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Cover Photo: CDC Staff monitoring air Benzene in an enameled wire factory in Tongling City, Anhui Province, 2020.

Preplanned Studies

Industry Distribution Characteristics of Benzene-Exposed Workers with Cytopenia — Four Provinces, China, 2020

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Summary

What is already known about this topic?

Benzene is harmful to the hematopoietic system and can cause leukemia. However, benzene is still being used in various industries including furniture, rubber, plastic products, and metal product manufacturing.

What is added by this report?

The white blood cell count of workers in general equipment, special equipment, chemical raw materials, and chemical products manufacturing decreased significantly. The enterprises in which benzene concentration exceeded the occupational exposure limit were small enterprises and private enterprises.

What are the implications for public health practice?

Regular health examinations are necessary for benzene-exposed workers. In addition, the monitoring of benzene concentration in small enterprises and private enterprises should be strengthened.

Benzene is a common organic solvent, and it is the basic raw material or intermediate for industrial production, such as in the manufacturing of rubber, lubricants, fuels, detergents, and pesticides. Benzene is widely used in furniture manufacturing, printing and recording media reproduction, housing service, maintenance, and other service industries (*1*). Benzene is hemotoxic and carcinogenic, and long-term exposure to low levels (<6 mg/m^3) of benzene can cause a decrease in peripheral blood counts and increase the risk of developing aplastic anemia (AA), myelodysplastic syndrome (MDS), and acute myeloid leukemia (AML) (*2*). This study aims to analyze the industry distribution of benzene-exposed workers with cytopenia. Four provinces were selected for the study. Sichuan, Jiangsu and Zhejiang are high-incidence areas of chronic benzene poisoning (CBP) and benzene-induced leukemia (BIL) (*3–4*), while Fujian was selected because it has high manufacturing productivity (*1*). From 2005 to 2019, CBP and BIL cases in the four provinces were mainly distributed in general equipment, special equipment, chemical raw materials, and chemical products manufacturing (*3–4*). The industrial distribution of benzene-exposed workers with significantly lower white blood cell (WBC), neutrophil (NEUT), and platelet (PLT) counts was compared with that of workers with more CBP and BIL in Sichuan, Jiangsu, and Zhejiang Provinces.

The results suggested that workers whose WBC counts decreased significantly were mainly distributed in general equipment, special equipment, chemical raw materials, and chemical products manufacturing. These were also the main industries with CBP and BIL. Small enterprises and private enterprises had benzene exposure concentrations exceeding the occupational exposure limit (PC-TWA=6 mg/m^3), with benzene-exposed workers experiencing a significant reduction in WBC, NEUT, and PLT counts. Therefore, strengthening the health supervision of workers — in general equipment, special equipment, chemical raw material, and chemical product manufacturing — and improving the safety and health management system of small and private enterprises will effectively reduce the risk of hematotoxicity and leukemia caused by benzene.

The local Centers for Disease Control and Prevention (CDC) measured 8-hour time-weighted average concentrations of benzene by gas chromatography with flame ionization detection after obtaining air samples through sentinel sampling. Hematological indicators of workers were assessed through medical examinations. Standardized classification of the benzene industry was performed using the *Industrial Classification for National Economic Activities* (GB/T 4754–2017). Data were statistically analyzed using EXCEL software (version Home and Student 2019, Microsoft Office, USA) and SPSS software (version 25.0, SPSS Inc., Chicago, IL, USA).

A total of 2,530 benzene-exposed workers were

recruited from 17 industries in four provinces, and 526 unexposed age- and sex-matched workers from Jiangsu, Beijing and Tianjin were selected as controls. The mean age of the exposed group was 39.77±9.38 years, comprised of 1,521 males (60.1%) and 1,009 females (39.9%). The mean age of the control group was 40.56±10.00 years, comprised of 326 males (62.0%) and 200 females (38.0%). There was no statistical difference in age or gender between the two groups. As shown in Table 1, WBC, NEUT, erythrocytes (RBC) and hemoglobin (HGB) were significantly lower in the exposed group compared to the control group (P<0.05). The WBC counts of workers among the general equipment and special equipment manufacturing, chemical raw materials and chemical products manufacturing, furniture manufacturing, and wood processing and wood, bamboo, rattan, palm, and grass products manufacturing were also significantly lower than in the control group (P<0.05). The median benzene exposure concentrations in general equipment and special equipment manufacturing (median=2 mg/m^3); computer, communication and other electronic equipment manufacturing (median=2 mg/m^3); and chemical raw materials and chemical products manufacturing (median=1.4 mg/m^3) ranked in the top three of all industries.

Given that decreased WBC, NEUT or PLT counts are the main clinical indicators of benzene-induced hematotoxicity (*5*), differences in these three clinical indicators among benzene-exposed workers were further analyzed. The results suggest that benzene-exposed workers with significantly lower levels of these three indicators were mainly distributed in seven industries: general and special equipment manufacturing; chemical raw materials and chemical products manufacturing; furniture manufacturing; wood processing and wood, bamboo, rattan, palm and grass products manufacturing; railroad, ship, aerospace and other transportation equipment manufacturing; cultural, educational, industrial, aesthetic, sports and recreational goods manufacturing; and retail trade. Further comparison between these seven industries and the industries with high prevalence of CBP and BIL (*3*–*4*) revealed that general equipment and special equipment manufacturing as well as chemical raw materials and chemical products manufacturing were industries with high prevalence of CBP and BIL. Enterprise size and ownership type of the above seven industries were also further analyzed. As shown in Table 2, most of the enterprises were small enterprises, and medium-sized enterprises had the most employees. The majority of the enterprises were private, and private enterprises had the greatest number of employees. Excessive benzene exposure concentrations were found only in small enterprises and private enterprises.

DISCUSSION

Workers exposed to high concentrations of benzene for a long time can have pancytopenia, and the persistent deterioration of symptoms can lead to benzene poisoning and leukemia (*6*). This study found that WBC counts of benzene-exposed workers were significantly lower in general and special equipment manufacturing and in chemical raw materials and chemical products manufacturing. These industries were also ones with high incidences of CBP and BIL. This may be related to the relatively high exposure to benzene in the two industries. From 1983 to 2014, the median benzene exposure in general and special equipment manufacturing, chemical raw materials and chemicals manufacturing, and leather, fur, feather and feather products and footwear manufacturing ranked in the top three of all benzene exposure industries (*6*). In 2020, the median benzene exposure concentration in general and special equipment manufacturing and chemical raw materials and chemical products manufacturing industries remained in the top three of the 17 industries in this study. It was found that chronic low benzene exposure (<3.25 mg/m^3) resulted in hematopoietic toxicity and significantly increased micronucleus frequency and sister chromatid exchange frequency, resulting in pancytopenia and an increased risk of leukemia (*7*–*8*). Therefore, the study suggests that workers in general and special equipment manufacturing and chemical raw materials and chemical products manufacturing may be at high risk of developing CBP and BIL, and that monitoring of benzene concentration in these two industries should be strengthened.

In industries that had a majority of workers with significantly reduced WBC, NEUT or PLT counts, excessive benzene exposure concentrations were found only in small enterprises and private enterprises. It is important to note that private enterprises also had the largest number of enterprises. The excessive benzene concentration may be related to their substandard protective equipment, poor occupational health conditions and lack of corporate supervision. In 2020, the concentration monitoring results of benzene-exposed enterprises in six provinces of China showed

TABLE 1. Analysis of blood cell counts of workers exposed to benzene in different benzene industries in Sichuan, Jiangsu, Zhejiang, and Fujian, 2020.

Groups	Median CTWA (range) (mg/m^3)	Number of workers	WBC	NEUT	RBC	HGB	PLT
Control	0	526	6.6 (3.6–9.5)	3.8 (1.9–6.3)	4.9 (4.3–5.8)	149 (130–175)	208 (125–350)
Benzene	0.6 (0.1–84.8)	2,530	6.3 (3.0–9.7)*	3.7 (1.3–7.2)*	4.8 (3.4–6.3)**	146 (89–187)**	226 (52–357)**
General and special equipment manufacturing	2.0 (0.2–4.0)	320	6.3 (3.4–9.7)*	3.6 (1.5–6.9)*	4.9 (3.5–6.1)	148 (92–187)	221 (73–352)*
Computer, communications and other electronic equipment manufacturing	2.0 (0.6–2.0)	98	7.2 (4.0–9.6)**	3.9 (1.9–5.9)	4.8 (3.7–5.8)*	147 (90–181)*	228 (131–335)**
Chemical raw materials and chemical products manufacturing	1.4 (0.1–8.0)	148	5.8 (3.6–9.7)**	3.1 (1.6–5.7)**	4.9 (3.9–6.1)	150 (91–185)	202 (98–348)*
Printing and recording media reproduction	0.7 (0.6–84.8)	189	6.5 (3.4–9.5)	3.6 (1.8–6.8)	5.1 (4.0–6.2)**	152 (90–181)*	221 (102–344)*
Metal product manufacturing	0.6 (0.2–1.5)	34	6.1 (3.9–9.4)	3.8 (1.9–7.0)	4.8 (3.6–5.7)	148 (90–172)	222 (85–340)
Non-ferrous metal smelting and rolling processing industry	0.6 (0.1–0.6)	37	6.1 (4.2–9.1)	4.1 (2.1–4.8)	5.1 (4.0–5.8)*	150 (121–173)	226 (150–337)**
Rubber and plastic products industry	0.6 (0.6–0.6)	118	6.2 (3.0–9.4)	3.7 (1.5–6.3)	5.2 (4.0–5.8)**	160 (123–175)**	231 (120–329)**
Railway, ship, aerospace and other transportation equipment manufacturing	0.6 (0.6–0.6)	50	6.2 (3.5–9.5)	3.5 (2.0–6.1)*	4.8 (3.7–5.8)*	142 (100–173)*	236 (81–342)*
Automobile manufacturing	0.6 (0.1–1.4)	60	6.2 (3.7–9.4)	3.9 (1.9–5.7)	5.0 (4.0–6.2)	152 (115–183)	212 (121–356)
Retailing	0.6 (0.1–2.1)	17	5.9 (3.8–8.7)	2.9 (1.7–4.7)*	5.1 (4.6–5.9)	150 (133–175)	243 (143–346)*
Motor vehicle, electronic products and daily products repair industry	0.6 (0.1–80.7)	24	6.5 (4.4–9.2)	3.5 (2.0–5.5)	5.3 (4.3–6.0)**	159 (135–174)**	251 (145–329)**
Wholesale of petroleum and petroleum products	0.6 (0.6–0.6)	409	6.5 (3.1–9.6)	3.8 (1.7–7.2)	4.7 (3.5–6.3)**	140 (89–182)**	239 (76–357)**
Leather, fur, feather and their products and shoemaking	0.5 (0.1–2.6)	311	6.5 (3.8–9.7)	3.7 (1.8–6.2)	4.4 (3.4–6.0)**	135 (90–173)**	215 (101–356)
Culture and education, arts and crafts, sports, and entertainment products manufacturing	0.1 (0.1–0.9)	141	6.5 (3.2–9.5)	3.8 (1.7–6.3)	4.6 (3.5–5.7)**	136 (91–173)**	199 (52–349)*
Wood processing and wood, bamboo, rattan, palm, and grass products	0.1 (0.1–73.9)	289	6.1 (3.0–9.5)**	3.4 (1.3–6.1)**	4.9 (3.6–5.9)	149 (96–176)	233 (108–346)**
Furniture manufacturing	0.1 (0.1–15.5)	243	6.2 (3.3–9.4)**	3.6 (2.0–5.1)	4.8 (3.6–5.8)**	145 (92–175)**	241 (70–354)**
Electrical machinery and equipment manufacturing	0.1 (0.1–10.8)	42	6.2 (3.6–9.3)	3.2 (1.8–6.0)	4.8 (4.0–5.7)	147 (118–166)	216 (99–341)

Abbreviation: CTWA=concentrations of time weighted average; WBC=white blood cell; NEUT=neutrophil; RBC=erythrocytes; HGB=hemoglobin; PLT=platelet.

