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Association of modifiable risk factors and infectious diseases among individuals with hypertension: a prospective cohort study

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Abstract

Background A comprehensive assessment of combined modifiable risk factors in relation to infectious diseases among individuals with hypertension is lacking, and the potential mechanisms of these associations remain unclear. To investigate the prospective associations of a combination of lifestyle behaviors and cardiometabolic factors with the risk of infectious diseases among individuals with hypertension and to estimate whether and to what extent blood biomarkers mediate these associations.

Methods This cohort study included 147,188 participants with hypertension and complete data on modifiable risk factors from the UK Biobank. Health score was constructed from eight modifiable risk factors, including four lifestyle behaviors (diet, physical activity, smoking, and sleep duration) and four cardiometabolic factors (body mass index, blood lipids, blood glucose, and blood pressure). Cox proportional hazards regression analysis was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the health score and infectious diseases. The mediation analysis was performed to assess the potential intermediation effects of blood biomarkers.

Results Over a median follow-up of 12.5 years, 27,398 participants with infectious diseases were documented, with 960 respiratory infectious diseases and 7940 digestive infectious diseases. After adjusting for potential confounders, the HR (95% CI) for the highest versus the lowest quartile of health score was 0.64 (0.62, 0.66) for infectious diseases, 0.72 (0.60, 0.86) for respiratory infectious diseases, and 0.66 (0.62, 0.71) for digestive infectious diseases. Stratified factors including duration of hypertension did not modify the associations between the health score and infectious diseases. In addition, biomarkers including inflammation and renal function collectively explained 46.60% of the associations between the combined lifestyle factors and infectious disease risk among individuals with hypertension.

Conclusions and relevance Ideal management of combined modifiable risk factors was associated with lower risks of infectious diseases and might produce profound changes in blood biomarkers among individuals with hypertension. Additionally, specific biomarkers appeared to serve as an intermediate between combined lifestyle factors and infectious diseases. These insights highlighted the important role of a combination of healthy lifestyle

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and favorable cardiometabolic status in reducing disease burden and facilitated the understanding of biological mechanisms underlying modifiable risk factors with infectious diseases.

Keywords Modifiable risk factor, Health risk, Biomarkers, Hypertension, Mediation analysis

Introduction

The growing pandemic of hypertension poses an enormous public health issue for almost every country [1–3]. In addition to well-established increased risks of premature death and cardiovascular diseases (CVD) [1], hypertension may contribute to the burden of infectious diseases [4–6]. Hypertension has been associated with a greater risk of infection death in the cohort study [4]. Although single factors have been association with outcomes regarding hypertension [7], evidence for cost-effective strategies to prevent infectious diseases in individuals with hypertension is sparse.

Beyond taking medications properly, the American Heart Association has emphasized the integral roles of adhering to a healthy lifestyle and maintaining a healthy weight in preventing and managing hypertension [8]. However, the combined beneficial effect of these modifiable factors on infectious diseases are not comprehensively quantified [9–11]. Therefore, a large longitudinal study is warranted to investigate the combined effect of lifestyle and cardiometabolic risk factors on infectious diseases among people with hypertension, which may facilitate impactful translation of epidemiology findings into public health practice. In addition, the mechanisms underlying the above associations remain undiscovered, leaving practical obstacles to capturing the complexity of modifiable risk factors with diseases [8]. Exploring whether, and to what extent, these blood biomarkers link modifiable risk factors to infectious diseases could enhance our understanding of the mechanisms underlying these associations.

To narrow these knowledge gaps, we aim to investigate the associations between combined modifiable risk factors and the risk of infectious diseases (e.g., respiratory and digestive infectious diseases) among individuals with hypertension, while also assessing the possible mediating effects of blood biomarkers on these associations.

Methods

Study population

The UK Biobank is a large population-based cohort study, which recruited around half a million participants aged 40–69 years in 2006–2010 across England, Scotland, and Wales. Each participant completed touchscreen questionnaires, underwent physical examinations, and provided biological samples. The study design and methods have been described in detail previously [12]. The UK Biobank received ethical approval from the North West Multi-Centre Research Ethical Committee and all participants provided written informed consent. The data were accessed for research purposes on June 3, 2023. The authors did not have access to information that could identify individual participants during or after data collection.

