



Research article

Meteorological rhythms of respiratory and circulatory diseases revealed by Harmonic Analysis

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ABSTRACT

The intricately fluctuating onset of respiratory and circulatory diseases displays rhythms of multi-scaled meteorological conditions due to their sensitivity to weather changes. The intrinsic meteorological rhythms of these diseases are revealed in this bio-meteorological study via Fourier decomposition and harmonic analysis. Daily emergency room (ER) visit data for respiratory and circulatory diseases from three comprehensive hospitals in Haidian district of Beijing, China were used in the analysis. Meteorological data included three temperature metrics, relative humidity, sunshine duration, daily mean air pressure, and wind speed. The Fourier decomposition and harmonic analysis on ER visits and meteorological variables involve frequency, period, and power of all harmonics. The results indicated that: i) for respiratory morbidity, a strong climatic annual rhythm responding to annual temperature change was firstly revealed; its ratio of spectral density was 16–33%. Moreover, significant correlations existed between the high-frequency fluctuations (<30 d) of morbidity and short-term harmonics of humidity and solar duration. High-frequency harmonics of temperature and pressure showed no statistically significant effect. ii) With regard to all types of circulatory morbidity, their annual periodicity was weaker than that of respiratory diseases, whose harmonic energy took a ratio less than 8%. Besides, the power of all high-frequency harmonics of circulatory morbidity accounted for up to 70–90% in the original sequences, and their relationship to many short-term meteorological factors were significant, including the mean and maximum temperatures, wind speed, and solar duration. iii) The weekly rhythm appeared in respiratory ER visits with 15% of harmonic variance but not prominent in circulatory morbidity. In summary, by decomposing the sequence of respiratory and circulatory diseases as well as recognizing their meteorological rhythms, different responses to meteorological conditions on various time scales were identified.

1. Introduction

The significant impact of climate (change) and extreme weather conditions on human health has been reported substantially in recent studies (Liu et al., 2017; Burkart et al., 2014; Costello et al., 2009; Luber and Mcgeehin, 2008; Turner et al., 2012). Both the onset of diseases and their meteorological inducers (e.g., alternation of seasons and short-term weather changes) contain complex and multi-scaled variations (Ban et al., 2017; Modesti, 2013; Onozuka and Hagihara, 2016). It is self-evident that the alternation of seasons follow the climatic cycles due

to the annual change of Earth-Sun relationship. So meteorological variables are partially characterized by the annual cycle (Wu et al., 2008). Furthermore, massive atmospheric motions accompanied by short-waves transfer energy and water vapor constantly. With complex terrain and earth surface conditions, various time-scaled weather systems bring about fast-changing weather (Hoskins et al., 1983).

However, the observed meteorological factors are results of superposition of two processes, namely, long-term climate background and short-term weather events (Barry and Chorley, 2003). In the study of health effects from meteorological conditions, in the time domain, the

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effects of these two meteorological concepts have always been analyzed as a whole, owing to the single meteorological observation data. As a result, their health effects at different time scales were also readily to be counterbalanced or obscured.

Separating the impacts of different disease inducers, especially seasonal factors and short-term weather changes, has been an important goal for researchers in this domain for decades. Efficient progress has been made, for example, when identifying the association between meteorological factors and their health outcome by time-series models (e.g., the generalized additive models, GAM), effect of each factor was described through function fitting, which including spline functions, linear functions, or dummy variables, etc. (Gasparrini, 2011; Gasparrini et al., 2015; Ding et al., 2015). Specifically, when removing the long-term fluctuations of a morbidity, which mainly indicating its seasonal cycles, the GAM model was adjusted for trends by including a counter variable for each day of the time-series and fitting a smooth spline. And a short-term effect of certain meteorological factor could be estimated by using suitable functions with optimum degrees of freedom afterwards (Liang et al., 2017; Breitrner et al., 2014).

Time-series models are advantageous in covering or controlling various artificial and natural inducers of diseases in the time domain. However, the frequency characteristics of chronic diseases (Maetzler et al., 2015; Abboud et al., 1986), or their prominent meteorological inducers on different time scales (Xirasagar et al., 2007; Pilar et al., 2016), were less noticed and underexplored. Health impact from meteorological conditions of various scales were not clear (Modesti, 2013).

Hence, analyzing the frequency spectrum is obviously the most direct way to observe the multi-periodic characteristics of time series, which is also a classical mathematical method. According to literature investigations, the medical applications of frequency domain analysis have mostly been focused on image recognition, biological signal processing, or storage of patient medical records (Rodríguez et al., 1996; You et al., 2002). For example, frequency domain analysis was applied to ultrasonic signals from the liver, to evaluate structural changes in diffuse liver disease (Suzuki et al., 1993). Techniques based on Fourier Transform were also adapted for interleaving patient information with medical images to reduce storage overheads, in both spatial and frequency domain (Nayak et al., 2004; Acharya et al., 2004).

In the meantime, harmonic analysis has been successfully applied in examining the atmospheric motion in meteorology, as well as separating weather systems on varied scales (Chelton and Schlax, 1996; Wheeler and Kiladis, 1999). Atmospheric motion is regarded as the superposition of numerous simple harmonics with different frequencies and amplitudes, e.g., synoptic scale troughs and ridges are superimposed on the mean zonal circulation. And a certain scale system could be extracted and discussed individually.