* denotes $P \leq 0.05$ as tested by Mann-Whitney U when compared to the control group,

** denotes $P \leq 0.001$ as tested by Mann-Whitney U when compared to the control group.

that private enterprises accounted for the largest proportion of benzene exposure levels exceeding the PC-TWA (*1*). Therefore, the monitoring of benzene exposure concentration in private enterprises should be strengthened. The majority of the CBP and BIL cases were found in small enterprises and private enterprises in China from 2005 to 2019 (*3*–*4*), suggesting that health screening among workers in small enterprises and private enterprises is also essential.

This research had the following limitations: 1) the blood cell count of workers may be affected by recently ingested drugs and food. As a result, the data from a single physical examination may have information bias. It is necessary to obtain information on diet and medication of workers in conjunction with epidemiological questionnaires. 2) This study only analyzed the information of benzene-exposed workers in four provinces, which does not accurately reflect the real health situation of benzene-exposed workers in China. Expanding the scope of investigation will help suggest and implement better prevention strategies and measures.

TABLE 2. Distribution of enterprise scale and ownership type in industries with significantly reduced WBC, NEUT, and PLT counts in Sichuan, Jiangsu, Zhejiang, and Fujian, 2020.

Item	Number of enterprises	Number of workers	Median CTWA (rang) (mg/m³)	Number of enterprises exceeding PC-TWA (%)
Enterprise scale				
Large	8	222	0.1 (0.1–0.6)	0
Medium	23	696	0.8 (0.1–3.6)	0
Small	54	365	0.6 (0.1–73.9)	18 (33)
Mini-sized	5	23	0.1 (0.1–4.5)	0
Ownership type				
State-owned	12	208	2.0 (0.2–2.0)	0
Joint-stock	3	105	0.1 (0.1–3.6)	0
Foreign-owned	5	25	0.6 (0.6–0.6)	0
Hong Kong-, Macao- and Taiwan-invested enterprises	7	116	0.1 (0.1–2.0)	0
Private	61	846	0.1 (0.1–73.9)	18 (30)
Unknown	2	6	0.6 (0.6–0.6)	0

Abbreviation: CTWA=concentrations of time weighted average; PC-TWA=permissible concentration-time weighted average; WBC=white blood cell; NEUT=neutrophil; PLT=platelet.

According to the results of this investigation, targeted prevention for healthy benzene-exposed workers should be the most proactive, effective and economical measure: 1) Early detection and diagnosis of cytopenia for workers in general and special equipment manufacturing and in chemical raw materials and chemical product manufacturing, including regular physical examinations and occupational contraindications (i.e., various hematological diseases, severe systemic dermatoses, etc.), are key to control the development of malignant hematological diseases. 2) Through technical transformation and ventilation measures (i.e., such as replacing benzene with non-toxic or low-toxic substances and applying automated machinery to reduce workers' contact time), the concentration of benzene can be reduced to the lowest possible level. 3) Management measures should be taken to control the risk factors that may cause CBP and BIL in small enterprises and private enterprises. Measures include strengthening the monitoring of benzene concentration in the workplace, promoting the wearing of protective equipment and improving the employee safety and health management system.

Conflicts of interest: No conflicts of interest.

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Preplanned Studies

Characteristics of Lung Function and Prevalence of Airflow Obstruction Among Individuals Aged 18–74 Years — Beijing, China, 2017–2018

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Summary

What is already known about this topic?

Airflow obstruction is the hallmark of many chronic respiratory diseases and may indicate the potential for the development of other progressive diseases. There are currently no representative studies of lung function in Beijing. An up-to-date estimation of the characteristics of lung function and airflow obstruction is thus needed.

What is added by this report?

The estimated prevalence of airflow obstruction was 14.68% in Beijing, 2017–2018. The values of vital capacity, forced vital capacity, and forced expiratory volume in the first second were 3.09 L, 2.66 L, 2.22 L, respectively.

What are the implications for public health practice?

Effective public health strategy for lung in Beijing should target older people, current or former smokers, and individuals who live in urban environments, have a low education level, exhibit a high smoking index, and/or have an abnormal body mass index.

Pulmonary function is a crucial parameter for the comprehensive evaluation of respiratory system functions such as airway ventilation capacity. Pulmonary function tests are mainly used to detect the patency of the airway and the lung capacity, including a variety of diagnostics that assess how well the lungs work; the most basic pulmonary function test is spirometry (*1*). The interpretation of spirometric test results, such as airflow obstruction (AFO) levels, can help identify abnormal patterns that may be related to the presence of disease (*2*).

The physiological definition of AFO is a reduction in the ratio of forced expiratory volume in the first second (FEV_1) to forced vital capacity (FVC). Importantly, AFO has been found to be a critical element of certain diseases, such as chronic obstructive pulmonary disease (COPD) (*2*). Among individuals with AFO, 43%–74% are COPD patients (*3*–*5*), and COPD has become a major public health problem in China (*6*). The aim of this study was thus to estimate the level and characteristics of lung function and AFO in a sample population of adults living in Beijing in order to better serve populations such as those suffering from COPD.

The study was performed using baseline data (from September 2017 to May 2018) obtained from the Beijing Population Health Cohort Study. It is a large, prospective dynamic cohort study with a total of 24,990 subjects aged 18–74 years. The details of this study's design are discussed in another publication (*7*). This study's methodology excluded individuals who did not meet the age requirements and/or lacked important information, such as lung function indicator values, which left 21,426 participants in the analysis.

A standardized questionnaire was administered by trained staff. Smoking severity was determined by the smoking index (SI) [SI, calculated as (daily smoking count) × (years of smoking). Light: SI≤200; Moderate: 200<SI<400; Severe: SI≥400]. Weight and height were measured by trained staff, and body mass index (BMI) was subsequently calculated. Spirometry tests were conducted by trained technicians on participants in a sitting position with a nose clip using a spirometer. The spirometer was calibrated daily. Participants completed three tests of lung function. This study then used the GOLD lung function criteria (FEV_1/FVC <70%) to define individuals with AFO. The participants provided written informed consent. The Ethics Review Committee of the Beijing Center for Disease Prevention and Control approved the study protocol [No. 2017D(6)].

This study estimated standardized prevalence using the 2010 census of the Chinese population. Categorical data are shown as numbers (percentages). The mean±standard deviation is used to represent the continuous variables. This investigation assessed the

statistical significance of differences either by one-way ANOVA or the Kruskal-Wallis H test for continuous variables and used the chi-squared test to compare prevalence. *P* values for trends were calculated using the Cochran-Armitage trend test for proportions. All statistical tests were two-sided, and $P<0.05$ was considered statistically significant. All statistical analyses were performed using Stata 16.0 (StataCorp LLC, College Station, Texas, USA).

The basic characteristics of the study subjects are listed in Table 1 and Table 2. Of the 21,426 subjects, 9,876 were males and 11,550 were females. Overall, males had higher vital capacity (VC), FVC, and FEV_1, but males had slightly lower FEV_1/FVC than females. The results of lung function testing are shown in Table 3. In males, the mean values of VC and FVC

TABLE 1. Basic characteristics of the sample population.

Variable	Total (*n*=21,426)	Male (*n*=9,876)	Female (*n*=11,550)
Age (years), mean (±SD)	45.97 (14.28)	45.95 (14.52)	45.99 (14.08)
Age group, *n* (%)			
18–29	3,332 (15.55)	1,620 (16.40)	1,712 (14.82)
30–39	4,876 (22.76)	2,226 (22.54)	2,650 (22.94)
40–49	4,079 (19.04)	1,723 (17.45)	2,356 (20.40)
50–59	4,274 (19.95)	1,996 (20.21)	2,278 (19.72)
60–74	4,865 (22.71)	2,311 (23.40)	2,554 (22.11)
BMI (kg/m^2), mean (±SD)	25.14 (3.84)	25.91 (3.67)	24.47 (3.86)
BMI group, *n* (%)			
<18.5	496 (2.31)	117 (1.18)	379 (3.28)
18.5–23.9	8,783 (38.19)	2,871 (29.07)	5,312 (45.99)
24.0–27.9	8,277 (38.63)	4,362 (44.17)	3,915 (33.90)
≥28.0	4,470 (20.86)	2,526 (25.58)	1,944 (16.83)
Residence, *n* (%)			
Urban	7,400 (34.54)	3,095 (31.34)	4,305 (37.27)
Suburban	14,026 (65.46)	6,781 (68.66)	7,245 (62.73)
Education level, *n* (%)			
Primary and below	1,765 (8.24)	657 (6.65)	1,108 (9.59)
Middle and high school	8,793 (41.04)	4,434 (44.90)	4,359 (37.74)
College and above	10,868 (50.72)	4,785 (48.45)	6,083 (52.67)
Smoking status, *n* (%)			
Current smoker	5,090 (23.76)	4,839 (49.00)	251 (2.17)
Former smoker	1,143 (5.33)	1,083 (10.97)	60 (0.52)
Never smoker	15,193 (70.91)	3,954 (40.04)	11,239 (97.31)
Smoking index level*, *n* (%)			
Light	1,418 (32.07)	1,334 (31.51)	84 (44.68)
Moderate	1,008 (22.80)	962 (22.72)	46 (24.47)
Severe	1,996 (45.14)	1,938 (45.77)	58 (30.85)
VC (L), mean (±SD)	3.09 (0.90)	3.59 (0.87)	2.66 (0.68)
FVC (L), mean (±SD)	2.66 (0.89)	3.12 (0.90)	2.27 (0.67)
FEV_1 (L), mean (±SD)	2.22 (0.83)	2.60 (0.87)	1.90 (0.63)
FEV_1/FVC (%), mean (±SD)	83.63 (15.04)	83.41 (15.31)	83.82 (14.81)

Note: Data are the number (percentage) for categorical variables and the mean±standard deviation for continuous variables.
* For smoking index level, the total number was 4,422, including 4,234 males and 188 females.
Abbreviation: SD=standard deviation; BMI=body mass index; VC=vital capacity; FVC=forced vital capacity; FEV_1=forced expiratory volume in the first second.

TABLE 2. Distribution of sample population by residence, educational level and smoking status by age group.

Variable	Total (*n*=21,426)	18–29 (*n*=3,332)	30–39 (*n*=4,876)	40–49 (*n*=4,079)	50–59 (*n*=4,274)	60–74 (*n*=4,865)
Residence, *n* (%)						
Urban	7,400 (34.54)	1,234 (37.03)	1,616 (33.14)	1,239 (30.38)	1,485 (34.74)	1,826 (37.53)
Suburban	14,026 (65.46)	2,098 (62.97)	3,260 (66.86)	2,840 (69.62)	2,789 (65.26)	3,039 (62.47)
Education level, *n* (%)						
Primary and below	1,765 (8.24)	18 (0.54)	30 (0.62)	82 (2.01)	315 (7.37)	1,320 (27.13)
Middle and high school	8,793 (41.04)	751 (22.54)	826 (16.94)	1,312 (32.16)	2,778 (65.00)	3,126 (64.25)
College and above	10,868 (50.72)	2,563 (76.92)	4,020 (82.44)	2,685 (65.82)	1,181 (27.63)	419 (8.61)
Smoking status, *n* (%)						
Current smoker	5,090 (23.76)	783 (23.50)	1,116 (22.89)	899 (22.04)	1,169 (27.35)	1,123 (23.08)
Former smoker	1,143 (5.33)	83 (2.49)	145 (2.97)	192 (4.71)	261 (6.11)	462 (9.50)
Never smoker	15,193 (70.91)	2,466 (74.01)	3,615 (74.14)	2,988 (73.25)	2,844 (66.54)	3,280 (67.42)
Smoking index level, *n* (%)*						
Light	1,418 (32.07)	545 (88.33)	501 (54.22)	152 (19.64)	110 (10.26)	110 (10.63)
Moderate	1,008 (22.80)	67 (10.86)	337 (36.47)	240 (31.01)	237 (22.11)	127 (12.27)
Severe	1,996 (45.14)	5 (0.81)	86 (9.31)	382 (49.35)	725 (67.63)	798 (77.10)
BMI group, *n* (%)						
<18.5	496 (2.31)	254 (7.62)	147 (3.01)	36 (0.88)	15 (0.35)	44 (0.90)
18.5–23.9	8,183 (38.19)	1,726 (51.80)	2,159 (44.28)	1,539 (37.73)	1,267 (29.64)	1,492 (30.67)
24.0–27.9	8,277 (38.63)	818 (24.55)	1,639 (33.61)	1,641 (40.23)	1,994 (46.65)	2,185 (44.91)
≥28.0	4,470 (20.86)	534 (16.03)	931 (19.09)	863 (21.16)	998 (23.35)	1,144 (23.51)

Note: Data are the number (percentage).
* For smoking index level, the total number was 4,422.
Abbreviation: BMI=body mass index.

were significantly different in the age, residence, education level, smoking status, smoking index level, and BMI groups. The mean value of FEV_1 was not significantly different among the different BMI groups. In females, the mean value of VC was significantly different in the age, education level, and BMI groups. The mean values of FVC and FEV_1 were not significantly different among the different smoking index levels.