Prevalent hypertension was defined as blood pressure results exceeding 90/140 mm Hg for diastolic and systolic blood pressure, respectively, or self-reported use of hypertension medication, along with hospitalization records coded (International Classification of Diseases, Tenth Revision [ICD-10]: I10.0–I15.9), and 227,761 participants with hypertension were identified at the baseline. After exclusion of participants who subsequently withdrew from the study ($n=117$), with cancer ($n=8865$) and those with incomplete data on modifiable risk factors ($n=71,659$), 147,118 were included for the association analyses (Supplementary Fig. 1).

Definition of health score

The health score was computed based on the Life's Essential 8 (LE8) metrics, as defined by the American Heart Association in 2022 [8]. LE8 comprises four health behaviors (diet, physical activity, smoking, and sleep duration) and four cardiometabolic factors (body mass index [BMI], blood lipids, blood glucose, and blood pressure). Self-reported data were collected on diet (validated food frequency questionnaire), physical activity (minutes of moderate or vigorous physical activity per week), smoking (smoking status), sleep duration, and the use of antihypertensive and antidiabetic medication. Weight, height, and blood pressure were measured during a physical examination, with BMI calculated as weight in kilograms divided by the square of height in meters. Blood biomarkers, such as total cholesterol, high-density lipoprotein cholesterol, glucose levels, and glycosylated hemoglobin, were obtained from random blood samples taken at baseline. These biomarkers have undergone external validation in the UK Biobank and are outlined in detail within the document [13]. Each component was assigned a score from 0 to 100 based on pre-specified categories in the LE8 metrics, using the available data. For example, five smoking categories including current smoker, former smoker (quit < 1 year), former smoker (quit 1 to < 5 years), former smoker (quit ≥ 5 years), and never smoker, corresponding to 0, 25, 50, 80, and 100 points, respectively. The details of the assessment of the health score are shown in Supplementary Table 1. The health score was calculated as the average of all eight

component metric scores and ranged between 0 and 100, with higher scores indicating healthier status.

Assessment of covariates

At baseline, demographic information (age, sex, and ethnicity), socioeconomic factors (household income, educational attainment, employment status, and Townsend deprivation index), alcohol consumption, and hypertension-related details (duration of hypertension and use of hypertension medication) were collected through both touchscreen questionnaires and interviews conducted by nurses. Educational attainment was categorized into three groups: high (college or university degree), intermediate (A levels, AS levels, or equivalent; O levels, GCSEs, or equivalent; CSEs or equivalent; NVQ, HND, HNC, or equivalent; other professional qualifications), and low qualification (none of the above). Employment status was divided into employed (including those in paid employment or self-employed, retired individuals, individuals engaged in unpaid or voluntary work, or full or part-time students) and unemployed (comprising individuals who were unemployed, caring for their home and/or family, or unable to work due to sickness or disability). The Townsend Deprivation Index scores, derived from national census data based on postcodes of residence and considering factors such as car ownership, household overcrowding, home ownership, and unemployment, represent the extent of socioeconomic deprivation, with higher scores indicating greater area-level deprivation. These values range from −6.26 to 3.41. The estimated glomerular filtration rate (eGFR) was determined using the Chronic Kidney Disease Epidemiology Collaboration equation [14].

Ascertainment of outcomes

Information on incident infectious diseases were identified through linkage with hospital inpatient admissions, self-reported data, primary care data, and death registries. The primary outcome was the incidence of all-cause infectious diseases, defined using ICD-10 code (A00-B99 and J00-J22) [15]. The most prevalent conditions among these were gastroenteritis and colitis of unspecified origin (18.5%) and unspecified septicemia (11.6%). Furthermore, we also defined three subtypes of infectious diseases as secondary outcomes: respiratory infectious diseases (A15, A37, A39, B01, B02, B05, B06, B26, and J09-J11), digestive infectious diseases (A00-A09, B15, B17.2, B67, B68, B77, B80, and B82), blood or sexually transmitted infectious diseases (A50-A64, B16, B17.1, B18.0, B18.1, B18.2 and B20-B24). Date of diagnosis was defined by the earliest diagnosed date for the outcomes during follow-up.