Despite the varied inducers for onset of diseases, their temporal change contain high-frequency oscillations and seasonal fluctuations (Marshall et al., 1988; Cohen et al., 2014; Modesti et al., 2006), as well as some social rhythms or random factors. The number of emergency room (ER) visits are considered as the comprehensive results of the multiple factors, each factor can be assumed to be a harmonic component that corresponds to a specific amplitude and cycle, and thus, can be decomposed or superimposed. Therefore, the combined characteristics of meteorological variables, meteorological rhythms, and prominent meteorological inducers of morbidity can be explored based on their harmonics.

It has been explicitly proposed that the underlying factors threatening human health in modern days have shifted from infectious diseases to chronic diseases (Zhou et al., 2019; GBD, 2016 Causes of Death Collaborators, 2017). As the main connection between human body and the external environment, respiratory system is affected directly by meteorological and/or atmospheric conditions. Circulatory diseases (cardio-cerebrovascular diseases) pose a serious threat to middle-aged and elderly people nowadays (Chen et al., 2016). And they both rank among the top few in the spectrum of treatments and deaths and are sensible to

meteorological conditions (GBD, 2017 Causes of Death Collaborators, 2018).

Beijing (39°54'N, 116°23'E) is located in the warm temperate zone, with semi-humid continental monsoon climate. It has strong meteorological rhythms, which are characterized by hot and rainy summer, as well as cold and dry winter. As the capital city of China, Beijing has a population of 13.63 million (<http://www.stats.gov.cn/>, 2016) and its climate has evident responses to the global climate change (Solomon et al., 2007; Zheng et al., 2011). Investigation of the harmonic distributions of respiratory and circulatory ER visits in Beijing, and their relationship with meteorological conditions, may provide more insight in predicting and preventing these diseases among the large population. Further, this study may also offer a different idea and referential results for related researches.

The objectives of this study are to: i) explore the harmonic spectra from frequency domain of ER visits for respiratory and circulatory diseases in Beijing, China; ii) reveal their meteorological rhythms and typical social cycles from harmonic characteristics; and iii) analyze the statistical correlations between harmonics of meteorological variables and diseases.

2. Materials and methods

2.1. Data source

Disease data were collected from three comprehensive hospitals in Beijing, upon approval of data-use application and confidentiality agreement being signed. A total of 264,075 cases of ER visits for respiratory diseases from 1 Jan 2009 to 31 Dec 2012, as well as 49,555 ER visits for circulatory diseases from 1 Jan 2008 to 31 Dec 2012, were obtained. The data included the date and reason of ER visit, age, gender, primary diagnosis, and address. Visitors living outside of Beijing were excluded. All medical data were classified according to the tenth revision of International Classification of Diseases (Hude et al., 2005).

From the cases of respiratory diseases (J00–J99), 158,231 upper respiratory tract infection (URI) (J00–J06, J30–J39) and 37,406 lower respiratory tract infection (LRI) (J20–J22, J40–J47) were extracted, accounting for 59.92% and 14.16% of the total, respectively. The total circulatory diseases (I00–I99, G45–46) were classified into cardiovascular diseases (28,833 cases) and cerebrovascular diseases (20,722 cases). Moreover, 1,808 cases of intra-cerebral hemorrhage (I61–I62) and 13,723 cases of cerebral infarction (I63–I64) were separated from cerebrovascular diseases. Total numbers of ER visits for hypertension (I10–I15) and coronary heart diseases (I25.1) were 16,205 and 22,540, respectively.

Meteorological data for Beijing from 1 Jan 2008 to 31 Dec 2012 were obtained from the China Meteorological Data Sharing Service System (<http://cdc.nmic.cn/home.do>). Observed parameters included daily maximum and minimum temperatures, daily mean temperature, relative humidity, sunshine duration, daily mean air pressure, and wind speed.

2.2. Fourier series and spectral analysis

The Fourier series is often used to represent any periodic function in the form of the sum of a set of simple oscillating functions, namely sine and cosine functions. And it is easy to understand that a certain sine or cosine function has fixed frequency. Fourier series was originally applied to solve the heat equation, later the same techniques was found applicable with a wide array of mathematical and physical problems, as well as in electrical engineering, vibration analysis, acoustics, optics, and signal processing (Cattermole, 2000; Thomson, 2005). As a generalization of the notations, Fourier analysis, also known as harmonic analysis or spectral analysis, is a branch of mathematics concerned with the representation of functions or signals as the superposition of basic waves. Correspondingly, the Fourier transformation of a function, is a

complex-valued function of frequency, whose absolute value represents the weight of that frequency present in the original function.

As an effective method of cycle identification, harmonic analysis converts the original sequence from the time domain to the frequency domain. By the transformation, the frequency spectrum and the corresponding power spectral density are obtained. The value of spectral density represents harmonic energy or its variances, then the proportion (or weight) of a certain harmonic in all harmonics for a sequence can be quantified. Then the original sequence can be split into multiple series by extracting or combining trigonometric functions flexibly.

The Fourier series of a stable series X_t ($t = 1, 2, 3, \dots, N$) can be expressed as:

$$X_t = A_0 + \sum_{m=1}^n \left(\frac{A_m \cos 2\pi mt}{N} + \frac{B_m \sin 2\pi mt}{N} \right) + \epsilon t, \tag{1}$$

where $t (=1, 2, \dots, N)$ represents the time, N is the sample size, n is the maximum count of harmonics for X_t , and $N = 2n$; $m = 1, 2, \dots, n$, representing each harmonic function; the reciprocal of sample size ($1/N$) denotes the basic frequency, then m/N represents the m_{th} harmonic wave; ϵt is a random error.