A total of 3,415 (15.94%) participants had a FEV_1∶FVC ratio less than 70% and were therefore diagnosed with AFO. The standardized prevalence of AFO in Beijing adults aged 18–74 years was estimated to be 14.68%. The prevalence of AFO did not differ significantly (P=0.062) between men (16.44%) and women (15.51%). The prevalence was significantly different by age group, residence, education level, and smoking status (Table 4). People with poor lung function and high prevalence of AFO were mainly those who were older, lived in an urban environment, were current or former smokers, and/or had a low education level, high smoking index, and an abnormal BMI.

DISCUSSION

To date, this is the first large-scale, community-based study working to estimate the level of lung function and the prevalence of AFO among adults in Beijing. Based on results, this research concluded that the prevalence of AFO among adults aged 18–74 years in Beijing was 15.94%, and that the standardized prevalence of AFO was 14.68%. Compared to the 2010 census data, the proportion of people aged 18–29 and 40–49 in this study is higher, and the proportion of people aged 50–59 and 60–74 is lower. With increased age, lung function decreases and the prevalence of AFO increases. Therefore, the crude prevalence in this study will decrease after standardization. Compared to the China Pulmonary Health (CPH) Study, which was a survey of 10 provincial-level administrative divisions (PLADs) in China (Beijing Municipality, Shanghai Municipality, Liaoning, Shanxi, Shaanxi, Sichuan, Guizhou, Hubei, Zhejiang and Guangdong Provinces) from June 2012 to May 2015, this study revealed a higher prevalence of AFO than the prevalence of COPD in adults aged 20

TABLE 3. Levels of pulmonary function indicators in the sample population aged 18–74 years old.

Variable	Total (*n*=21,426)				Male (*n*=9,876)				Female (*n*=11,550)			
	n	VC (L) (mean)	FVC (L) (mean)	FEV_1 (L) (mean)	*n*	VC (L) (mean)	FVC (L) (mean)	FEV_1 (L) (mean)	*n*	VC (L) (mean)	FVC (L) (mean)	FEV_1 (L) (mean)
Age group (years)												
18–29	3,332	3.45 (0.94)	2.97 (1.01)	2.54 (0.91)	1,620	4.02 (0.83)	3.50 (0.99)	2.98 (0.90)	1,712	2.92 (0.70)	2.47 (0.73)	2.11 (0.68)
30–39	4,876	3.36 (0.90)	2.93 (0.92)	2.50 (0.84)	2,226	3.95 (0.81)	3.46 (0.90)	2.96 (0.83)	2,650	2.87 (0.64)	2.49 (0.68)	2.12 (0.63)
40–49	4,079	3.12 (0.84)	2.71 (0.82)	2.30 (0.75)	1,723	3.68 (0.79)	3.23 (0.81)	2.75 (0.76)	2,356	2.70 (0.59)	2.34 (0.59)	1.98 (0.55)
50–59	4,274	2.91 (0.82)	2.51 (0.77)	2.06 (0.72)	1,996	3.37 (0.76)	2.91 (0.76)	2.40 (0.73)	2,278	2.51 (0.64)	2.15 (0.58)	1.76 (0.56)
60–74	4,865	2.69 (0.80)	2.28 (0.74)	1.80 (0.67)	2,311	3.07 (0.75)	2.62 (0.71)	2.04 (0.70)	2,554	2.34 (0.67)	1.96 (0.61)	1.57 (0.56)
P value		<0.001	<0.001	<0.001		<0.001	<0.001	<0.001		<0.001	<0.001	<0.001
Residence												
Urban	7,400	3.03 (0.90)	2.47 (0.87)	2.04 (0.79)	3,095	3.53 (0.88)	2.90 (0.91)	2.40 (0.85)	4,305	2.66 (0.72)	2.15 (0.69)	1.79 (0.63)
Suburban	14,026	3.12 (0.90)	2.77 (0.88)	2.31 (0.83)	6,781	3.62 (0.86)	3.22 (0.87)	2.69 (0.86)	7,245	2.65 (0.66)	2.34 (0.65)	1.96 (0.63)
P value		<0.001	<0.001	<0.001		<0.001	<0.001	<0.001		0.422	<0.001	<0.001
Education level												
Primary and below	1,765	2.61 (0.83)	2.16 (0.73)	1.68 (0.68)	657	3.05 (0.79)	2.57 (0.78)	1.96 (0.78)	1,108	2.35 (0.73)	1.92 (0.58)	1.52 (0.55)
Middle and high school	8,793	2.92 (0.86)	2.49 (0.83)	2.04 (0.77)	4,434	3.35 (0.81)	2.89 (0.82)	2.37 (0.80)	4,359	2.48 (0.66)	2.09 (0.62)	1.71 (0.57)
College and above	10,868	3.30 (0.89)	2.88 (0.90)	2.45 (0.82)	4,785	3.89 (0.82)	3.41 (0.89)	2.90 (0.83)	6,083	2.84 (0.64)	2.46 (0.66)	2.10 (0.62)
P value		<0.001	<0.001	<0.001		<0.001	<0.001	<0.001		<0.001	<0.001	<0.001
Smoking status												
Current smoker	5,090	3.52 (0.87)	3.07 (0.90)	2.56 (0.86)	4,839	3.57 (0.85)	3.12 (0.89)	2.60 (0.85)	251	2.60 (0.75)	2.14 (0.64)	1.73 (0.60)
Former smoker	1,143	3.41 (0.88)	2.94 (0.88)	2.38 (0.86)	1,083	3.45 (0.87)	2.99 (0.87)	2.41 (0.86)	60	2.61 (0.68)	2.17 (0.69)	1.83 (0.63)
Never smoker	15,193	2.92 (0.86)	2.50 (0.83)	2.09 (0.78)	3,954	3.66 (0.88)	3.15 (0.91)	2.64 (0.88)	11,239	2.66 (0.68)	2.27 (0.67)	1.90 (0.63)
P value		<0.001	<0.001	<0.001		<0.001	<0.001	<0.001		0.425	0.003	<0.001
Smoking index level												
Mild	1,418	3.80 (0.89)	3.35 (0.94)	2.84 (0.88)	1,334	3.87 (0.84)	3.42 (0.91)	2.91 (0.85)	84	2.67 (0.80)	2.20 (0.65)	1.81 (0.58)
Moderate	1,008	3.62 (0.88)	3.14 (0.91)	2.64 (0.86)	962	3.67 (0.85)	3.19 (0.88)	2.68 (0.84)	46	2.58 (0.82)	2.04 (0.68)	1.69 (0.66)
Severe	1,996	3.25 (0.77)	2.83 (0.78)	2.30 (0.77)	1,938	3.27 (0.76)	2.86 (0.77)	2.32 (0.76)	58	2.44 (0.66)	2.09 (0.63)	1.59 (0.57)
P value		<0.001	<0.001	<0.001		<0.001	<0.001	<0.001		0.210	0.368	0.105
BMI group												
<18.5	496	2.92 (0.84)	2.49 (0.82)	2.13 (0.78)	117	3.39 (0.90)	2.95 (0.96)	2.47 (0.92)	379	2.77 (0.76)	2.34 (0.72)	2.02 (0.69)
18.5–23.9	8,183	3.00 (0.86)	2.59 (0.86)	2.17 (0.80)	2,871	3.56 (0.89)	3.09 (0.93)	2.58 (0.89)	5,312	2.70 (0.67)	2.32 (0.68)	1.95 (0.65)
24.0–27.9	8,277	3.14 (0.91)	2.72 (0.90)	2.25 (0.83)	4,362	3.61 (0.84)	3.14 (0.88)	2.61 (0.85)	3,915	2.61 (0.67)	2.24 (0.65)	1.86 (0.61)
≥28.0	4,470	3.17 (0.96)	2.72 (0.92)	2.27 (0.86)	2,526	3.61 (0.89)	3.12 (0.90)	2.61 (0.86)	1,944	2.61 (0.73)	2.20 (0.64)	1.81 (0.60)
P value		<0.001	<0.001	<0.001		0.004	0.021	0.151		<0.001	<0.001	<0.001

Abbreviation: BMI=body mass index; VC=vital capacity; FVC=forced vital capacity; FEV_1=forced expiratory volume in the first second.

TABLE 4. Prevalence of airflow obstruction in the sample population aged 18–74 years old.

Variable	Total (*n*=21,426)		Male (*n*=9,876)		Female (*n*=11,550)	
	Cases/*N*	Prevalence of AFO (%) (95% *CI*)	Cases/*N*	Prevalence of AFO (%) (95% *CI*)	Cases/*N*	Prevalence of AFO (%) (95% *CI*)
Age group (years)						
18–29	423/3,332	12.70 (11.60–13.86)	205/1,620	12.65 (11.10–14.34)	218/1,712	12.73 (11.22–14.38)
30–39	562/4,876	11.53 (10.65–12.44)	242/2,226	10.87 (9.63–12.22)	320/2,650	12.08 (10.88–13.36)
40–49	509/4,079	12.48 (11.49–13.52)	202/1,723	11.72 (10.27–13.31)	307/2,356	13.03 (11.72–14.44)
50–59	758/4,274	17.74 (16.61–18.90)	360/1,996	18.04 (16.40–19.77)	398/2,278	17.47 (15.95–19.07)
60–74	1,163/4,865	23.91 (22.72–25.12)	615/2,311	26.61 (24.84–28.44)	548/2,554	21.46 (19.90–23.08)
P value*		<0.001		<0.001		<0.001
Residence						
Urban	1,300/7,400	17.57 (16.71–18.45)	563/3,095	18.19 (16.86–19.58)	737/4,305	17.12 (16.02–18.27)
Suburban	2,115/14,026	15.08 (14.49–15.68)	1,061/6,781	15.65 (14.80–16.53)	1,054/7,245	14.55 (13.75–15.37)
P value		<0.001		0.002		<0.001
Education level						
Primary and below	478/1,765	27.08 (25.05–29.19)	211/657	32.12 (28.63–35.76)	267/1,108	24.10 (21.65–26.68)
Middle and high school	1,688/8,793	18.97 (18.16–19.80)	857/4,434	19.33 (18.19–20.51)	811/4,359	18.61 (17.47–19.78)
College and above	1,269/10,868	11.68 (11.08–12.29)	556/4,785	11.62 (10.73–12.55)	713/6,083	11.72 (10.93–12.55)
P value*		<0.001		<0.001		<0.001
Smoking status						
Current smoker	832/5,090	16.35 (15.35–17.38)	780/4,839	16.12 (15.10–17.18)	52/251	20.72 (16.06–26.05)
Former smoker	226/1,143	19.77 (17.54–22.16)	220/1,083	20.31 (18.00–22.79)	6/60	10.00 (4.28–19.45)
Never smoker	2,357/15,193	15.51 (14.94–16.10)	624/3,954	15.78 (14.67–16.94)	1,733/11,239	15.42 (14.76–16.10)
P value		<0.001		0.001		0.036
Smoking index level						
Mild	188/1,418	13.26 (11.57–15.10)	169/1,334	12.67 (10.97–14.53)	19/84	22.62 (14.69–32.39)
Moderate	138/1,008	13.69 (11.67–15.92)	132/962	13.72 (11.66–16.00)	6/46	13.04 (5.63–24.92)
Severe	419/1,996	20.99 (19.25–22.82)	403/1,938	20.79 (19.03–22.64)	16/58	27.59 (17.37–39.97)
P value*		<0.001		<0.001		0.583
BMI group						
<18.5	69/496	13.91 (11.08–17.16)	21/117	17.95 (11.82–25.64)	48/379	12.66 (9.60–16.29)
18.5–23.9	1,267/8,183	15.48 (14.71–16.28)	485/2,871	16.89 (15.56–18.30)	782/5,312	14.72 (13.79–15.69)
24.0–27.9	1,373/8,277	16.59 (15.80–17.40)	740/4,362	16.96 (15.87–18.10)	633/3,915	16.17 (15.04–17.35)
≥28.0	706/4,470	15.79 (14.75–16.89)	378/2,526	14.96 (13.61–16.40)	328/1,944	16.87 (15.26–18.59)
P value*		0.233		0.057		0.003