Statistical analysis

Baseline characteristics were examined using *chi*-squared test or *t* test (Wilcoxon rank-sum test for non-normal distributed continuous variables) according to the quartiles of health score. Person-time was computed from the date of attending the assessment center until the date of outcome diagnosis, death, or the end of follow-up, whichever came first. Multivariable Cox proportional hazards regression model was used to calculate associated hazard ratios (HRs) and 95% confidence intervals (CIs) between health score and infectious diseases. Schoenfeld residuals were used to test the proportional hazards assumption, and no violation was observed. Multivariable models were adjusted for age (continuous, years), sex (male, female), ethnicity (white, non-white), Townsend deprivation index (continuous), education attainment (high, intermediate, and low qualifications), employment status (employed, unemployed), household income (<£18 000, £18 000–30 999, £31 000–51 999, £52 000-100 000, >£100 000), alcohol consumption (yes, no), hypertension duration (continuous, years), and use of hypertension medication (yes, no). The percentage of missing values are present in Supplementary Table 2. The missing values of covariates were imputed and analyzed using multiple imputations with 5 imputations. In addition, a restricted cubic spline model with three knots (10th, 50th, and 90th percentiles) was performed to explore the dose-response relationship between health score and infectious diseases. We performed stratified analyses to examine the association of health score with risks of infectious diseases by age (<60 or ≥60 years), sex (male or female), education (College or university, or others), employment status (employed or unemployed), drinking status (non-current drinker, or current drinker), Townsend deprivation index (<median or ≥median), duration of hypertension (<5.0 or ≥5.0 years), and eGFR (<60 or ≥60 ml/min/1.73m^2). Interactions between health score and stratified factors on risk of outcomes were examined using the likelihood ratio test by adding multiplicative terms in the multivariable-adjusted Cox models. To assess the strength of our findings, we replicated the analyses using the weighted health score and excluding individuals who died or reached endpoints within two years of follow-up. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) and R software (version 4.3.1; R Foundation for Statistical Computing). *P* values after the Benjamini–Hochberg false discovery rate (FDR) adjustment <0.05 were considered statistically significant.

Results

Among 147,118 participants with hypertension, 67,501 (45.9%) were female, with a mean age of 58.6 years. The baseline characteristics of participants according to health score are shown in Table 1. Overall, participants

Table 1 Baseline characteristics of the study population according to quartiles of the health score

	The health score				*P* value
	Q1	Q2	Q3	Q4	
Number of patients	36,586	34,633	38,833	37,066	
Age	57.8 (7.5)	58.7 (7.4)	59.0 (7.4)	58.7 (7.6)	< 0.001
Male	22,505 (61.5)	19,711 (56.9)	20,430 (52.6)	16,971 (45.8)	< 0.001
Ethnic, White[†]	34,768 (95.3)	33,053 (95.7)	37,068 (95.7)	35,563 (96.2)	< 0.001
College or university degree[†]	8905 (24.6)	9678 (28.2)	12,432 (32.3)	14,092 (38.3)	< 0.001
Employed[†]	32,209 (88.3)	31,758 (92.0)	36,120 (93.2)	34,529 (93.4)	< 0.001
TDI[†]	-0.9 (3.3)	-1.4 (3.0)	-1.7 (2.9)	-1.9 (2.7)	< 0.001
Current drinkers[†]	33,748 (92.3)	32,103 (92.7)	36,102 (93.0)	34,463 (93.0)	< 0.001
eGFR	90.3 (15.3)	91.8 (14.5)	93.3 (14.2)	95.7 (13.7)	< 0.001
Use of blood pressure medication	15,816 (43.2)	13,180 (38.1)	13,038 (33.6)	10,273 (27.7)	< 0.001
Diet score	32.4 (27.7)	44.2 (28.5)	53.2 (27.1)	68.8 (22.5)	< 0.001
Physical activity score	73.3 (30.8)	85.2 (24.5)	91.4 (18.6)	96.0 (12.0)	< 0.001
Smoking score	59.1 (40.0)	79.0 (29.4)	87.6 (21.0)	93.3 (13.5)	< 0.001
Sleep score	81.7 (23.6)	88.2 (19.0)	91.7 (15.8)	95.2 (12.0)	< 0.001
BMI score	44.7 (27.8)	58.2 (27.1)	69.7 (24.2)	83.8 (19.2)	< 0.001
Blood lipid score	34.1 (26.4)	40.5 (26.7)	46.1 (26.3)	60.9 (26.7)	< 0.001
Blood glucose score	76.4 (27.2)	86.9 (22.3)	92.2 (18.1)	96.8 (12.0)	< 0.001
Blood pressure score	25.6 (18.2)	29.2 (18.3)	32.7 (18.2)	39.0 (18.4)	< 0.001

