regression to appropriately model it[25, 26]. The model examined the association of the exposure variables, in this case dietary nutrients and physical activity, with the outcome variable (CCI) in two parts. Specifically, Part 1 models CCI for those at risk of having CCI equals to nonzero, and Part 2 models the odds of CCI equals to zero. The rate ratios (RRs) or odds ratios (ORs) of a covariate in the ZINB model means how the response variable varies with one-unit change of the explanatory variable while the other covariates remain unchanged. Seven covariates including age, gender, race, education, income, smoking and drinking were adjusted for both in the Part 1 and Part 2.

All analyses account for clusters pseudo-strata, pseudo-sampling units and participant weights to accommodate the complex sampling of the data, which were performed by using Stata/SE, version 15.1 statistical software. Two-sided $P < 0.05$ was considered significant for statistical inferences.

Results

Table 1 and *Table 2* shows descriptive statistics of the weighted, descriptive statistics of the complete case sample, which includes observed frequencies and weighted percentages of categorical variable, means and 95% confidence interval(CI) of continuous variables.The frequency distribution of CCI was shown in *Figure 1,* and there are too much zero.

Table 3 contains weighted RRs of CCI from Part 1 of ZINB regression models, which were adjusted for seven baseline covariates (age, gender, race, education, income, smoking and drinking). In Part 1 of the model, taking an extra gram of niacin resulted in 1.621 times of CCI versus eating less (RR = 1.621, p = 0.016). Conversely, lutein and zeaxanthin were associated with 0.974 times of CCI with every milligram of increased intake (RR = 0.974, p = 0.031). Besides, sedentary time was also concerned significantly with CCI (RR = 1.035, p = 0.005). Moreover, those who do not have vigorous work activity would be more likely to have higher CCI than those who have (RR = 1.275, P = 0.045).

In particular, *Table 3* shows weighted ORs of CCI (equals to zero) versus any CCI (zero and nonzero) from Part 2 of ZINB regression models as well, which were also adjusted for the baseline covariates (age, gender, race, education, income, smoking and drinking). Moreover, those who do not have vigorous

recreational activity have 0.541 times of taking CCI scored zero versus those who have (OR = 0.541, p = 0.004), and those who do not have moderate recreational activity have 0.708 times of taking CCI equals zero versus those who have (OR = 0.708, p = 0.017).

Discussion

Principal findings

After adjusting for the baseline covariates (age, gender, race, education, income, smoking and drinking), we have the following principal findings. With the increasing intakes of niacin, participants were more likely to suffer from chronic diseases. However, lutein and zeaxanthin might have beneficial impact on individuals' health and decrease mortality. In the respect of physical activity, the death rate among people who have higher sedentary time and do not have vigorous work activity will be more likely to increase. In addition, persons do not have vigorous or moderate physical activity have the risk of death compared with those who have.

Niacin

In our study, we found the higher the total niacin intake, the higher the risk of death. Recently, Park et al. [27] indicated that the higher the total niacin intake, the higher the risk of skin cancer. This is true only for men, but not for women. However, previous studies have reported that niacin is a protective factor for skin cancer[28, 29]. On the one hand, niacin promote the synthesis of sex hormones, and affect the development of melanocytes, and higher estrogen exposure increases the risk of skin melanoma[27, 30]. On the other hand, niacin may protect the skin from DNA damage caused by UV radiation through cellular processes such as DNA repair, genomic stability and transcription[28, 31]. Heinken et al.[32] have shown that niacin can be synthesized by large intestinal microbiota. Additionally, several studies have documented that niacin is able to improve the gut microbiome, and influence intestinal development[33, 34]. Moreover, as a kind of lifestyle intervention strategies, increasing intakes of niacin may have a role in reducing liver fat[35]. However, the intakes of niacin always accompanied with other B group vitamins or other nutrients, and this might mask the opposite relationship. More further researches in this area are needed in the future.