Abbreviation: AFO=airflow obstruction; BMI=body mass index; *CI*=confidence interval.
* *P* value from Cochran-Armitage trend test for prevalence.

years or older (8.6%) (*8*). In the study mentioned above, bronchodilators were used to identify patients with COPD. The use of bronchodilators could lead to the exclusion of some patients with bronchial asthma. Therefore, the prevalence of AFO is higher than that of COPD, which is a finding that is consistent with other studies (*3*,*5*).

Males always have higher index values of lung function. The results of this study were consistent with this phenomenon. With increasing age, various organs of the human body gradually age, and because people are exposed to risk factors such as smoking starting when they are young, the cumulative effect of these factors increases with age, causing lung function to decline with age. According to a previous study, the prevalence of COPD was higher in rural areas (*6*). This

may be due to the lower economic status in rural areas, which leads to people being exposed to many risk factors that affect lung function. Beijing, the capital of China, is a modern international city with generally favorable economic conditions and lower exposure to life-threatening factors than rural areas. People in urban areas, however, may be exposed to more car exhaust than people in suburban areas due to traffic congestion. Urban populations had worse lung function and a higher prevalence of AFO in this study. People with lower education levels had lower levels of lung function and a higher prevalence of AFO, possibly because they are less aware of lung function protection and are more likely to be exposed to risk factors. People with low BMI are generally more likely to develop COPD, whereas being overweight or obese is often a protective factor for COPD (*9*), which is not entirely consistent with this study's findings. In this study, females had worse lung function and a higher prevalence of AFO with increasing BMI. This result is however consistent with the findings of a study in the United States demonstrating that overweightness and obesity are risk factors for COPD (*10*). A BMI that is too high or too low can have an impact on lung function, so maintaining a normal weight is vital for health. Women who were current smokers and men who were former smokers had the worse lung function and the highest prevalence of AFO. The findings in males are consistent with another Chinese study (*11*). It may be that former smokers who are male have too much damage to lung function due to prior smoking habits and that their lung function has not fully recovered with smoking cessation. Nonsmokers have the best lung function, so it is essential to avoid cigarettes for health.

This study had several limitations. First, this study used the GOLD criteria ($FEV_1/FVC<70\%$). The ERS and the ATS promote the use of the lower limit of normal (LLN). However, using the LLN as a threshold can potentially exclude subjects with mild AFO. Therefore, this study decided to use the GOLD criteria. Second, this study did not use bronchodilators. In fact, bronchodilators have many side effects, such as dizziness. For safety reasons, bronchodilators were not used. Thirdly, when considering the prevalence of AFO in different age groups, it is necessary to analyze prevalence across different risk factors by age group. In this study, however, there were some overlapping risk factors exhibited by the same study participants.

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Preplanned Studies

Physical Activity and Different Recommendations Associated with the Dynamic Trajectory of Cardiometabolic Diseases — UK, 2006–2021

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Summary

What is already known about this topic?

Previous studies have illustrated the benefits of physical activity on cardiometabolic multimorbidity (CMM), while limited studies have concentrated on the trajectory of CMM progression.

What is added by this report?

Through multi-stage regression analysis, we found that physical activity could reduce the risk of CMM incidence. Participants initially free of cardiometabolic diseases (CMDs) may benefit more from engaging in recommended physical activity.

What are the implications for public health practice?

Adults, especially those initially free of CMDs, should engage in WHO-recommended physical activity as early as possible to prevent CMD incidence and further progression.

While many studies have investigated the associations between physical activity and cardiometabolic diseases (CMDs), evidence remains scarce regarding the relationship between physical activity and different stages of cardiometabolic multimorbidity (CMM) progression. Using data from the United Kingdom (UK) Biobank study from 2006 to 2021, we adopted traditional Cox proportional hazard regression models and multi-state regression models to examine the associations between physical activity and CMM progression (Supplementary Figure S1, available in http://weekly.chinacdc.cn/). CMD was defined as any of the following three diseases, including ischemic heart disease (IHD) (I20 to I25), stroke (I60 to I64), and type 2 diabetes (T2D), (E11, and E14), which were determined via the International Classification of Diseases (10th Revision) (*1*). Incidence of the first CMD (FCMD) was identified as the earliest occurrence of any of these three diseases (IHD, stroke, and T2D), and incident of CMM was defined as the subsequent occurrence of any of the remaining CMDs. Inverse associations were observed between physical activity and almost all phases of CMM progression, albeit to different extents. The associations were stronger in transitions from baseline to FCMD [hazard ratio (HR): 0.880, 95% confidence intervals (*CI*): 0.853, 0.908 and HR: 0.892, 95% *CI*: 0.864, 0.920 for moderate and high physical activity levels]. Adults, especially those free of CMDs, showed the most conspicuous health benefits when meeting the World Health Organization (WHO) Guidelines.

UK Biobank (UKB), an ongoing cohort study, recruited over half a million participants across the UK between 2006 and 2010. Data from the UK Biobank are available upon reasonable request (https://www.ukbiobank.ac.uk/). The study was approved by the Northwest Multi-Centre Research Ethics Committee (06/MRE08/65). Informed consent was obtained, and detailed information on the study protocols has been described elsewhere (*2*). All participants were followed up from recruitment to study until they were deceased, lost of subsequent follow-up from the health record, or March 31, 2021, whichever came first. A group of potential confounders were selected as presented in Table 1, and 307,411 participants were included in the final analysis (Supplementary Figure S2, available in http://weekly.chinacdc.cn/).

Self-reported physical activity was categorized as low, moderate, and high levels according to widely-used criteria of the International Physical Activity Questionnaire (IPAQ). This criterion corresponds to <150 minutes/week, 150–750 minutes/week, and ≥ 750 minutes per week of moderate-intensity physical activity. The cut-off value of 600 MET-min/week is set by the WHO physical activity recommendations (*3*). Considering the more physically active cohort, four recommendations (Guideline Low, 2017 Physical Activity Guidelines, Guideline 300, and Guideline 450) were further defined to examine whether participants would harvest more benefits if they take

higher-level physical activity (details of definitions of physical activity seen in Supplementary Methods, available in http://weekly.chinacdc.cn/) (*4*).

Two incrementally adjusted Cox proportional hazard regression models were constructed to examine the associations between physical activity, FCMD, CMM, and all-cause death. The model plotted the data against follow-up time. Multi-state regression models (*5*) were used to assess the relationships between physical activity and the different phases of CMM progression, resulting in 5 transitions in trajectory pattern A (Supplementary Figure S1). Considering participants might enter the stages of FCMD/CMM or all-cause death simultaneously, we determined the entering date of the theoretically prior stage as the entering date of the theoretically latter stage minus 0.5 days (*1*). Several sensitivity analyses were conducted to examine the robustness of our results (Supplementary Methods) (*6*).

All statistical analyses were conducted using R software (version 3.3.2, R Foundation for Statistical Computing, Vienna, Austria). A two-sided *P* value of <0.05 was considered statistically significant.

A total of 307,411 participants with an average age of 55.46 [standard deviation (SD): 8.09] years at baseline were included (Table 1). During a mean follow-up of 11.92 years, 29,373 (9.56%) participants developed at least one CMD (3.67% were self-reported cases); among them, 7.13% developed CMM later, and 22.67% died from CMM eventually (Supplementary Figure S1).

In traditional Cox regression analysis, higher physical activity levels were associated with lower FCMD, CMM, and all-cause mortality incidence (Table 2). For moderate physical activity level, the fully adjusted HRs [95% confidence intervals (*CI*)] relative to low physical activity level were 0.880 (0.853, 0.908) for FCDM, 0.840 (0.749, 0.942) for CMM, and

TABLE 1. Baseline characteristics of the participants by incident disease status during follow-up*.

Levels	Total	FCMD survivor	CMM survivor	Death with FCMD	Death with CMM†	Death without CMD†	Non-cases
Number of participants	307,411	23,273	1,620	4,005	475	9,772	268,266
Age at recruitment (years)	55.46 (8.09)	58.60 (7.34)	59.92 (6.85)	61.48 (6.46)	63.08 (5.49)	60.46 (6.89)	54.87 (8.05)
Years of follow-up	11.92 (1.47)	12.18 (0.83)	12.22 (0.81)	8.16 (3.19)	9.45 (2.54)	7.57 (3.26)	12.12 (0.94)
Sex							
Female	164,962 (53.66)	9,247 (39.73)	568 (35.06)	1,312 (32.76)	140 (29.47)	4,341 (44.42)	149,354 (55.67)
Male	142,449 (46.34)	14,026 (60.27)	1,052 (64.94)	2,693 (67.24)	335 (70.53)	5,431 (55.58)	118,912 (44.33)
Ethnicity							
White	292,433 (95.13)	21,980 (94.44)	1,494 (92.22)	3,880 (96.88)	451 (94.95)	9,512 (97.34)	255,116 (95.10)
Non-white	14,173 (4.61)	1,221 (5.25)	119 (7.35)	114 (2.85)	24 (5.05)	230 (2.35)	12,465 (4.65)
Unknown	805 (0.26)	72 (0.31)	7 (0.43)	11 (0.27)	0 (0.00)	30 (0.31)	685 (0.26)
BMI, kg/m^2							
Normal	106,760 (34.73)	4,939 (21.22)	200 (12.35)	1,006 (25.12)	84 (17.68)	3,142 (32.15)	97,389 (36.30)
Underweight	1,512 (0.49)	67 (0.29)	2 (0.12)	29 (0.72)	3 (0.63)	100 (1.02)	1,311 (0.49)
Overweight	134,015 (43.59)	10,389 (44.64)	688 (42.47)	1,838 (45.89)	207 (43.58)	4,255 (43.54)	116,638 (43.48)
Obese	65,124 (21.18)	7,878 (33.85)	730 (45.06)	1,132 (28.26)	181 (38.11)	2,275 (23.28)	52,928 (19.73)
Education							
Higher degree	159,486 (51.88)	1,0492 (45.08)	615 (37.96)	1,632 (40.75)	147 (30.95)	4,338 (44.39)	142,262 (53.03)
School degree	91,542 (29.78)	6,367 (27.36)	449 (27.72)	1,018 (25.42)	114 (24.00)	2,551 (26.11)	81,043 (30.21)
Vocational degree	17,332 (5.64)	1,818 (7.81)	122 (7.53)	306 (7.64)	41 (8.63)	713 (7.30)	14,332 (5.34)
Other	39,051 (12.70)	4,596 (19.75)	434 (26.79)	1,049 (26.19)	173 (36.42)	2,170 (22.21)	30,629 (11.42)
Employment							
Paid	195,130 (63.48)	12,180 (52.34)	735 (45.37)	1,453 (36.28)	137 (28.84)	4,012 (41.06)	176,613 (65.84)
Retired	23,384 (7.61)	1,906 (8.19)	189 (11.67)	383 (9.56)	56 (11.79)	888 (9.09)	19,962 (7.44)
Unpaid	88,897 (28.92)	9,187 (39.47)	696 (42.96)	2,169 (54.16)	282 (59.37)	4,872 (49.86)	71,691 (26.72)