Data are presented as mean (SD) for continuous variable and n (%) for categorical variables. [†] The missing values of these covariates ranged from 0.1–2.4%. *P* values for differences in baseline characteristics were estimated by ANOVA or chi-squared test

TDI, Townsend deprivation index; eGFR, estimated glomerular filtration rate; BMI, body mass index

with higher health score were relatively older, were more likely to be female, non-white, employed, and have a higher education qualification, better economic status, and were current drinkers.

During a median follow up of 12.5 years, we documented 27,398 incident infectious diseases including 960 respiratory infectious diseases, 7940 digestive infectious diseases, and 160 blood or sexually transmitted infectious diseases. Associations of quartiles of the health score with incident infectious diseases are shown in Table 2. In the fully adjusted model, compared with patients who had the lowest quartile of the health score, the multivariable-adjusted HRs (95% CI) for patients had the highest quartile of the health score were 0.64 (0.62, 0.66) for infectious diseases, 0.72 (0.60, 0.86) for respiratory infectious diseases, 0.66 (0.62, 0.71) for digestive infectious diseases. After adjusting for confounding factors, the association between the health score and blood or sexually transmitted infectious diseases was not significant. The health score was associated with lower risk of incident infectious diseases in a dose-response manner (Supplementary Fig. 2, $P_{overall} < 0.001$, and $P_{nonlinearity} = 0.007$).

In stratified analyses, the associations between the health score and risk of infectious diseases were consistent across various subgroups, including age, sex, education levels, employment status, drinking status, deprivation, duration of hypertension, and eGFR, with no significant multiplicative interaction observed ($P_{interaction} > 0.05$, Fig. 1).

In mediation analysis, all the biomarkers were significantly associated with the overall lifestyle score except for aspartate aminotransferase and total cholesterol (Supplementary Table 3). The associations between the selected biomarkers and infectious diseases are shown in Supplementary Table 4. Eight significant mediators were detected on the associations of lifestyle score with risk of infectious diseases. Specifically, the relationship between the lifestyle score and risk of infectious diseases was mediated by hs-CRP, Cystatin C, GGT, HbA1c, Albumin, HDL, ALP, and Apolipoprotein A with the proportion of mediation effect ranging from 4.1 to 21.9% (Table 3). Collectively, the mediators explained 46.60% (42.80, 50.40) of the associations of the lifestyle score with infectious diseases (Table 3).

In sensitivity analyses, the weighted health score was constructed based on the association between individual components of the health score and infectious diseases (Supplementary Table 5). After adjusting for covariates and other components, diet, non-HDL cholesterol, and blood pressure were not significantly associated with infectious diseases. The results were generally robust when using the weighted health score (Supplementary Table 6). In addition, the results were largely consistent after excluding patients who developed infectious diseases within the first two years of follow-up (Supplementary Table 7), or repeating the analysis among participants with complete data on all covariates (Supplementary Table 8).