Based on the least squares estimation, the Fourier coefficients of X_t are expressed as:

$$A_0 = (x_1 + x_2 + \dots + x_n)/N = \sum_{t=1}^N x_t/N, \tag{2}$$

$$A_m = \frac{2}{N} \sum_{t=1}^n \frac{X_t \cos 2\pi mt}{N}, \quad m = 1, 2, \dots, n, \tag{3}$$

$$B_m = \frac{2}{N} \sum_{t=1}^n \frac{X_t \sin 2\pi mt}{N}, \quad m = 1, 2, \dots, n. \tag{4}$$

And the power spectral density of the m_{th} harmonic wave is:

$$I_m = \frac{N}{2} (A_m^2 + B_m^2), \quad m = 1, 2, \dots, n. \tag{5}$$

From the above analysis, spectral densities of all harmonics can be obtained, which range from the shortest (2) to the longest (N) periods.

In this study, the sequences of ER visits for each type of disease, as well as daily meteorological factors, were processed with the above

Fourier transformation method. The original sequences were decomposed into a series of simple harmonics (sines and cosines), and the spectral density (power) of each harmonic was obtained. In cases of some time series that were not strictly periodic and stable due to superposition of numerous periodic sequences and certain trends, the series was pre-processed by de-trending and stabilizing before harmonic analysis. And the subsequent analysis mainly focused on the first few harmonics with large spectral density and neglected the numerous insignificant ones. For the distinct length of respiratory and circulatory sequence (1661 and 1826), their total number of harmonics were 830 and 913, respectively.

3. Results

3.1. Basic statistics of variables

Table 1 shows a summary of numbers of daily ER visits of different diseases and the corresponding meteorological variables. The daily mean ER visits for respiratory diseases was 180.75, within which URI and LRI were 108.3 and 25.6, respectively. Daily average ER visits for circulatory disease was 27.12, and number of cardiovascular patients (15.78) was slightly higher than cerebrovascular counts (11.34). The annual range of mean temperature, air pressure, relative humidity, and wind speed in Beijing was -12.5–34.5 °C, 992.6–1041 hPa, 9–97 %, and 0.5–6.4 m/s, respectively.

The series of respiratory diseases were pretreated with logarithm for the reason that their variance exceeds the average significantly (Table 1). The other treatment was to remove the trends in ER-visit counts for all diseases. The trends were in form of polynomial functions for total respiratory disease and URI, and linear functions for LRI (Figure 1A, eFigure 1, the prefix “e” is used to reference the figures and tables in the supplemental materials) and all types of circulatory diseases (Figure 1B, eFigure 2). Furthermore, ER visits for total circulatory diseases increased at 730 yr⁻¹ rates from 2008 to 2012 in Beijing, which was indicative of a very prominent growth. All trends passed tests with a significance level of $p = 0.001$ and were removed before harmonic analysis. During the study period, no significant trends were identified in meteorological factors.

3.2. Results of fourier transformation

3.2.1. Harmonic spectra of meteorological variables

Harmonics of meteorological sequences were sorted in the descending order of spectral density, from which the top 10 harmonics are shown

Table 1. Summary statistics of daily ER visits for respiratory and circulatory diseases and of corresponding meteorological variables in Beijing from 2008 to 2012.

Variables	Mean	Median	Standard deviation	Variance	Minimum	Maximum
Total Respiratory Disease	180.75	169.0	64.97	4221.07	50.0	649.0
Upper Respiratory Infection	108.30	101.0	40.25	1619.77	28.0	447.0
Lower Respiratory Infection	25.60	23.0	12.72	161.84	2.00	90.0
Total circulatory disease	27.12	27.0	12.56	157.7	0.00	66.0
Cardiovascular disease	15.78	15.0	8.02	64.37	0.00	46.0
Cerebrovascular disease	11.34	11.0	5.77	33.35	0.00	38.0
Hypertensive disease	8.87	8.00	6.24	38.89	0.00	31.0
Coronary heart disease	12.34	12.0	6.87	47.24	0.00	37.0
Intracerebral hemorrhage	0.99	1.00	1.11	1.22	0.00	7.00
Cerebral infraction	7.51	7.00	4.38	19.15	0.00	29.0
Air pressure (hPa)	1015.02	1014.8	10.53	110.89	992.6	1041.0
Air temperature (°C)	13.08	15.1	11.62	135.04	-12.5	34.5
Maximum temperature (°C)	18.20	20.6	11.86	140.61	-8.50	40.6
Minimum temperature (°C)	8.37	9.60	11.45	131.06	-16.7	29.2
Relative humidity (%)	50.54	52.0	20.07	402.68	9.00	97.0
Wind speed (m/s)	2.23	2.10	0.92	0.85	0.50	6.40
Sunshine duration (hour)	6.73	7.80	4.04	16.31	0.00	14.0

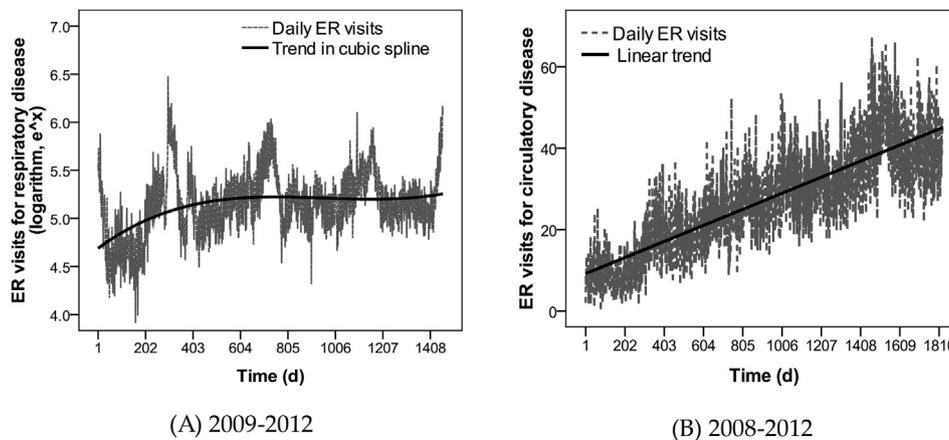


Figure 1. The time-series of daily ER visits for (A) the total respiratory diseases and (B) the total circulatory diseases in Beijing.