Lutein and zeaxanthin

Our study showed a negative correlation between the intakes of lutein and zeaxanthin and mortality. As a kind of carotenoids, lutein and its structural isomer zeaxanthin is widely distributed in the structure of plants exposed to sunlight and in the human retina[36, 37], and they are deemed as the only carotenoids in the neuroretina and lens[36]. In addition, acting as anti-oxidant, they also reduce oxidative damage indirectly by absorbing light[37, 38]. Early studies indicated that lutein and zeaxanthin may protect against inflammation by inhibiting the increase of oxidation-induced cytokines and upregulating the

expression of inflammation-related genes[39]. Moreover, recent evidence suggests that the more lutein and zeaxanthin consumed, the lower risk of colorectal cancer[40, 41], which might be attributed to the regulation of gene expression[40]. Furthermore, lutein and zeaxanthin may reduce the risk of cancer types especially breast and lung cancers, as well as suppressing heart disease and stroke[42]. Heinen et al.[43] indicated that lutein and zeaxanthin also plays a crucial role in skin cancer. It's function of controlling the occurrence of disease might contributed to the following functions. As antioxidants, zeaxanthin effectively remove water-soluble and lipid-soluble peroxyl radicals[44]. Animal studies suggested that lutein and zeaxanthin could reduce the adverse effects of inflammatory cytokines and low density lipoprotein on blood vessels[45, 46].

Sedentary time and physical activity

We concluded that individuals who have higher sedentary time and do not have vigorous work activity will be more likely to have higher rate of death. And people who do not have vigorous recreational activity or moderate recreational activity have the risk of death. Previous studies have reported that there is a negative correlation between health status and sedentary time, which is associated with chronic diseases and overall mortality[47, 48]. For adults and the elderly, inactivity in leisure time and high television time increase the incidence of chronic diseases[49]. Moreover, a research from NHANES 2009–2012 pointed out that increasing time spent on physical activity will lead to lower risk of chronic diseases[50]. However, some researchers suggested that high activity level could weaken the increased risk associated with excessive sedentary time[51]. Importantly, this provide us with a novel idea that our study could consider the interaction between physical activity and sedentary time in further studies.

Limitations

Several limitations of this study should be noted. Firstly, some of the participants were excluded due to the missing data. Secondly, we have a conservative assignment for CCI, and we consider those who have missing value of diseases as the healthy. Furthermore, a dietary recall is less accurate than a urine sample, which may result in a false estimate of dietary nutrients intake. Finally, we can't get a causal correlation due to the study was a cross-sectional survey.

Abbreviations

CCI: Charlson Comorbidity Index

NHANES: National Health and Nutrition Examination Survey

OR: odds ratio

RR: rate ratio

ZINB: zero-inflated negative binomial

Declarations

Availability of data and materials

Data sharing is not applicable to this article.

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Contributions

BL, LJ and HZ designed the study; HZ, CW and YP performed the study; HZ, NY and YG analyzed the data and drafted the manuscript; HZ and HW participated amending the manuscript. All authors approved the final version of the manuscript.

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Ethics declarations

Ethics approval and consent to participate

Study protocols for NHANES were approved by the National Center for Health Statistics ethnics review board. All the participants signed the informed consent before participating in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1 Descriptive characteristics of categorical variables, NHANES 2013-2014 (n=4386)

Variable	Study Participants	
	n	%*
Age		
20-39	1456	34.92
40-59	1501	37.14
60 and above	1429	27.94
Gender		
Male	2154	49.57
Female	2232	50.43
Race/ethnicity		
Hispanic	946	13.79
Non-Hispanic White	2018	68.72
Non-Hispanic Black	863	10.49
Other Races (Including Multi-Racial)	559	7
Educational attainment		
Less than High school	842	13.63
GED/AA degree	2396	55.18
College and higher	1148	31.2
Income		
0-24999	1343	22.51
25000-54999	1275	27.14
55000-74999	470	12
75000 and above	1298	38.35
Smoking		
Yes	1942	43.81
No	2444	56.19
Drinking		
Yes	3219	78.61
No	1167	21.39
Vigorous work activity		
Yes	847	20.07
No	3539	79.93
Moderate work activity		
Yes	1516	36.88
No	2870	63.12
Vigorous recreational activity		
Yes	1017	25.28
No	3369	74.72
Moderate recreational activity		
Yes	1870	45.59
No	2516	54.41

*All data are weighted to be nationally representative.