TABLE 1. (Continued)

Levels	Total	FCMD survivor	CMM survivor	Death with FCMD	Death with CMM†	Death without CMD†	Non-cases
Smoking status							
Never	174,910 (56.90)	11,544 (49.60)	722 (44.57)	1,616 (40.35)	152 (32.00)	4,258 (43.57)	156,618 (58.38)
Previous	102,212 (33.25)	8,837 (37.97)	655 (40.43)	1,564 (39.05)	217 (45.68)	3,770 (38.58)	87,169 (32.49)
Current	30,289 (9.85)	2,892 (12.43)	243 (15.00)	825 (20.60)	106 (22.32)	1,744 (17.85)	24,479 (9.12)
Alcohol intake							
Never	20,073 (6.53)	1,951 (8.38)	173 (10.68)	350 (8.74)	52 (10.95)	789 (8.07)	16,758 (6.25)
Occasional	64,093 (20.85)	5,252 (22.57)	423 (26.11)	805 (20.10)	100 (21.05)	1,977 (20.23)	55,536 (20.70)
Moderate	156,506 (50.91)	11,025 (47.37)	686 (42.35)	1,781 (44.47)	209 (44.00)	4,416 (45.19)	138,389 (51.59)
Heavy	66,739 (21.71)	5,045 (21.68)	338 (20.86)	1,069 (26.69)	114 (24.00)	2,590 (26.50)	57,583 (21.46)
Household income							
Low	50,701 (16.49)	5,241 (22.52)	452 (27.90)	1,311 (32.73)	185 (38.95)	2,688 (27.51)	40,824 (15.22)
Moderate	207,405 (67.47)	14,522 (62.40)	915 (56.48)	2,118 (52.88)	214 (45.05)	5,592 (57.22)	184,044 (68.61)
High	18,066 (5.88)	869 (3.73)	31 (1.91)	108 (2.70)	8 (1.68)	293 (3.00)	16,757 (6.25)
Unknown	31,239 (10.16)	2,641 (11.35)	222 (13.70)	468 (11.69)	68 (14.32)	1,199 (12.27)	26,641 (9.93)
Fruit & vegetable intake							
Low	87,443 (28.44)	7,193 (30.91)	490 (30.25)	1,356 (33.86)	151 (31.79)	3,011 (30.81)	75,242 (28.05)
Moderate	156,342 (50.86)	11,360 (48.81)	791 (48.83)	1,859 (46.42)	227 (47.79)	4,807 (49.19)	137,298 (51.18)
High	63,626 (20.70)	4,720 (20.28)	339 (20.93)	790 (19.73)	97 (20.42)	1,954 (20.00)	55,726 (20.77)
Family history of CMM							
No	240,798 (78.33)	16,832 (72.32)	1,089 (67.22)	3,076 (76.80)	344 (72.42)	7,780 (79.62)	211,677 (78.91)
Yes	66,613 (21.67)	6,441 (27.68)	531 (32.78)	929 (23.20)	131 (27.58)	1,992 (20.38)	56,589 (21.09)
Physical activity level							
Low	55,116 (17.93)	4,721 (20.29)	360 (22.22)	841 (21.00)	108 (22.74)	1,920 (19.65)	47,166 (17.58)
Moderate	125,837 (40.93)	9,148 (39.31)	630 (38.89)	1,561 (38.98)	179 (37.68)	4,049 (41.43)	110,270 (41.10)
High	126,458 (41.14)	9,404 (40.41)	630 (38.89)	1,603 (40.02)	188 (39.58)	3,803 (38.92)	110,830 (41.31)
Meeting the 2017 physical activity guidelines§							
No	54,427 (17.70)	4,518 (19.41)	328 (20.25)	797 (19.90)	100 (21.05)	1,800 (18.42)	46,884 (17.48)
Yes	252,984 (82.30)	18,755 (80.59)	1,292 (79.75)	3,208 (80.10)	375 (78.95)	7,972 (81.58)	221,382 (82.52)
Meeting the WHO guidelines§							
No	54,590 (17.76)	4,651 (19.98)	343 (21.17)	821 (20.50)	105 (22.11)	1,908 (19.53)	46,762 (17.43)
Yes	252,821 (82.24)	18,622 (80.02)	1,277 (78.83)	3,184 (79.50)	370 (77.89)	7,864 (80.47)	221,504 (82.57)

Abbreviation: BMI=Body mass index; CMD=Cardiometabolic diseases; FCMD=First cardiometabolic disease; CMM=Cardiometabolic multimorbidity; 2017 Physical Activity Guidelines=the 2017 UK Physical Activity Guidelines; IHD=Ischemic heart disease; T2D=Type 2 diabetes.

* Results are presented as mean (standard deviation) for continuous variables or number (percentage) for categorical variables.

† CMD include IHD, stroke, and T2D. CMM is defined as the co-occurrence of two or more diseases mentioned above.

§ Meeting the 2017 Physical Activity Guidelines means participants take 150 minutes of walking or moderate-intensity activity, 75 minutes of vigorous-intensity activity per week. WHO Guidelines mean participants take 150 minutes of moderate-intensity physical activity, 75 minutes of vigorous-intensity physical activity, or an equivalent combination of moderate- and vigorous-intensity physical activity.

0.872 (0.833, 0.912) for all-cause mortality, respectively.

Multi-state regression analyses generated similar results regarding the results yielded by traditional Cox regression models (Table 3). The inverse associations were found between physical activity and almost all transitions in CMM progression, as the HRs (95% *CIs*) of transition from baseline to death were 0.886 (0.838, 0.936) and 0.815 (0.771, 0.862) for moderate and high level of physical activity. Meeting the WHO Guidelines showed the most conspicuous benefits among all five transitions (Supplementary Table S2,

TABLE 2. Associations between physical activity and FCMD, CMM, and all-cause death among 307,411 participants in the UK Biobank.

Outcomes*	Physical activity	No. of cases (total number)	Model 1†		Model 2†	
			HR (95% *CI*)	*P*	HR (95% *CI*)	*P*
FCMD	Physical activity level					
	Low	6,030 (55,116)	1.000	–	1.000	–
	Moderate	11,518 (125,837)	0.800 (0.775, 0.825)	<0.001	0.880 (0.853, 0.908)	<0.001
	High	11,825 (126,458)	0.798 (0.773, 0.823)	<0.001	0.890 (0.862, 0.919)	<0.001
	Meeting the 2017 PA guidelines					
	No	5,743 (54,427)	1.000	–	1.000	–
	Yes	23,630 (252,984)	0.826 (0.803, 0.851)	<0.001	0.906 (0.880, 0.933)	<0.001
	Meeting the WHO guidelines§					
	No	5,920 (54,590)	1.000	–	1.000	–
	Yes	23,453 (252,821)	0.805 (0.783, 0.829)	<0.001	0.895 (0.869, 0.921)	<0.001
CMM	Physical activity level					
	Low	468 (55,116)	1.000	–	1.000	–
	Moderate	809 (125,837)	0.718 (0.641, 0.805)	<0.001	0.840 (0.749, 0.942)	<0.001
	High	818 (126,458)	0.702 (0.627, 0.787)	<0.001	0.824 (0.734, 0.926)	<0.001
	Meeting the 2017 PA guidelines					
	No	428 (54,427)	1.000	–	1.000	–
	Yes	1,667 (252,984)	0.770 (0.692, 0.856)	<0.001	0.887 (0.796, 0.988)	0.029
	Meeting the WHO guidelines§					
	No	448 (54,590)	1.000	–	1.000	–
	Yes	1,647 (252,821)	0.738 (0.665, 0.819)	<0.001	0.869 (0.781, 0.966)	0.009
All-cause death	Physical activity level					
	Low	2,869 (55,116)	1.000	–	1.000	–
	Moderate	5,789 (125,837)	0.825 (0.789, 0.863)	<0.001	0.872 (0.833, 0.912)	<0.001
	High	5,594 (126,458)	0.782 (0.747, 0.818)	<0.001	0.819 (0.782, 0.857)	<0.001
	Meeting the 2017 PA guidelines					
	No	2,697 (54,427)	1.000	–	1.000	–
	Yes	11,555 (252,984)	0.974 (0.958, 0.990)	0.002	0.961 (0.945, 0.977)	<0.001
	Meeting the WHO guidelines§					
	No	2,834 (54,590)	1.000	–	1.000	–
	Yes	11,418 (252,821)	0.803 (0.771, 0.837)	<0.001	0.851 (0.816, 0.887)	<0.001

Note: "–" means not applicable.
Abbreviation: FCMD=First cardiometabolic disease; CMM=Cardiometabolic multimorbidity; CMD=Cardiometabolic diseases; PA=Physical activity; No.=Number; HR=Hazard ratio; *CI*=Confidence interval; IHD=Ischemic heart disease; T2D=Type 2 diabetes.
* CMD include IHD, stroke, and T2D. CMM is defined as the co-occurrence of two or more diseases mentioned above.
† Model 1 was adjusted for age (per 5-year interval), sex, and ethnicity; Model 2 was further adjusted for body mass index, total household income, employment, education, smoking status, alcohol intake, fruit and vegetable intake, and family history of CMM. All results were calculated by the traditional Cox proportional hazard regression models.
§ Meeting the 2017 Physical Activity Guidelines means participants take 150 minutes of walking or moderate-intensity activity or 75 minutes of vigorous-intensity activity per week. WHO Guidelines means participants take 150 minutes of moderate-intensity physical activity, 75 minutes of vigorous-intensity physical activity, or an equivalent combination of moderate- and vigorous-intensity physical activity.

available in http://weekly.chinacdc.cn/). All our findings remained substantially stable after conducting several sensitivity analyses (Supplementary Tables S2–S3, available in http://weekly.chinacdc.cn/).

DISCUSSION

Our study investigated the impact of physical activity levels and recommendations on different

TABLE 3. Associations between 5 transitions of CMM progression and physical activity levels among 307,411 participants in the UK Biobank.

Transition*	Physical activity level	No. of cases (total number)	HR (95% *CI*)†	*P*
Baseline → FCMD	Low	6,030 (55,116)	1.000	
	Moderate	11,518 (125,837)	0.880 (0.853, 0.908)	<0.001
	High	11,825 (126,458)	0.892 (0.864, 0.920)	<0.001
Baseline → Death	Low	1,920 (55,116)	1.000	
	Moderate	4,049 (125,837)	0.886 (0.838, 0.936)	<0.001
	High	3,803 (126,458)	0.815 (0.771, 0.862)	<0.001
FCMD → CMM	Low	468 (6,030)	1.000	
	Moderate	809 (11,518)	0.951 (0.848, 1.068)	0.398
	High	818 (11,825)	0.942 (0.838, 1.059)	0.315
FCMD → Death	Low	841 (6,030)	1.000	
	Moderate	1,561 (11,518)	0.908 (0.834, 0.988)	0.026
	High	1,603 (11,825)	0.916 (0.841, 0.998)	0.045
CMM → Death	Low	108 (468)	1.000	
	Moderate	179 (809)	0.882 (0.690, 1.127)	0.314
	High	188 (818)	1.009 (0.790, 1.288)	0.943

Abbreviation: FCMD=First cardiometabolic disease; CMM=Cardiometabolic multimorbidity; HR=Hazard ratio; *CI*=Confidence interval; IHD=Ischemic heart disease; T2D=Type 2 diabetes; BMI=Body mass index.