Table 2 Associations between the health score and infectious diseases among patients with hypertension

	The health score				P_{trend}
	Q1 (*N* = 36586)	Q2 (*N* = 34633)	Q3 (*N* = 38833)	Q4 (*N* = 37066)	
Infectious diseases					
Number of events	8773	6626	6531	5468	
Model 1	Reference	0.74 (0.72, 0.77)	0.63 (0.61, 0.65)	0.56 (0.54, 0.57)	< 0.001
Model 2	Reference	0.78 (0.75, 0.80)	0.68 (0.66, 0.71)	0.61 (0.59, 0.64)	< 0.001
Model 3	Reference	0.79 (0.77, 0.82)	0.70 (0.68, 0.73)	0.64 (0.62, 0.66)	< 0.001
Respiratory infectious diseases					
Number of events	301	225	219	215	
Model 1	Reference	0.74 (0.62, 0.88)	0.62 (0.52, 0.74)	0.64 (0.54, 0.76)	< 0.001
Model 2	Reference	0.77 (0.65, 0.92)	0.67 (0.56, 0.80)	0.70 (0.58, 0.83)	< 0.001
Model 3	Reference	0.78 (0.66, 0.93)	0.68 (0.57, 0.81)	0.72 (0.60, 0.86)	< 0.001
Digestive infectious diseases					
Number of events	2484	1918	1949	1580	
Model 1	Reference	0.77 (0.72, 0.82)	0.68 (0.64, 0.72)	0.57 (0.53, 0.60)	< 0.001
Model 2	Reference	0.81 (0.76, 0.86)	0.73 (0.69, 0.78)	0.63 (0.59, 0.67)	< 0.001
Model 3	Reference	0.82 (0.77, 0.87)	0.76 (0.71, 0.81)	0.66 (0.62, 0.71)	< 0.001
Blood or sexually transmitted infectious diseases					
Number of events	54	33	44	29	
Model 1	Reference	0.68 (0.44, 1.05)	0.82 (0.55, 1.23)	0.60 (0.38, 0.94)	0.007
Model 2	Reference	0.70 (0.42, 1.13)	1.00 (0.64, 1.53)	0.75 (0.44, 1.23)	0.187
Model 3	Reference	0.79 (0.51, 1.22)	1.06 (0.70, 1.59)	0.82 (0.51, 1.30)	0.314

Cox proportional hazards models were used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) of infectious diseases according to the health score

Model 1: adjusted for age (continuous, years), sex (male or female), and ethnicity (white, non-white)

Model 2: Model 1 + drinking status (never drinker, former drinker, or current drinker), education levels (college or university, high school or equivalent, or others), employment status (employed, unemployed), household income (<£18 000, £18 000–30 999, £31 000–51 999, £52 000-100 000, >£100 000), and Townsend deprivation index (continuous)

Model 3: Model 2 + hypertension duration (continuous, years) and use of hypertension medication (yes or no)

Discussion

In this prospective cohort study, we observed a significant inverse association between the combination of healthy lifestyles and favorable metabolic status with infectious diseases including respiratory infectious diseases and digestive infectious diseases among individuals with hypertension. Compared to individuals in the lowest quartile, those in the highest quartile of health score had a 36% lower risk of developing overall infectious diseases. Furthermore, blood biomarkers, including those related to inflammation and renal function, collectively explained nearly half of the associations between lifestyle factors and infectious diseases.

Our study contributes to the literature regarding the influence of the combination of healthy lifestyles and favorable metabolic status on the risk of infectious diseases. To date, although many studies have evaluated the relationship between individual lifestyle behaviors (e.g., smoking) and risk of infectious diseases [7, 16], the joint association of multiple lifestyle behaviors and biomarkers with infectious diseases remains unknown. For example, previous cohort study has demonstrated that risk of infectious diseases was significantly associated with multiple lifestyle behaviors [17, 18]. In addition, the associations were consistent across different subgroups (e.g., socioeconomic status) [15]. Regarding metabolism, elevated adiposity status was causally associated with higher risk of infectious diseases [9]. Additionally, there's evidence suggesting an inverse relationship between HDL cholesterol (HDL-C) levels and the risk of infectious hospitalizations, while no such association was found for LDL cholesterol (LDL-C) or triglyceride levels [19]. However, the evidence regarding the combined beneficial effect of these modifiable factors on infectious diseases are not comprehensively quantified. This study also added evidence about the consistent protective effect on different infection subtypes, including respiratory infectious diseases and digestive infectious diseases. Further trials with appropriate designs are necessary to confirm the effect of modifiable variables (e.g., dietary patterns) and validate our findings in the future.