in Table 2. The spectral density (harmonic energy) is presented as a ratio of single (or several) spectral density to the total energy of the original sequence, which is measured in percentage (%). Obviously, the annual cycle took the leading role for all variables, representing the significant climatic rhythm. The annual cycle of the mean temperature, in particular, showed a ratio of 93.3% (Table 2), being the strongest periodicity among all variables. Moreover, semi-annual cycle also appeared in temperature, humidity, and wind (Table 2). The remaining harmonics was insignificant for their minor proportion. It should be noted that long-term climate change was not considered, due to the lack of matched medical data.

3.2.2. Harmonic characteristics of respiratory and circulatory ER visits

In a similar pattern, the top 10 harmonics for the two types of diseases are shown in Tables 3 and 4, respectively, with more details in eTables 1 and 2. Figure 2 displays the distribution of harmonic spectral density of the total respiratory diseases. For three respiratory sequences, the harmonic period of 365 d was also the leading one, whose ratio of spectral density varied within the range of 16–33 % (Table 3, Figure 2). The 6–8 d and 2–4 d periods took the second and third place, which represents the weekly fluctuations known as the day-of-the-week phenomenon, and the intra-week oscillations, respectively (Figure 2, Table 3). The next few harmonics that were common to the total respiratory diseases and URI and had >5% spectral density included 292 d, 104.29 d, and 146 d, which reflected the intra-annual and intra-seasonal fluctuations (Table 3). Several harmonics reflecting longer than annual fluctuations of LRI were also identified, in addition to the annual and weekly cycles (Table 3).

In summary, for all respiratory diseases, spectral density of low-frequency (>30 d) part took a large proportion (>60%) with 49

components, the remaining (<40%) high-frequency part included up to 683 harmonics (eTable 3).

In all the subgroups of circulatory diseases, many high frequency harmonics (2–4 d) were identified (Table 4, Figure 3). And their ratios of spectral density for the total circulatory diseases, cardiovascular disease, and cerebrovascular diseases were 38.74%, 41.02%, and 41.39%, respectively. Some other intra-week cycles (4.01–6 d) also appeared, their summed ratio ranged in 12–15%. Compared to respiratory diseases, circulatory diseases had lower ratios in the annual-cycle (365 d), which only took 0.94% and 7.84% for cerebrovascular and cardiovascular morbidity, respectively (Table 4, eTable 2). Particularly, the day-of-the-week phenomenon was not significant for circulatory diseases, with a ratio around 6% (Figure 3).

In summary, circulatory morbidity was dominated by large quantity of high-frequency oscillations (>70%, eTable 3). It should also be noted that for cerebrovascular diseases, fraction of low-frequency harmonics (>30 d) was especially low (eTable 3).

3.3. The association between harmonics of ER visits and meteorological variables

According to harmonic spectra of the total respiratory diseases, its annual-cycle harmonic was extracted firstly (Figure 4A), then the superposition of non-annual low-frequency (>30 d) harmonics was separated (Figure 4B), and the remaining numerous high-frequency waves is shown in Figure 4C. The regular annual-periodic harmonic reflected the change of morbidity with climate background, other periodic intra-annual trends were also obvious in respiratory ER visits, and the

Table 2. The top 10 harmonics of main meteorological variables, which sorted in the descending order of spectral density, was characterized as the ratio of single harmonic energy to the total energy of the original sequence.

	Temperature		Air pressure		Relative humidity		Wind	
	Harmonic period (d)	Ratio (%)						
1	365.2	93.3	365.2	72.3	365.2	28.7	365.2	9.75
2	182.6	1.02	28.98	0.63	182.6	1.34	182.6	0.95
3	913.0	0.11	166.0	0.46	608.7	1.30	29.93	0.86
4	53.71	0.09	83.0	0.42	17.56	0.91	6.54	0.71
5	166.0	0.09	121.7	0.42	10.14	0.86	10.14	0.71
6	608.7	0.09	31.48	0.40	11.41	0.83	121.7	0.69
7	19.02	0.09	23.41	0.36	304.3	0.75	8.23	0.66
8	140.5	0.08	21.48	0.34	121.7	0.71	9.00	0.66
9	23.41	0.08	8.53	0.32	15.61	0.70	8.78	0.65
10	152.2	0.08	182.6	0.31	27.25	0.69	2.81	0.64
Sum		95.03		75.96		36.79		16.28

Table 3. The top 10 harmonics of respiratory ER visit counts in Beijing. The ratio (%) was defined in the same way as in Table 2.