* CMD include IHD, stroke, and T2D. CMM is defined as co-occurrence of two or more diseases mentioned above. Trajectory pattern A consists of 5 transitions, including transitions from baseline to FCMD and all-cause death, transitions from FCMD to CMM and all-cause death, and to transition from CMM to all-cause death.

† Multivariable models were adjusted by age at recruitment (5-year interval) to sex, ethnicity, BMI, total household income, employment, education, smoking status, alcohol intake, fruit and vegetable intake, and family history of CMM.

trajectories of CMM progression. The results of both traditional Cox regression and multi-state regression analyses yielded the inverse associations between physical activity and CMD incidence and further progression, albeit to different degrees. More substantial impacts of physical activity were found on transitions from baseline to FCMD and all-cause death. The WHO Guidelines seemed to possess more pronounced health benefits than the other four recommendations.

In traditional Cox regression analyses, increasing physical activity levels were associated with lower FCMD, CMM, and death incidence. A stronger association was found in transition from the baseline to CMM. The findings differed from previous studies reporting a more beneficial role physical activity played in the transition from the baseline to single CMD than CMM (*7*). The heterogeneity might be due to multiple factors, albeit largely unclear. First, CMM incidence in traditional Cox regression models consisted of several transitions in multi-state regression models. Different transitions might have reshaped the characteristics of the study population, consequently leading to different effect estimates. Second, as Albrecht et al. suggested (*8*), the disability paradox might largely influence the fundamental relationship between life quality and diseases. The influence of physical activity might thus be exaggerated as adults may be influenced to have higher levels of physical activity after being diagnosed with CMDs. Notably, such speculation seemed contradictory to the findings in multi-state regression models, where stronger associations were observed in the transition from the baseline to FCMD than in the transition from FCMD to CMM. Further studies are warranted to confirm our findings and to investigate the underlying mechanisms.

Inverse relationships between physical activity and almost all the transition incidences were observed in multi-state regression models, with stronger associations observed in transitions from baseline to FCMD/death. In contrast, a recent study of the China Kadoorie Biobank (CKB) found that physical inactivity significantly impacted the transition from FCMD to death/CMM (*1*). Foremost, the percentage of low physical activity levels was relatively more prominent in the CKB (about 50%) than UKB (about 20%) (*1*), indicating the Chinese adults were more physically inactive, albeit the CKB participants might

not represent the general Chinese population well. Physical activity has been well-confirmed to be associated with lower risks of numerous chronic diseases (*9*). The relatively low percentage of taking physical activity in China would therefore imply more significant health benefits if Chinese adults could take more physical activity. Furthermore, a higher prevalence of CMDs in CKB (19%) than in UKB (9.55%) indicated that the Chinese population was more sensitive to adverse health outcomes, such as CMM. Physical activity could play a more notable role in CMM progression in CKB than UKB, considering the more vulnerable group of Chinese adults. Therefore, Chinese policymakers should encourage adults to take physical activity actively to help lower the risks of CMM in the Chinese population.

Meeting the WHO Guidelines showed the most notable benefits on almost all transitions compared with other higher-level recommendations. It was different from the current physical activity recommendations suggesting that adults already with chronic diseases should take more physical activity. The difference could be interpreted by the fact that the health benefits of increasing physical activity tend to hit a plateau when adults have met the WHO Guidelines (*10*).

Several limitations should be noted. First, we only adopted information at baseline levels. Changes in physical activity and other covariates over the follow-up may influence the estimates. However, we further conducted an additional analysis in a sub-sample of participants (n=15,894), finding most participants (63%) maintained their physical activity level. The distribution of physical activity levels among participants with or without CMDs was similar (Supplementary Table S1), indicating the changes were non-differentially distributed, our results would not be substantially affected. Second, for those diagnosed with two or more CMDs on the same date, we determined the entering date as the entering date of the theoretically latter stage minus 0.5 days, which may lead to a biased estimate. However, considering the small proportion [1,304 (0.4%)] and robust results of sensitivity analyses (Supplementary Table S3), the bias may not influence the results substantially. Third, almost 20% of the population was excluded at baseline, which may cause selection bias inevitably. However, we compared baseline characteristics between included and excluded participants, finding that the distribution of baseline characteristics was comparable between the two groups (data not shown). Furthermore, we conducted a multivariate imputation, and no substantial changes in results were found (data not shown).

In summary, our study suggested that physical activity could reduce CMD incidence and further progression, albeit to different extents. Adults should engage in physical activity, meeting the WHO Guidelines as early as possible, especially those initially free of CMDs.

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SUPPLEMENTARY MATERIALS

Supplementary Methods

Changes in Physical Activity between Baseline and Resurvey

We calculated the difference in total physical activity level (measured based on the criteria of the short form of IPAQ) between the 2006–10 baseline and 2014+ resurvey (*1*). The number (proportion) of change in physical activity by cardiometabolic disease status at 2014+ resurvey was calculated.

Definitions of Different Physical Activity Recommendations

Guideline low means participants take at least 150 minutes of walking each week, but fail to meet the WHO Guidelines. 2017 Physical Activity Guidelines mean participants take 150 minutes of walking or moderate-intensity activity, or 75 minutes of vigorous-intensity activity per week, or an equivalent combination of these activities. The WHO Guidelines mean participants take 150 minutes of moderate-intensity physical activity, or 75 minutes of vigorous-intensity physical activity, or an equivalent combination of both intensities (*2*). Guideline 300 means participants take 300 minutes of moderate-intensity physical activity, or 150 minutes of vigorous-intensity physical activity, or an equivalent combination of both intensities. And Guideline 450 means participants take 450 minutes of moderate-intensity physical activity, or 225 minutes of vigorous-intensity physical activity, or an equivalent combination of both intensities.

Analytical Protocol

We constructed two incrementally-adjusted models: Model 1 was adjusted for age at recruitment, sex, and ethnicity; Model 2 was further adjusted for BMI, household income, employment status, education, lifestyle factors (smoking status, alcohol consumption, and fruit and vegetable intake), and family history of cardiometabolic multimorbidity (CMM). Several sensitivity analyses were performed for the multi-state analyses on the trajectory pattern A, including: 1) determining the entering date of theoretically prior stage with different time intervals (0.5 year, 1 year, and 1.5 years) for participants entering different disease stages on the same date; 2) excluding participants entering different stages on the same date; 3) excluding cardiometabolic disease (CMD) cases occurring in the first two years of follow-up; 4) further adjusting for the history of hypertension; 5) in addition to the predefined 5 transitions, adding another transition directly from the baseline to CMM. Considering the fact that we excluded a relatively large number of participants due to missing baseline covariates, we additionally conducted a multivariate imputation via chained equation (MICE) (the number of imputations was five) to make sure that the representativeness of the cohort was not substantially affected by exclusion of participants (data not shown) (*3*).

SUPPLEMENTARY TABLE S1. Changes in physical activity levels between 2006–2010 baseline and resurvey between 2014 and 2020 by cardiometabolic disease status among 15,894 participants.

Change in physical activity level[*†]	Overall	Free of CMD	FCMD/CMM
Total number	15,894	15,554	340
Upward	3,652 (22.98)	3,586 (23.06)	66 (19.41)
Downward	2,154 (13.55)	2,111 (13.57)	43 (12.65)
Stable	10,088 (63.47)	9,857 (63.37)	231 (67.94)

Abbreviation: FCMD=First cardiometabolic disease; CMM=Cardiometabolic multimorbidity; CMD=Cardiometabolic diseases.
Cardiometabolic diseases include ischemic heart disease (IHD), stroke, and type 2 diabetes (T2D). Cardiometabolic multimorbidity is defined as co-occurrence of two or more diseases mentioned above.
* Results are presented as number (percentage) for categorical variables.
† Changes in physical activity between baseline and resurvey were classified into stable (at the same level), upward (from low level to moderate/high level, or from moderate level to high level), and downward (from high level to moderate/low level, or from moderate level to low level). The number (proportion) of change in physical activity by cardiometabolic disease status at 2014+ resurvey was calculated.

SUPPLEMENTARY TABLE S2. Associations between different physical activity recommendations and 5 transitions of CMM progression.

5 transitions in trajectory pattern A[†]	Physical activity recommendations[*§]				
	Guideline low	2017 UK physical activity guideline	WHO guidelines	Guideline 300	Guideline 450
Baseline → FCMD	0.935 (0.904, 0.968)[¶]	0.907 (0.880, 0.934)[¶]	0.894 (0.868, 0.920)[¶]	0.933 (0.911, 0.955)[¶]	0.963 (0.940, 0.985)[¶]
Baseline → Death	0.946 (0.891, 1.004)	0.884 (0.839, 0.931)[¶]	0.849 (0.807, 0.893)[¶]	0.891 (0.855, 0.930)[¶]	0.880 (0.845, 0.916)[¶]
FCMD → CMM	0.982 (0.865, 1.116)	1.000 (0.897, 1.114)	0.986 (0.886, 1.097)	0.997 (0.911, 1.090)	1.039 (0.952, 1.134)
FCMD → Death	0.950 (0.867, 1.042)	0.925 (0.854, 1.001)	0.934 (0.863, 1.010)	0.923 (0.865, 0.985)[¶]	0.972 (0.913, 1.035)
CMM → Death	0.800 (0.611, 1.051)	0.914 (0.729, 1.148)	0.916 (0.732, 1.145)	0.982 (0.813, 1.186)	1.084 (0.903, 1.301)

Abbreviation: FCMD=First cardiometabolic disease; CMM=Cardiometabolic multimorbidity; HR=Hazard ratio; *CI*=Confidence interval; CMD=Cardiometabolic diseases; IHD=Ischemic heart disease; T2D=Type 2 diabetes; UK=United Kingdom; WHO=World Health Organization.
* Multivariable models were adjusted for age (per 5-year interval), sex, ethnicity, body mass index, total household income, employment, education, smoking status, alcohol intake, fruit and vegetables intake, and family history of CMM. Estimates were presented as HRs and their 95% *CI*s with the reference group of not meeting corresponding guidelines.
† CMD include IHD, stroke, and T2D. CMM is defined as co-occurrence of two or more diseases mentioned above. Five transitions in trajectory pattern A consist of transitions from baseline to FCMD and all-cause death, transitions from FCMD to CMM and all-cause death, and transition from CMM to all-cause death.
§ Guideline low means participants take at least 150 minutes of walking each week, but fail to meet WHO Guidelines. 2017 UK Physical Activity Guidelines mean participants meet its standards. WHO Guidelines mean participants take 150 minutes of moderate-intensity physical activity; or 75 minutes of vigorous-intensity physical activity; or an equivalent combination of moderate- and vigorous-intensity physical activity. Guideline 300 means participants take 300 minutes of moderate-intensity physical activity; or 150 minutes of vigorous-intensity physical activity; or an equivalent combination of moderate- and vigorous-intensity physical activity. And guideline 450 means participants take 450 minutes of moderate-intensity physical activity; or 225 minutes of vigorous-intensity physical activity; or an equivalent combination of moderate- and vigorous-intensity physical activity.
¶ The statistically significant differences (P<0.05).

SUPPLEMENTARY TABLE S3. Sensitivity analysis of the associations between physical activity levels and 5 phases of CMM trajectory among 307,411 participants in the UK Biobank.