Associations between hypertension and infectious disease have been well-described [4, 20]. The hypertension, inflammation, and immune system are interconnected [21]. As defined by the American Heart Association, Life's Essential 8 serve as crucial benchmarks for enhancing and sustaining cardiovascular health, with several longitudinal studies investigating their relationships with adverse outcomes in the general population [22–26]. However, prospective studies examining the beneficial

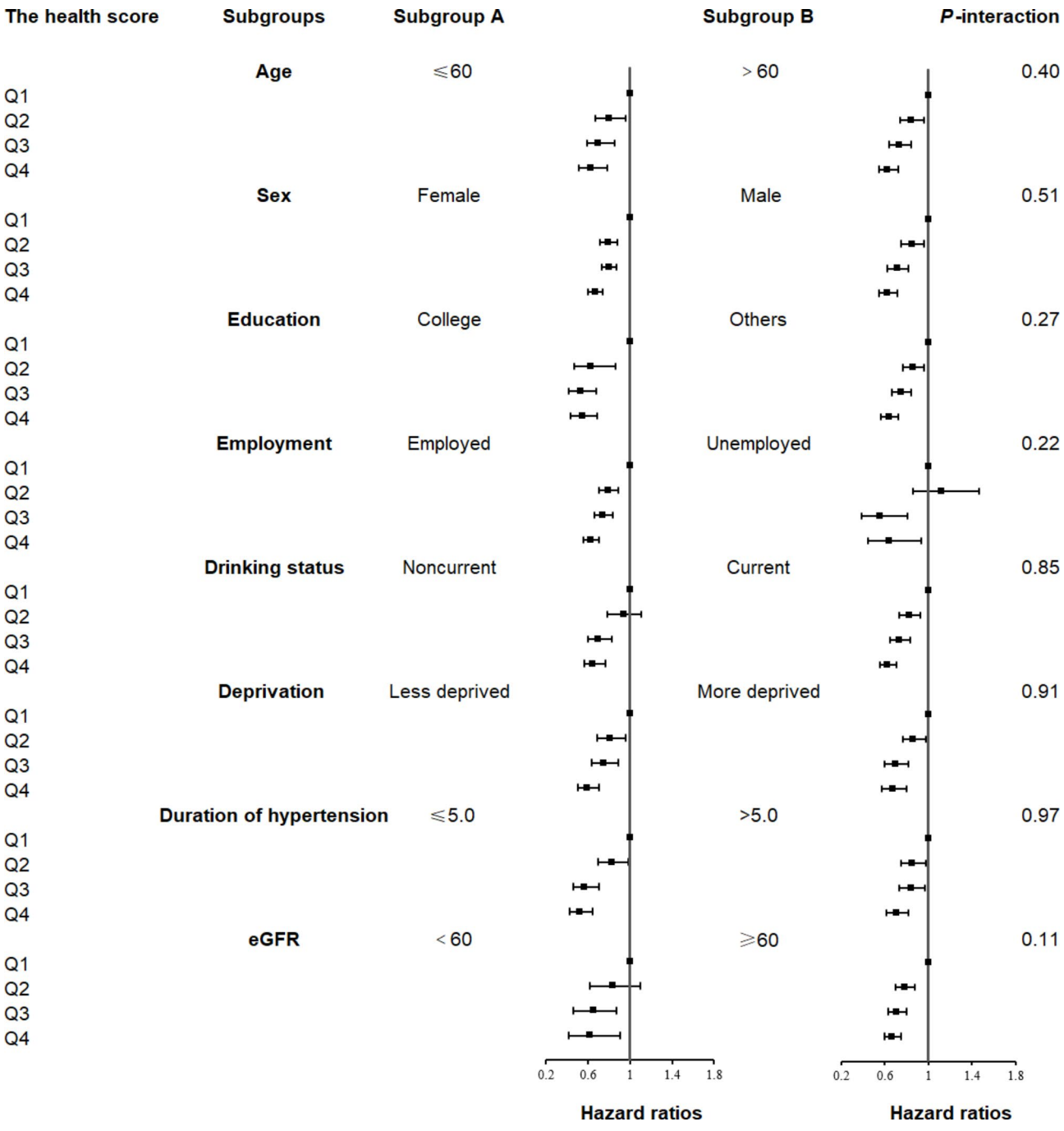

Fig. 1 Stratified analyses were conducted to examine the associations between the health score and infectious diseases among patients with hypertension. The models were adjusted for the aforementioned covariates. Interactions between the health score and stratified factors on the risk of outcomes were examined using the likelihood ratio test by adding product terms in the multivariable-adjusted Cox models