Table 2 Descriptive characteristics of continuous variables, NHANES 2013-2014 (n=4386) *

Variable	Study Participants	
	mean	CI
Protein (gm)	82.75	(80.75, 84.74)
Carbohydrate (gm)	245.3	(241.47, 249.13)
Dietary fiber (gm)	16.99	(16.43, 17.56)
Total fat (gm)	80.43	(78.80, 82.05)
Vitamin A (mcg)	634.52	(602.07, 666.97)
Thiamin (Vitamin B1) (mg)	7.49	(4.86, 10.13)
Riboflavin (Vitamin B2) (mg)	4.62	(3.96, 5.27)
Niacin (mg)	37.1	(34.25, 39.96)
Vitamin B6 (mg)	7.36	(3.18, 11.54)
Folate (mcg)	526.76	(506.24, 547.29)
Vitamin B12 (mcg)	78.27	(64.21, 92.33)
Vitamin C (mg)	178.68	(159.52, 197.84)
Vitamin K (mcg)	133.82	(121.07, 146.58)
Vitamin D (D2 + D3) (mcg)	18.11	(16.48, 19.75)
Vitamin E (mg)	10.12	(9.65, 10.59)
Calcium (gm)	1.12	(1.08, 1.15)
Phosphorus (gm)	1.39	(1.35, 1.42)
Magnesium (mg)	331.94	(320.21, 343.67)
Iron (mg)	17.88	(17.16, 18.60)
Zinc (mg)	15.51	(14.86, 16.16)
Copper (mg)	1.52	(1.45, 1.59)
Sodium (gm)	3.47	(3.40, 3.53)
Potassium (gm)	2.66	(2.58, 2.73)
Selenium (mcg)	132.91	(129.40, 136.42)
Water (kg)	2.94	(2.84, 3.04)
Cholesterol (mg)	292.52	(283.01, 302.03)
Lycopene (mg)	5.08	(4.84, 5.31)
Lutein + zeaxanthin (mg)	1.77	(1.64, 1.89)
Alpha-carotene(mcg)	419.27	(370.40, 468.13)
Beta-carotene (mg)	2.29	(2.08, 2.50)
Beta-cryptoxanthin (mcg)	84.92	(78.29, 91.55)
Total choline (mg)	336.22	(325.92, 346.53)
Hours sedentary activity	7.12	(6.91, 7.32)

*All data are weighted to be nationally representative.

Table 3 Adjusted RRs and adjusted ORs of Carlson comorbidity index *

Variable	Part 1		Part 2	
	RR	p-Value	OR	p-Value
Protein (kg)	0.171	0.211	36.039	0.140
Carbohydrate (kg)	0.462	0.079	0.562	0.484
Dietary fiber (gm)	0.991	0.074	0.996	0.600
Total fat (kg)	0.223	0.132	0.167	0.386
Vitamin A (mg)	0.934	0.479	1.059	0.677
Thiamin (Vitamin B1) (gm)	0.820	0.538	0.089	0.506
Riboflavin (Vitamin B2) (gm)	25.700	0.371	25.482	0.439
Niacin (gm)	1.621	**0.016**	0.445	0.337
Vitamin B6 (gm)	15.134	0.183	3.590	0.783
Folate (mg)	1.085	0.240	1.021	0.890
Vitamin B12 (mg)	0.988	0.786	0.925	0.437
Vitamin C (gm)	1.111	0.239	0.860	0.479
Vitamin K (mg)	1.007	0.231	0.929	0.106
Vitamin D (D2 + D3) (mg)	2.242	0.152	0.383	0.594
Vitamin E (mg)	0.998	0.764	1.008	0.333
Calcium (gm)	1.072	0.170	1.206	0.065
Phosphorus (gm)	0.933	0.448	1.274	0.118
Magnesium (gm)	1.004	0.984	1.374	0.303
Iron (gm)	2.711	0.565	0.332	0.807
Zinc (gm)	7.067	0.350	3.406	0.854
Copper (mg)	1.018	0.482	1.042	0.537
Sodium (gm)	0.959	0.123	1.049	0.419
Potassium (gm)	0.924	0.157	1.045	0.432
Selenium (mg)	0.862	0.612	4.182	0.268
Water (kg)	0.983	0.559	1.052	0.273
Cholesterol (gm)	0.994	0.973	1.527	0.415
Lycopene (mg)	0.992	0.140	1.008	0.479
Lutein + zeaxanthin (mg)	0.974	**0.031**	0.972	0.477
Alpha-carotene(mg)	0.945	0.253	0.879	0.450
Beta-carotene (mg)	0.987	0.411	0.992	0.785
Beta-cryptoxanthin (mg)	0.863	0.133	0.602	0.240
Total choline (gm)	0.828	0.442	1.639	0.306
Hours sedentary activity	1.035	**0.005**	1.001	0.948
Vigorous work activity				
Yes	Reference		Reference	
No	1.275	**0.045**	1.501	0.060
Moderate work activity				
Yes	Reference		Reference	
No	0.984	0.788	0.842	0.457
Vigorous recreational activity				
Yes	Reference		Reference	
No	0.977	0.828	0.541	**0.004**
Moderate recreational activity				
Yes	Reference		Reference	
No	1.030	0.680	0.708	**0.017**

*All data are weighted to be nationally representative.