Physical activity levels	Time interval	Different trajectory phases of CMM progression[†]					
		Baseline → FCMD	Baseline → Death	FCMD → CMM	FCMD → Death	CMM → Death	Baseline → CMM
Low level	–	1.000	1.000	1.000	1.000	1.000	1.000
Moderate level	**Different time intervals**						
	0.5 days	0.880 (0.853, 0.908)[§]	0.886 (0.838, 0.936)[§]	0.951 (0.848, 1.068)[§]	0.908 (0.834, 0.988)[§]	0.882 (0.690, 1.127)[§]	–
	0.5 years	0.880 (0.852, 0.908)[§]	0.886 (0.838, 0.936)[§]	0.967 (0.861, 1.086)[§]	0.900 (0.827, 0.980)[§]	0.948 (0.736, 1.220)[§]	–
	1 year	0.880 (0.853, 0.908)[§]	0.886 (0.838, 0.936)[§]	0.967 (0.861, 1.086)[§]	0.900 (0.827, 0.980)[§]	0.948 (0.736, 1.220)[§]	–
	3 years	0.880 (0.853, 0.908)[§]	0.886 (0.838, 0.936)[§]	0.967 (0.861, 1.086)[§]	0.900 (0.827, 0.980)[§]	0.948 (0.736, 1.220)[§]	–
	5 years	0.880 (0.853, 0.908)[§]	0.886 (0.838, 0.936)[§]	0.967 (0.861, 1.086)[§]	0.900 (0.827, 0.980)[§]	0.948 (0.736, 1.220)[§]	–
	Excluding participants who entered different stages on the same date						
	–	0.879 (0.851, 0.908)[§]	0.886 (0.839, 0.936)[§]	0.953 (0.847, 1.073)	0.868 (0.786, 0.960)[§]	0.863 (0.655, 1.135)	–
	Additionally adjusted for whether having the history of hypertension						
	–	0.878 (0.851, 0.906)[§]	0.885 (0.838, 0.935)[§]	0.949 (0.845, 1.065)	0.908 (0.834, 0.989)[§]	0.881 (0.689, 1.128)	–
	Excluding events occurred in the first two-year of follow-up						
	–	0.878 (0.850, 0.908)[§]	0.896 (0.847, 0.949)[§]	1.039 (0.892, 1.212)	0.857 (0.732, 1.004)	0.712 (0.457, 1.110)	–
	Adding a transition from free of CMD to CMM directly						
	–	0.881 (0.853, 0.909)[§]	0.742 (0.604, 0.911)[§]	0.886 (0.839, 0.936)[§]	0.957 (0.853, 1.073)	0.908 (0.834, 0.988)[§]	0.946 (0.759, 1.179)
High level	**Different time intervals**						
	0.5 days	0.892 (0.864, 0.920)[§]	0.815 (0.771, 0.862)[§]	0.942 (0.838, 1.059)[§]	0.916 (0.841, 0.998)[§]	1.009 (0.790, 1.288)[§]	–
	0.5 years	0.892 (0.864, 0.920)[§]	0.815 (0.771, 0.862)[§]	0.950 (0.844, 1.069)[§]	0.910 (0.835, 0.991)[§]	1.046 (0.812, 1.346)[§]	–
	1 year	0.892 (0.864, 0.92)[§]	0.815 (0.771, 0.862)[§]	0.950 (0.844, 1.069)[§]	0.910 (0.835, 0.991)[§]	1.046 (0.812, 1.346)[§]	–
	3 years	0.892 (0.864, 0.920)[§]	0.815 (0.771, 0.862)[§]	0.950 (0.844, 1.069)[§]	0.910 (0.835, 0.991)[§]	1.046 (0.812, 1.346)[§]	–
	5 years	0.892 (0.864, 0.920)[§]	0.815 (0.771, 0.862)[§]	0.950 (0.844, 1.069)[§]	0.910 (0.835, 0.991)[§]	1.046 (0.812, 1.346)[§]	–
	Excluding participants who entered different stages on the same date						
	–	0.889 (0.861, 0.918)[§]	0.815 (0.771, 0.863)[§]	0.925 (0.820, 1.042)	0.854 (0.772, 0.946)[§]	0.899 (0.680, 1.187)	–
	Additionally adjusted for whether having the history of hypertension						
	–	0.891 (0.863, 0.92)[§]	0.815 (0.770, 0.862)[§]	0.942 (0.838, 1.058)	0.916 (0.841, 0.998)[§]	1.008 (0.789, 1.289)	–
	Excluding events occurred in the first two-year of follow-up						
	–	0.898 (0.868, 0.928)[§]	0.836 (0.789, 0.886)[§]	0.934 (0.798, 1.094)	0.819 (0.697, 0.962)[§]	0.657 (0.413, 1.045)	–
	Adding a transition from free of CMD to CMM directly						
	–	0.892 (0.865, 0.921)[§]	0.704 (0.571, 0.869)[§]	0.816 (0.771, 0.863)[§]	0.947 (0.843, 1.064)	0.916 (0.841, 0.998)[§]	1.044 (0.835, 1.304)

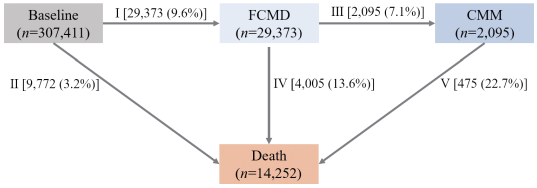
Note: "–" means not applicable.

Abbreviation: FCMD=First cardiometabolic disease; CMM=Cardiometabolic multimorbidity; CMD=Cardiometabolic diseases; *CI*=Confidence interval; HR=Hazard ratio; IHD=Ischemic heart disease; T2D=Type 2 diabetes; UK=United Kingdom.

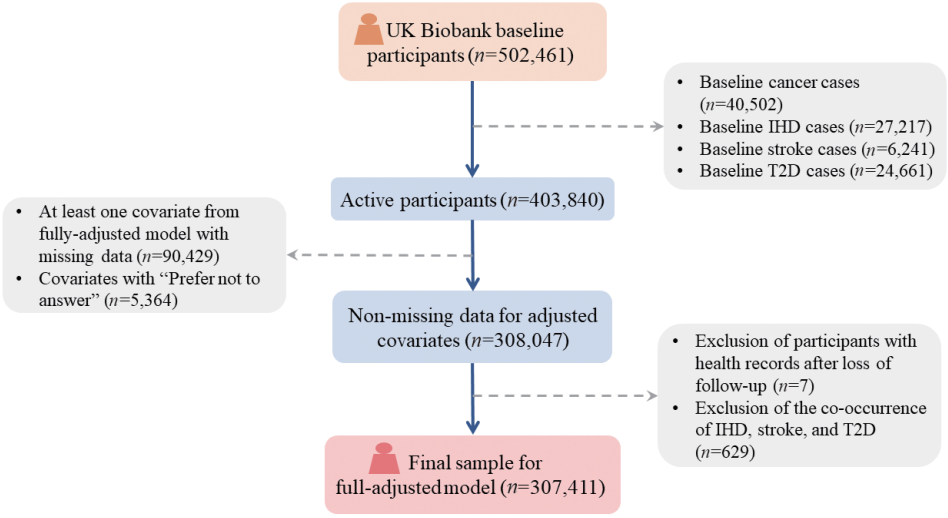
* Multivariable models were adjusted for age (per 5-year interval), sex, ethnicity, body mass index, total household income, employment, education, smoking status, alcohol intake, fruit and vegetables intake, and family history of CMM. Estimates were presented as HRs and their 95% *CI*s.

[†] CMD include IHD, stroke, and T2D. Cardiometabolic multimorbidity is defined as co-occurrence of two or more diseases mentioned above.

[§] The statistically significant differences ($P<0.05$).



SUPPLEMENTARY FIGURE S1. Numbers (percentages) of participants in trajectory pattern A from baseline to the first cardiometabolic diseases (FCMD) to cardiometabolic multimorbidity (CMM), and to death.
Note: FCMD was identified as the earliest occurrence of any of these three diseases (ischemic heart disease, stroke, and type 2 diabetes). CMM is defined as subsequent occurrence of any of the remaining CMDs.
Abbreviation: FCMD=First cardiometabolic disease; CMD=Cardiometabolic diseases.



SUPPLEMENTARY FIGURE S2. Flowchart of selection of participants.
Abbreviation: IHD=Ischemic heart disease; T2D=Type 2 disease.

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Preplanned Studies

Relationship between Maternal Postpartum Intention to Breastfeed and Actual Breastfeeding Duration — Four Provinces, China, 2015–2017

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Summary

What is already known about this topic?

Several studies have reported that maternal antenatal intention to breastfeed is a strong predictor of actual breastfeeding duration. However, little research has investigated whether maternal postpartum intention also extends breastfeeding duration.

What is added by this report?

Maternal postpartum intention to breastfeed was a protective factor for extending actual breastfeeding duration after controlling potential confounders.

What are the implications for public health practice?

It is crucial to address and promote intrinsic and extrinsic factors that influence a mother's intention to breastfeed after delivery, thereby extending the actual breastfeeding duration.

Breast milk is universally recognized as the optimal source of nutrition for infants. The World Health Organization (WHO) and United Nations International Children's Emergency Fund (UNICEF) recommend exclusive breastfeeding until 6 months old, with continued breastfeeding to 2 years old or beyond (*1*). Nevertheless, breastfeeding duration in China is still far below the global nutrition targets (*2*). Several studies have reported that maternal antenatal intention to breastfeed is a strong predictor of actual duration of breastfeeding (*3*). Maternal postpartum intention could be much more associated with actual breastfeeding duration because of shorter time intervals and fewer impeding factors present during pregnancy, compared to maternal antenatal intention. However, very little research has been done to determine if the maternal postpartum intention to breastfeed increases the duration of feeding in some mothers (*4*). This study was performed to examine the relationship between maternal postpartum intention and actual breastfeeding duration to provide data on the impact of extended breastfeeding duration. Data used in this study (e.g., infants' breastfeeding status) were drawn from "Maternal and Child Health Monitoring Project", which was implemented by the National Center for Women and Children's Health of China CDC in five districts in four provinces (Hebei, Liaoning, Hunan, and Fujian) from 2015–2017. The results showed that maternal postpartum intention to breastfeed was a protective factor for extending actual breastfeeding duration. Addressing key factors influencing a mother's postnatal intention to breastfeed may be important for prolonging this duration.

The data were collected during a surveillance project founded by the Central Financial Project called the "Maternal and Child Health Monitoring Project" (2015–2019), which aimed to promote infants' health. This surveillance project was implemented by the National Center for Women and Children's Health of China CDC. Five districts in four provinces (Hebei, Liaoning, Hunan, and Fujian) were selected as monitoring sites in this project. These districts were selected based on their good compliance and their existing management systems for child health according to the requirements of the National Basic Public Health Service Project covering the whole area. Pregnant women in their third trimester were recruited as participants, and their children were followed for 3 years. To be included in the project, pregnant women had to have a gestational age between 28 and 36 weeks, have a singleton birth, and have lived in the monitoring site for more than half a year. Additionally, they would have to be registered residents at the site, be expected to live in the monitoring site until the child reaches 3 years of age and ensure their child receives routine child health care, possess a handbook for maternal health care containing complete records of antenatal examination, and agree to participate for the entire duration of the follow-up including the provision of informed consent. Pregnant women with mental illness, brain diseases, cardiovascular and cerebrovascular diseases, endocrine diseases, and cancer

were excluded. Ultimately, 2,731 mother–infant pairs were included in the project.

Of the 2,731 mother–infant pairs recruited; 228 pairs were excluded from the study because breastfeeding information was missing. Ultimately, 2,503 eligible mother–infant pairs were assessed in this study. Data on maternal postpartum intention to breastfeed were acquired from mothers 1 month after birth. Investigators collected information on breastfeeding duration at face-to-face physical examinations of infants at two follow-up time points (ages 6 and 12 months). Both maternal postpartum intentions to breastfeed and the actual duration of breastfeeding were divided into three classes: ≤6 months, 7–12 months, and >12 months. Breastfeeding was defined as feeding with milk (direct from the breast or expressed) with or without other drinks, formula, or other infant foods (*5*).