effect of modifying risk factors on infectious diseases among individuals with hypertension were sparse [7, 20]. Previous research has revealed important interactions between socioeconomic status (SES) and various lifestyle factors, indicating that individuals with lower SES face an elevated risk of overall infections, particularly evident among males and non-white populations [15]. While the current study extends these findings by consistently demonstrating significant associations between combinations of modifiable risk factors and infectious diseases across different subgroups of individuals with hypertension. These findings highlight the significance of addressing multiple modifiable risk factors as part of comprehensive health promotion efforts for individuals with hypertension. Further trials employing appropriate

Table 3 Association of lifestyle score with infectious diseases mediated by biomarkers among patients with hypertension*

	Total effect				Natural direct effect				Natural indirect effect				Proportion mediated	
	Beta	Lower	Upper	*P*	Beta	Lower	Upper	*P*	Beta	Lower	Upper	*P*	% (95%CI)	*P*
Infectious diseases														
hs-CRP	-0.0127	-0.0150	-0.0104	< 0.001	-0.0095	-0.0119	-0.0071	< 0.001	-0.0032	-0.0039	-0.0025	< 0.001	21.85 (19.66, 24.03)	< 0.001
Cystatin C	-0.0123	-0.0146	-0.0100	< 0.001	-0.0089	-0.0113	-0.0065	< 0.001	-0.0034	-0.0039	-0.0029	< 0.001	20.31 (18.52, 22.09)	< 0.001
GGT	-0.0125	-0.0148	-0.0102	< 0.001	-0.0107	-0.0131	-0.0084	< 0.001	-0.0018	-0.0023	-0.0014	< 0.001	9.60 (8.32, 10.89)	< 0.001
HbA1c	-0.0124	-0.0147	-0.0101	< 0.001	-0.0114	-0.0137	-0.0091	< 0.001	-0.0010	-0.0013	-0.0007	< 0.001	8.94 (7.92, 9.96)	< 0.001
Albumin	-0.0125	-0.0148	-0.0102	< 0.001	-0.0109	-0.0132	-0.0086	< 0.001	-0.0016	-0.0020	-0.0013	< 0.001	8.05 (7.13, 8.97)	< 0.001
HDL	-0.0125	-0.0148	-0.0102	< 0.001	-0.0118	-0.0141	-0.0095	< 0.001	-0.0007	-0.0011	-0.0003	< 0.001	5.10 (3.80, 6.40)	< 0.001
ALP	-0.0124	-0.0147	-0.0101	< 0.001	-0.0115	-0.0138	-0.0092	< 0.001	-0.0009	-0.0012	-0.0006	< 0.001	5.08 (4.33, 5.84)	< 0.001
Apolipoprotein A	-0.0153	-0.0161	-0.0144	< 0.001	-0.0146	-0.0156	-0.0137	< 0.001	-0.0006	-0.0008	-0.0005	< 0.001	4.11 (3.17, 5.05)	< 0.001
Total mediation													46.60 (42.80, 50.40)	< 0.001

*The levels of biomarkers were nature log-transformed before analyses. Multivariable-adjusted models were adjusted for age (continuous, years), sex (male or female), ethnicity (white, non-white), drinking status (never drinker, former drinker, or current drinker), education levels (college or university, high school or equivalent, or others), employment status (employed, unemployed), household income (<£18 000, £18 000–30 999, £31 000–51 999, £52 000-100 000, >£100 000), Townsend deprivation index (continuous), hypertension duration (continuous, years), and use of hypertension medication (yes or no). 95% CI was computed by 1,000 bootstrap resampling. CI, confidence interval; CRP, C-reactive protein; HDL, high-density lipoprotein; GGT, gamma-glutamyl transferase; ALP, Alkaline phosphatase

designs are necessary to confirm our findings in future research.