	Total respiratory disease		URI		LRI	
	Harmonic period (d)	Ratio (%)	Harmonic period (d)	Ratio (%)	Harmonic period (d)	Ratio (%)
1	365	17.73	365	16.16	365	32.55
2	6.01–8.0	13.35	2.0–4.0	13.42	2.0–4.0	18.52
3	2.0–4.0	8.49	6.01–8.0	12.08	6.01–8.0	7.59
4	104.29	7.02	292	7.55	4.01–6.0	5.91
5	292	6.80	104.29	7.25	730	4.85
6	146	6.05	146	5.63	1460	3.62
7	486.67	5.00	4.01–6.0	4.64	486.67	3.01
8	208.57	3.63	208.57	2.92	292	2.56
9	4.01–6.0	2.91	76.84	2.76	104.29	2.26
10	76.84	2.53	486.67	2.70	121.67	2.02
Sum		73.51		75.11		82.89

superposed high-frequency harmonics still oscillated intensively and disorderly.

Similarly, Figure 5 shows the decomposed harmonics of the total circulatory diseases. Compared to the its annual and other low-frequency cycles (Figure 5A-B), high-frequency harmonics took obviously higher proportion and indicated the irregular onset of circulatory diseases (Table 4, Figure 5C).

Typical annual-periodic harmonics of both types of diseases (Figures 6 and 7), as well as main meteorological variables (air temperature, relative humidity, and wind speed, in eFigure 3), were extracted to explore the relationship between them. Figure 6 presents that the annual harmonic of respiratory morbidity had almost an inversed phase of the annual harmonic of mean temperature, the lower the temperature, the higher the morbidity. Moreover, LRI matched with temperature better than did URI.

The annual periods of CVD also displayed an inverse relationship with mean temperature (Figure 7), whereas CBD didn't contain obvious

annual cycle (Table 4, Figure 7). Thus, obviously reverse associations between the annual cycles of air temperature and the basal morbidity of respiratory and cardiovascular diseases were identified.

After filtering out the annual and weekly periodic harmonics of ER visits and meteorological variables, the Spearman's correlation showed that respiratory ER visits had no relevance with all of the temperature metrics, air pressure, and wind speed, but significantly related with relative humidity and solar duration (Table 5). In contrast, correlation analysis indicated a significant association between the onset of circulatory diseases and short-term change of mean and maximum temperature, solar duration, and wind speed (Table 6).

4. Discussion

The meteorological rhythm of the onset of two common diseases, respiratory and circulatory diseases, were explored from frequency domain based on Fourier decomposition. Through harmonic periodicity

Table 4. The top 10 harmonics of circulatory ER visit counts in Beijing. The ratio (%) was defined in the same way as in Table 2.

	Total circulatory diseases		Cardiovascular disease		Hypertension		Coronary heart disease	
	Harmonic period (d)	Ratio (%)	Harmonic period (d)	Ratio (%)	Harmonic period (d)	Ratio (%)	Harmonic period (d)	Ratio (%)
1	2.0–4.0	38.74	2.0–4.0	41.02	2.0–4.0	40.84	2.0–4.0	42.57
2	4.01–6.0	12.47	4.01–6.0	12.42	4.01–6.0	14.48	4.01–6.0	12.89
3	365.2	5.76	365.2	7.84	6.01–8.0	7.19	365.2	7.23
4	6.01–8.0	5.44	6.01–8.0	5.74	365.2	6.23	6.01–8.0	6.45
5	608.67	5.12	8.01–10.0	3.91	8.01–10.0	5.15	8.01–10.0	3.23
6	8.01–10.0	4.31	10.01–12.0	2.39	608.67	3.88	12.01–14.0	2.80
7	913	2.83	12.01–14.0	2.38	10.01–12.0	2.22	1826	2.29
8	10.01–12.0	2.58	913	2.04	456.5	1.76	10.01–12.0	2.21
9	1826	1.88	608.67	1.92	182.6	1.37	182.6	1.85
10	182.6	1.76	304.33	1.89	12.01–14.0	1.34	228.25	1.48
Sum		80.89		81.55		84.46		83.00

	Cerebrovascular disease		Intra-cerebral hemorrhage		Cerebral infraction	
	Harmonic period (d)	Ratio (%)	Harmonic period (d)	Ratio (%)	Harmonic period (d)	Ratio (%)
1	2.0–4.0	41.39	2.0–4.0	45.83	2.0–4.0	42.38
2	4.01–6.0	13.59	4.01–6.0	14.87	4.01–6.0	12.77
3	6.01–8.0	7.80	6.01–8.0	8.33	6.01–8.0	7.55
4	608.67	5.04	8.01–10.0	5.95	8.01–10.0	5.38
5	8.01–10.0	4.55	10.01–12.0	4.19	608.67	4.68
6	10.01–12.0	2.87	14.01–16.0	2.08	10.01–12.0	3.74
7	913	2.10	12.01–14.0	1.88	913	3.11
8	12.01–14.0	1.99	16.01–18.0	1.81	12.01–14.0	1.60
9	1826	1.51	1826	1.39	14.01–16.0	1.53
10	14.01–16.0	1.33	608.67	0.93	304.33	1.12
Sum		82.17		87.26		83.86

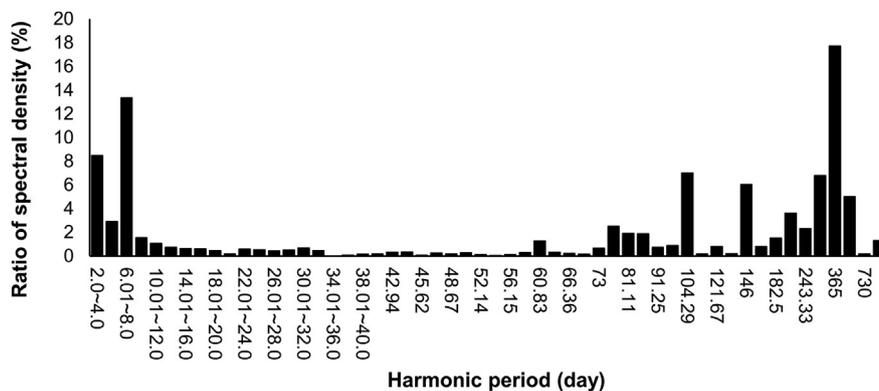


Figure 2. The harmonic power spectrum of the total respiratory diseases, which showed in ratio (%) of partitioned or single harmonic energy to the total energy.

and spectral density of variables, the possible associations between diseases and multi-scaled meteorological conditions were investigated.