The chi-square test was used to investigate the correlation between maternal postpartum intention to breastfeed and actual breastfeeding duration. Multinomial logistic regression was performed to analyze the association between the maternal postpartum intended period of breastfeeding and the actual period of breastfeeding after controlling potential confounders that could be related to breastfeeding duration (including sex, gestational age at birth, method of delivery, birth weight, the timing of beginning complementary food, maternal age, parity, maternal education, annual family income, and region of the country). All data analyses were performed in SAS (version 9.4; SAS Institute). $P<0.05$ was considered statistically significant.

The sociodemographic characteristics of the study population are shown in Table 1.

Of the mothers who intended to breastfeed up to 6 months, only 50.72% were still breastfeeding at 6 months after birth, compared to 89.58% of mothers who had intended to breastfeed for 7 to 12 months and 94.30% of mothers who had intended to breastfeed for more than 12 months. There was a positive correlation between maternal postpartum intention to breastfeed and actual breastfeeding duration (Pearson contingency coefficient=0.42; $P<0.05$) (Table 2).

As shown in Table 3, after adjustment for confounding factors, multinomial logistic regression showed that relative to mothers intending to breastfeed less than 6 months at 1 month after birth, the intention to breastfeed more than 6 months or more than 12 months was a protective factor for extending actual breastfeeding duration to more than 6 months [*OR*=5.77, 95% confidence interval (*CI*)=4.04–8.24; *OR*=8.61, 95% *CI*=5.93–12.50, respectively] and to more than 12 months (*OR*=9.47, 95% *CI*=6.09–14.75; *OR*=21.26, 95% *CI*=13.84–32.66, respectively).

Moreover, the timing for beginning complementary food, parity, and region of the country was statistically significantly associated with actual breastfeeding duration ($P<0.05$). Starting complementary food ≥6 months, multiparity, and living in South China were protective factors for longer breastfeeding duration.

DISCUSSION

In the monitored regions, 87.06% and 50.46% of mothers continued breastfeeding at 6 months and 12 months, respectively, which was far below global nutrition targets. The result of this study suggests that health guidelines and education should continue to be strengthened in monitoring regions to extend the duration of breastfeeding. In addition, this study found that maternal intention to breastfeed 1 month after birth was a protective factor for extending actual breastfeeding duration after controlling potential confounders, which implied that promoting a mother's postnatal intention to breastfeed may be an essential measure for extending breastfeeding duration. Furthermore, regional variation was also seen in breastfeeding duration, the reasons for which might be different rates of maternal postpartum intention among the regions. The rate of maternal postpartum intention to breastfeed until 7–12 months was 37.78% in Liaoning and 69.87% in Hunan.

Li et al. determined that the mean duration of breastfeeding in China from 2007–2018 was only 10 months and a wide gap in the prevalence of breastfeeding remained among different cities (*6*), consistent with this study. Studies in China conducted in Shihezi (*7*) and Sichuan (*8*) also reported a positive association between maternal postpartum intention and actual breastfeeding duration. In a study in Thailand, mothers who intended to breastfeed more than 6 months after delivery were more likely to be breastfeeding at 6 months (*4*). In another study, infants whose mothers had the postpartum intention to breastfeed longer than 6 months were more likely to have been breastfed at 6 months (*9*); our results are consistent with these findings. Furthermore, even if mothers have a strong intention to breastfeed, they cannot achieve successful breastfeeding in reality because they are primiparous, concerned about the

TABLE 1. Sociodemographic characteristics of 2,503 mother–infant pairs in five districts of four provinces (Hebei, Liaoning, Hunan, and Fujian) in China from 2015–2017.

Sociodemographic characteristic	Total (*n*=2,503)	
	Number	Proportion (%)
Sex of infants		
Male	1,329	53.10
Female	1,174	46.90
Gestational age at birth (week)		
<37	87	3.48
≥37	2,416	96.52
Method of delivery		
Vaginal	1,325	52.94
Cesarean	1,178	47.06
Birth weight of infants (kg)		
<2.50	67	2.68
2.50–4.00	2,313	92.41
>4.00	123	4.91
Timing for starting complementary food (month)		
<6	1,572	62.80
≥6	931	37.20
Maternal age (year)		
<25	339	13.54
25–29	1,220	48.74
30–34	675	26.97
≥35	269	10.75
Parity		
Primiparous	1,156	46.18
Multiparous	1,347	53.82
Maternal education		
Less than high school	804	32.12
High school	650	25.97
College or above	1,049	41.91
Annual family income (CNY)		
<30,000	347	13.86
30,000–49,999	671	26.81
50,000–79,999	616	24.61
≥80,000	864	34.52
Missing	5	0.20
Region of the country*		
North China	630	56.85
South China	450	43.15

Abbreviation: CNY=China Yuan.
* North China includes Hebei and Liaoning provinces; South China includes Hunan and Fujian provinces.

TABLE 2. Correlation between maternal postpartum intention to breastfeed and actual breastfeeding duration.

Maternal postpartum intention to breastfeed (months)	Actual breastfeeding duration, *n* (%)			Total	Pearson contingency coefficient	χ^2	*P*
	≤6 months	7–12 months	>12 months				
≤6	137 (49.28)	81 (29.14)	60 (21.58)	278	0.42	536.14	<0.0001
7–12	133 (10.42)	600 (46.99)	544 (42.60)	1,277			
>12	54 (5.70)	235 (24.79)	659 (69.51)	948			
Total	324 (12.94)	916 (36.60)	1,263 (50.46)	2,503			

TABLE 3. Associations between maternal postpartum intention to breastfeed and other confounding factors with actual breastfeeding duration.

Factors	Actual breastfeeding duration (7–12 months)*		Actual breastfeeding duration (12 months)*	
	OR (95% *CI*)	*P*	*OR* (95% *CI*)	*P*
Maternal postpartum intention to breastfeed, months (ref. ≤6)				
7–12	5.77 (4.04–8.24)	<0.0001	8.61 (5.93–12.50)	<0.0001
>12	9.47 (6.09–14.75)	<0.0001	21.26 (13.84–32.66)	<0.0001
Sex of infants (ref. male)				
Female	1.13 (0.85–1.51)	0.394	1.16 (0.87–1.53)	0.311
Gestational age at birth, weeks (ref. <37)				
≥37	1.52 (0.73–3.18)	0.264	1.87 (0.90–3.91)	0.095
Method of delivery (ref. vaginal)				
Cesarean	0.87 (0.64–1.17)	0.354	0.86 (0.64–1.15)	0.315
Birth weight, kg (ref. 2.50–4.00)				
<2.50	0.56 (0.24–1.31)	0.181	0.49 (0.21–1.13)	0.093
>4.00	0.91 (0.46–1.80)	0.793	1.11 (0.59–2.11)	0.743
Timing for starting complementary food, months (ref. <6)				
≥6	1.85 (1.32–2.59)	0.0004	2.91 (2.08–4.06)	<0.0001
Maternal age, years (ref. 25–29)				
<25	1.49 (0.93–2.37)	0.101	1.48 (0.93–2.39)	0.100
30–34	0.83 (0.59–1.16)	0.272	0.90 (0.65–1.26)	0.537
≥35	0.83 (0.52–1.35)	0.462	0.98 (0.61–1.58)	0.928
Parity (ref. Primiparous)				
Multiparous	1.52 (1.09–2.11)	0.015	2.01 (1.45–2.79)	<0.0001
Maternal education (ref. Less than high school)				
High school	0.78 (0.54–1.11)	0.168	0.81 (0.57–1.15)	0.240
College or above	0.92 (0.63–1.35)	0.669	0.84 (0.58–1.22)	0.369
Annual family income, CNY (ref. <30,000)				
30,000–49,999	1.41 (0.88–2.25)	0.158	1.53 (0.97–2.39)	0.065
50,000–79,999	1.03 (0.64–1.63)	0.916	1.33 (0.85–2.08)	0.209
≥80,000	0.76 (0.49–1.19)	0.229	1.16 (0.75–1.78)	0.507
Region of the country (ref. North China)				
South China	5.46 (3.81–7.81)	<0.0001	0.74 (0.53–1.03)	0.076

Abbreviation: CNY=China Yuan.
* Actual breastfeeding duration <6 months is the reference category.

amount of breast milk or pain, lack professional support, or are required to return to an unsupportive work environment after giving birth (*10*–*11*). Thus, it may be that enhancing mothers' intrinsic power, including increasing their self-efficacy regarding breastfeeding, and their extrinsic support power, such as improving the support they receive from family and society for breastfeeding during the postnatal period, can enhance maternal breastfeeding postpartum intention, including breastfeeding duration intention.

The present study had some limitations. First, it was conducted at five monitoring sites in four provinces of China; the results cannot be generalized to China as a whole. Second, the need to return to work after giving birth may reduce overall breastfeeding duration; however, this variable was not collected in this study. Third, the presence of maternal illness, lack of breast milk, nipple pain during breastfeeding, and other factors that can affect breastfeeding were not considered, which may have affected the accuracy of the results. Finally, maternal intention to breastfeed at 1 month after birth may be more correlated with actual breastfeeding duration, though it seems that it is more practical to educate pregnant women before delivery or those who are hospitalized after delivery and improve their intention to breastfeed compared to educate mothers at 1 month after birth and improve their breastfeeding duration.

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Conflicts of interest: No conflicts of interest.

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Notifiable Infectious Diseases Reports

Reported Cases and Deaths of National Notifiable Infectious Diseases — China, September 2022

Diseases	Cases	Deaths
Plague	1	1
Cholera	4	0
SARS-CoV	0	0
Acquired immune deficiency syndrome*	4,389	1,847
Hepatitis	123,318	72
Hepatitis A	945	1
Hepatitis B	101,083	35
Hepatitis C	18,740	35
Hepatitis D	14	0
Hepatitis E	1,946	0
Other hepatitis	590	1
Poliomyelitis	0	0
Human infection with H5N1 virus	1	0
Measles	78	0
Epidemic hemorrhagic fever	205	0
Rabies	14	8
Japanese encephalitis	53	1
Dengue	28	0
Anthrax	42	0
Dysentery	3,134	0
Tuberculosis	58,638	347
Typhoid fever and paratyphoid fever	631	0
Meningococcal meningitis	2	0
Pertussis	3,849	0
Diphtheria	0	0
Neonatal tetanus	4	0
Scarlet fever	1,020	0
Brucellosis	5,311	0
Gonorrhea	8,598	0
Syphilis	44,470	9
Leptospirosis	43	2
Schistosomiasis	8	0
Malaria	96	2
Human infection with H7N9 virus	0	0
COVID-19[†]	7,172	0
Influenza	90,089	0
Mumps	11,041	0

Continued

Diseases	Cases	Deaths
Rubella	98	0
Acute hemorrhagic conjunctivitis	2,273	0
Leprosy	24	0
Typhus	174	0
Kala azar	19	0
Echinococcosis	140	0
Filariasis	0	0
Infectious diarrhea[§]	76,490	2
Hand, foot and mouth disease	44,872	1
Total	486,329	2,292

* The number of deaths of acquired immune deficiency syndrome (AIDS) is the number of all-cause deaths reported in the month by cumulative reported AIDS patients.
† The data were from the website of the National Health Commission of the People's Republic of China.
§ Infectious diarrhea excludes cholera, dysentery, typhoid fever and paratyphoid fever.
The number of cases and cause-specific deaths refer to data recorded in National Notifiable Disease Reporting System in China, which includes both clinically-diagnosed cases and laboratory-confirmed cases. Only reported cases of the 31 provincial-level administrative divisions in the mainland of China are included in the table, whereas data of Hong Kong Special Administrative Region, Macau Special Administrative Region, and Taiwan are not included. Monthly statistics are calculated without annual verification, which were usually conducted in February of the next year for de-duplication and verification of reported cases in annual statistics. Therefore, 12-month cases could not be added together directly to calculate the cumulative cases because the individual information might be verified via National Notifiable Disease Reporting System according to information verification or field investigations by local CDCs.

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