Many efforts have been made to identify the role of blood biomarkers in the health [27]. A cohort study identified that lifestyle modifications can decrease inflammatory burden [28]. Additionally, a lifestyle intervention trial revealed that combining a healthy diet with moderate-intensity physical activity notably lowers serum liver enzymes and enhances insulin resistance among individuals with severe obesity [29]. Previous research has identified an association between serum HDL-cholesterol and apolipoprotein A1 levels with the risk of severe infection, while higher BMI, type II diabetes, and HbA1c were associated with increased risks of infectious diseases [30, 31]. The current mediation analyses contributed to a better understanding of the lower risk of infectious diseases associated with lifestyle behaviors. We found that the associations of overall lifestyle factors with infectious diseases could be partially explained by improvements in glycemic control, renal function, liver function, lipid profile, and systemic inflammation. These findings were coherent with previous evidence [32, 33]. Consider the assumed causal relationship in the current study, the findings still need additional confirmation in future studies.

The current study is among the first to comprehensively investigate the relationship of the combination of lifestyle behaviors and cardiometabolic status with a wide range of infectious diseases among individuals with hypertension. The strengths of this study included the large sample size and long period of follow-up. The robust findings in the stratified analysis further strengthen the validity of our results. Additionally, extensive collection of data on blood biomarkers, which allowed us to comprehensively evaluate the potential mechanisms underlying the observed associations. Nevertheless, several limitations of this study warrant acknowledged. First, the self-reported and one-time assessment of lifestyle behaviors data are susceptible to measurement errors. Second, since the outcomes were identified through hospital inpatient records and death registries, there is a possibility of underreporting of cases. Third, mediation analysis presupposes causality between lifestyle behaviors and biological biomarkers, while both were assessed simultaneously in the UK Biobank. Future studies with repeatedly measured data are required to replicate our findings. Fourth, the UK Biobank does not adequately represent the broader population of the UK, especially concerning socioeconomic deprivation, lifestyles, and noncommunicable diseases, due to the presence of a healthy volunteer selection bias. Fifth, the ethnic homogeneity of the study (>85% Whites) may restrict the generalizable of our results to other ethnic groups. Sixth, residual or unknown confounding factors could not be entirely

ruled out due to the observational study design, despite our efforts to adjust for potential confounders. Finally, due to the observational study design, establishing causal relationships was not feasible, and residual or unknown confounding factors could not be entirely eliminated.

Conclusions

Our findings suggested that adherence to healthy lifestyle behaviors and favorable cardiometabolic status, including healthy diet, regular physical activity, reduced exposure to nicotine, adequate sleep duration, and recommended BMI, blood lipids, blood glucose, and blood pressure, was associated with lower risks of infectious disease among individuals with hypertension. Our findings bolster the importance of public health programs for improving modifiable risk factors in mitigating infectious diseases. Additionally, our data showed significant mediation effect of biomarkers involving of glycemic control, liver function, lipid profile, and systemic inflammation on the associations between combined modifiable risk factors and infectious disease. Further studies are warranted to confirm our findings.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-024-10064-1.

Supplementary Material 1

Supplementary Material 2

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Author contributions

W.L. and N.H. designed the research; N.H. and B.A. accessed and verified the data, performed statistical analysis, and drafted the manuscript. All the authors participated in the interpretation of the results and critical revision of the manuscript.

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Data availability

UK Biobank data are available to all researchers for health-related research and public interest through registration on the UK Biobank (www.ukbiobank.ac.uk).

Declarations

Ethics approval and consent to participate

This study was conducted using data from the UK Biobank, which has obtained ethics approval from the North West Multi-Centre Research Ethics Committee (REC reference: 11/NW/0157). All procedures were performed in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent to participate

Informed consent was obtained from all participants included in the study by the UK Biobank.

Transparency declaration

The lead author (WL) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Competing interests

The authors declare no competing interests.

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