4.1. Harmonic characteristics of meteorological variables

Meteorological variables were mainly characterized by the annual cycle, within which temperature displayed the strongest climate regularity, and air pressure came the second (Qian et al., 2010; Kang et al., 2009). It is self-evident that the changes of temperature and air pressure mainly obeyed the climatic cycles, due to earth rotation and change of seasons (Qian et al., 2011; Leathers et al., 1998). In contrast, the harmonics of humidity and wind were relatively irregular, which might relate to some other factors, such as the underlying surface, local terrain, short-term weather processes, precipitation, and evaporation (Moradi et al., 2016; Yu et al., 2007; Tao and Feng, 2015). Moreover, semiannual cycles were identified, which could be explained by the similarity of meteorological variables in transition seasons in Beijing (Zheng et al., 2011).

4.2. Meteorological rhythms of respiratory and circulatory diseases

For respiratory ER visits, its outstanding annual cycle matched well with annual change of meteorological variables, with the low-frequency harmonics indicating that the climatic rhythms were evident in the respiratory sequences. The widely reported seasonal high morbidity of many respiratory diseases, e.g., upper respiratory tract infection, asthma, or pneumonia, may help understand this issue (Derrick, 1966; Ramos et al., 2013; Qiu et al., 2016). Several studies indicated that cold and dry climate stimulates the respiratory tract inflammation, damages the respiratory mucosa, reduces its resistance, and leads to the opportunistic

pathogenic microbes (Wells et al., 1960; Mäkinen et al., 2009). In contrast, warm and moist air helps to maintain the normal function of respiratory tract (Schwartz, 1996).

Under certain climate background, frequent changes of humidity and sunshine duration related to short-term fluctuations of respiratory morbidity significantly. Gonçalves et al. (2005) reported that water vapor and solar radiation influenced respiratory morbidity in São Paulo City in summer, during which the levels of air pollutants were low. Wang et al. (2016) also revealed that extreme humidity related to higher risk of respiratory infection in short terms in Beijing, China. However, no association was found between asthma occurrence and changes in relative humidity or temperature by stratified analyses in Ottawa, Canada (Vileneuve et al., 2005). In summary, climate characteristics determined the basal morbidity of respiratory diseases to a large extent. Based on that, changes of weather caused high frequency oscillations being superimposed on the original base of patient number.

With regard to circulatory diseases, high-frequency harmonics (≤ 30 d) took the majority (70–90%) in the series, especially those with period 2–4 d (around 40%), whereas its low-frequency climatic rhythms were not as significant as in respiratory diseases. Some studies on mechanisms explained how changes of meteorological conditions increased the risk of circulatory diseases (Sartini et al., 2017; Wang et al., 2017). The sudden changes of temperature or pressure may lead to sympathetic and parasympathetic dysfunction, increased secretion of adrenaline, which resulted in small artery spasm, coronary vasoconstriction, platelet aggregation, thrombosis, as well as increased capillary resistance (Woodhouse et al., 1993; Dawson et al., 2008). Increased risks of cardiovascular diseases caused by high temperature was reported in Vietnam (Phung et al., 2016). Experiments also shown that long-term sustained hypertension

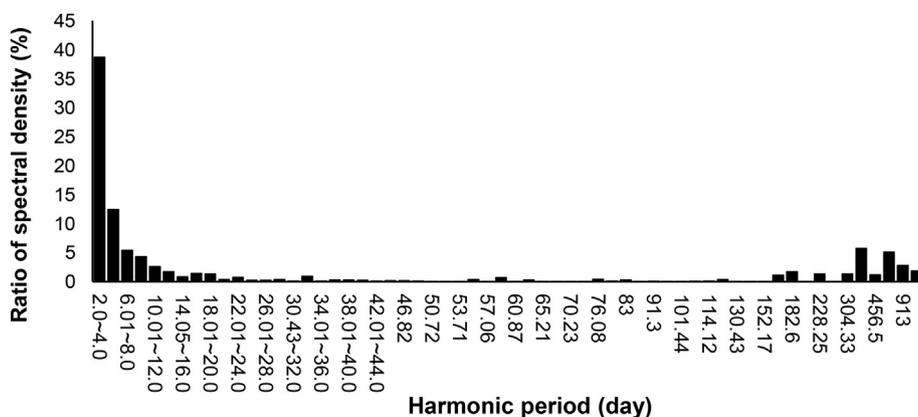


Figure 3. The harmonic power spectrum of the total circulatory diseases, showed in ratio (%) of partitioned or single harmonic energy to its total energy.