Figures

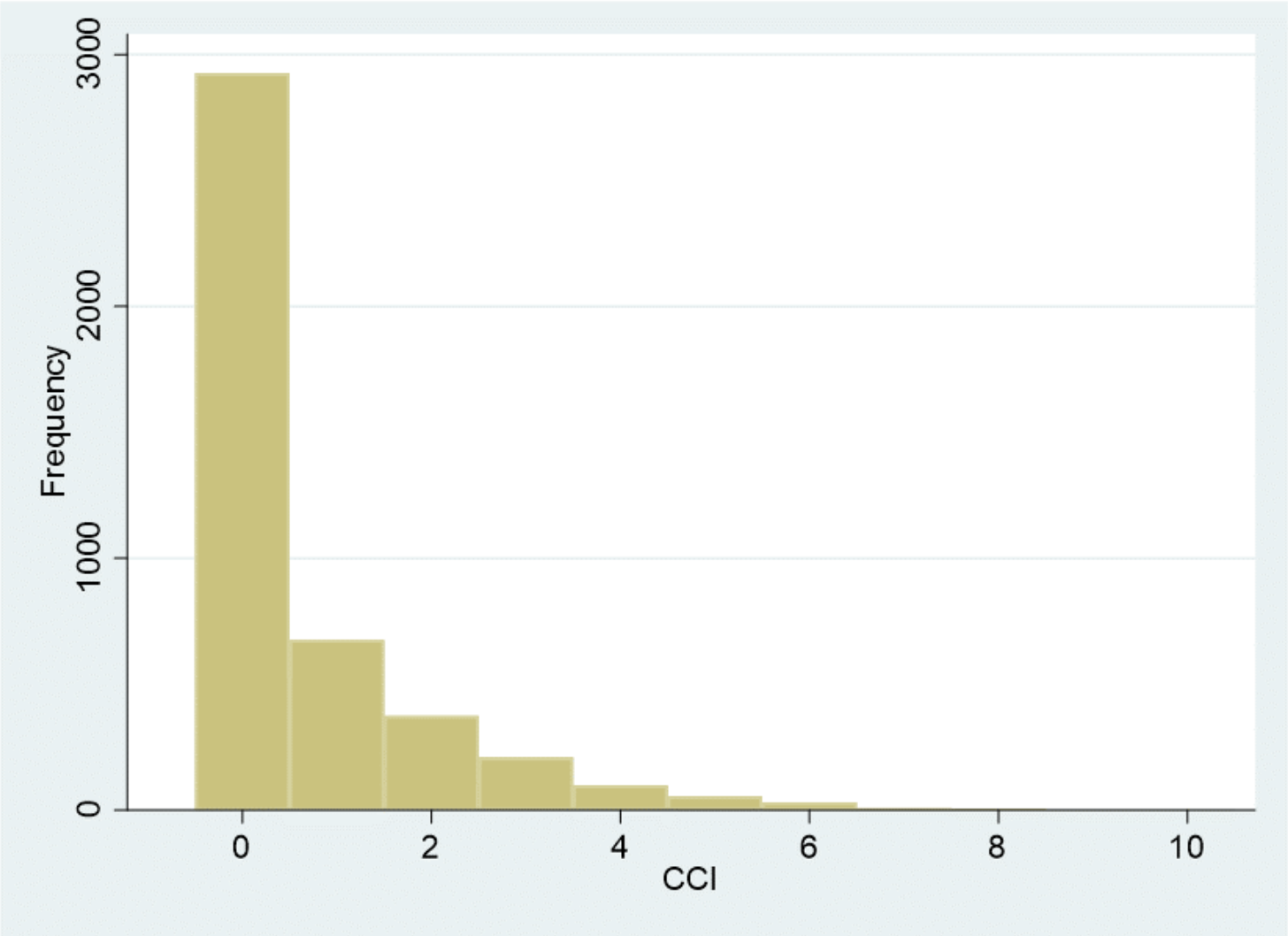


Figure 1

The frequency distribution of Carlson comorbidity index (CCI).

Supplementary Files

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- Additionalfile1.xlsx