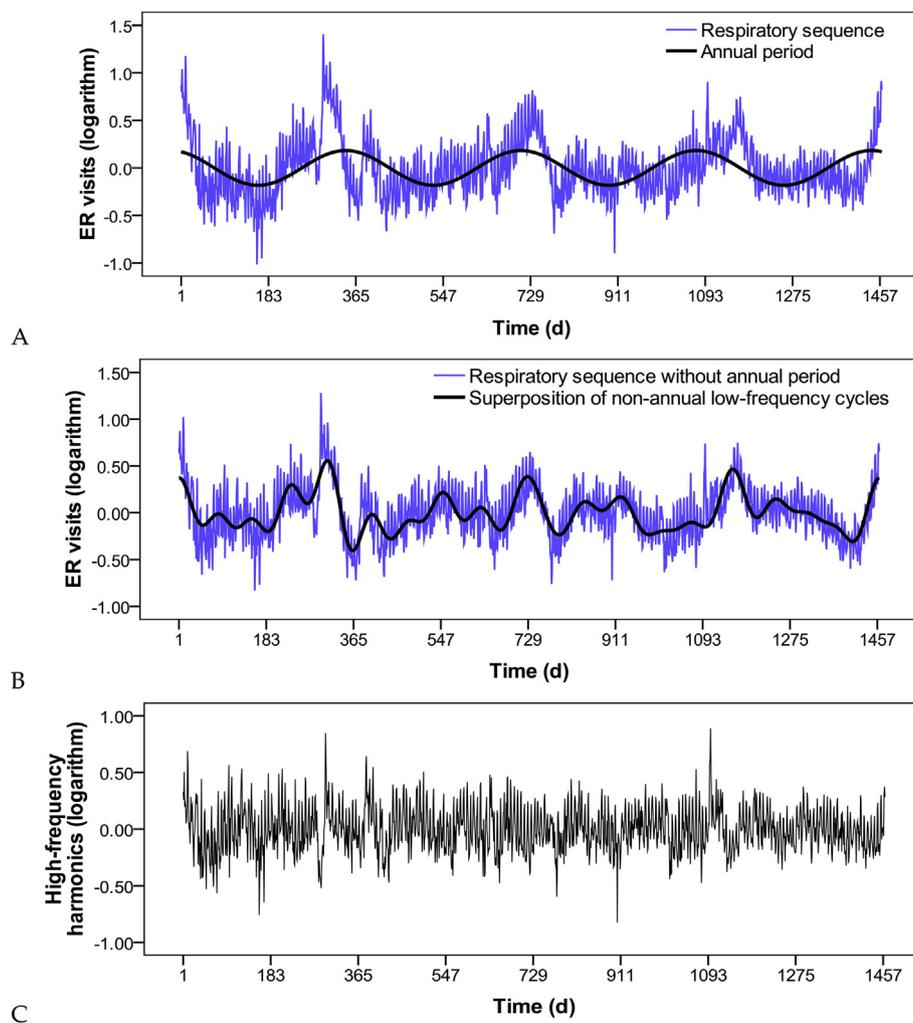


Figure 4. The (A) annual periods, (B) superimposed non-annual low-frequency harmonics (>30 d), and (C) the remaining numerous high-frequency waves for the pretreated series of respiratory ER visits.

damages the regulatory function of cerebral vascular endothelium, while decreased air temperature is a start factor (Claudio et al., 2016). Besides, the correlation between cerebral infarction and temperature varied between different regions, some reported a significant effect of high temperature on cerebral infarction (Lim et al., 2013), others concluded that no relationship exists between the former two (Cowperthwaite and Burnett, 2011). In a word, there existed many non-environmental, individualized, random, or unpredictable factors that affected the attack of circulatory diseases, which caused the inconsistency and complexity of related studies.

In addition, the weekly cycle was prominent in respiratory morbidity, which was originated from the weekly rhythm of human society instead of external environment and had been widely reported in epidemiological studies (Makie et al., 2002; Sundell et al., 2016). However, circulatory diseases didn't show obvious day-of-the-week rhythm, due to its sudden onset without delay. Moreover, for both diseases, considering the simultaneous influence by various socioeconomic factors, policy, or other uncertain reasons (Ma et al., 2011), cycles beyond one year was thought unrelated to meteorological conditions.

4.3. Strengths and limitations

Several strengths of our study should be noted. First, to our knowledge, this is the first study to operate harmonic analysis on the

number of ER visits for meteorologically sensitive diseases in China. Unlike the traditional analysis, the association between morbidity and multi-scale meteorological conditions in the view of frequency spectrum was explored and, fortunately, some interesting results were achieved as presented above. Second, depending on the Fourier decomposition of both disease and meteorological variables, the relationship between short-term weathers and circulatory morbidity was stronger than that of respiratory diseases, while the climate impact behaved the opposite. Third, at different time scales, the prominent meteorological variables influencing morbidity were identified to be distinct. This study could supply as a theoretical basis for targeted prevention of both respiratory and circulatory diseases.

Potential limitations should also be considered. First, data from only one city were analyzed. Thus, the conclusions may not be generalizable to other regions of different climates. Second, we chose the first 10 harmonics subjectively, slight bias of results may exist due to the truncation of the harmonics.

4.4. Future directions of this study

The next step, further explorations on the relevance between harmonic components of diseases and meteorological conditions of different time scales will be pursued, and clearer relationship might be revealed.

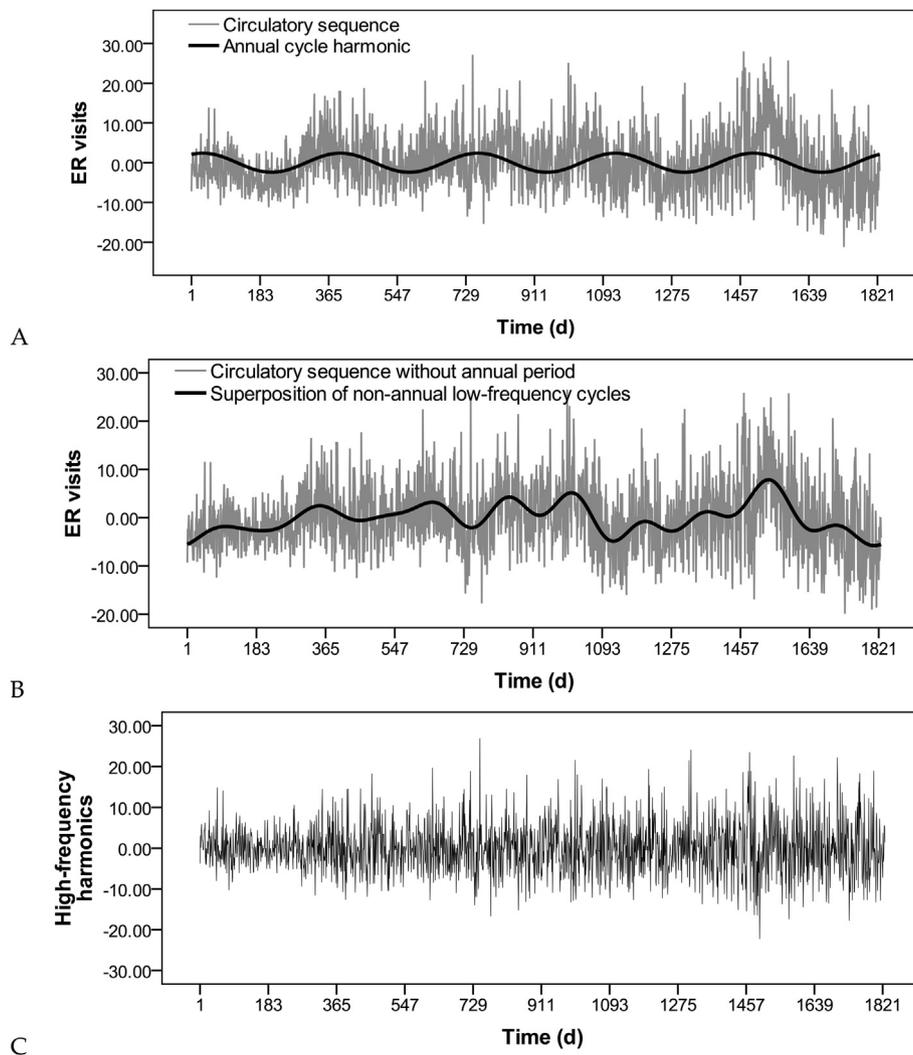


Figure 5. The (A) annual periods, (B) superimposed non-annual low-frequency harmonics, and (C) the remaining numerous high-frequency waves for the pretreated series of circulatory ER visits.

Based on these, multi-cycle superimposed predictive models could be constructed.

5. Conclusions

By recognizing the meteorological rhythms of both respiratory and circulatory diseases in Beijing, different responses to meteorological conditions at various time scales were revealed. Onset of respiratory diseases contained stronger climatic rhythms than that of circulatory

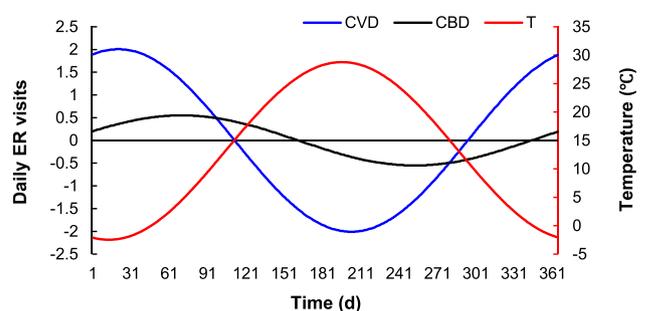


Figure 7. The annual cyclic wave of morbidity for CVD and CBD, relatively to annual cycle of air temperature.

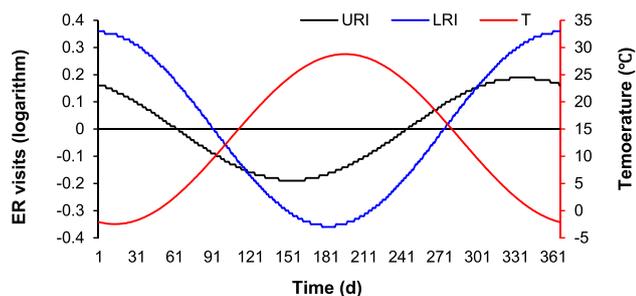


Figure 6. The annual periodic harmonics in morbidity of URI and LRI, as well as the annual cycle of air temperature (T).

Table 5. Spearman's correlation between respiratory morbidity and meteorological variables, the annual cycles of all series were filtered out.

	Total		URI		LRI	
	R	P	R	P	R	P
Air temperature (°C)	-0.010	0.716	-0.015	0.560	-0.011	0.679
Maximum temperature (°C)	0.011	0.663	0.005	0.856	0.007	0.796
Minimum temperature (°C)	-0.021	0.415	-0.030	0.249	-0.004	0.880
Air pressure (hPa)	-0.036	0.168	-0.045	0.086	0.010	0.708
Relative humidity (%)	-0.090**	0.001	-0.080**	0.002	-0.071**	0.007
Wind speed (m/s)	-0.017	0.518	-0.026	0.324	0.006	0.830
Solar duration (hour)	0.057*	0.030	0.052*	0.047	0.049	0.062

R is the correlation coefficient, P is the corresponding statistical significance level, ** and * indicate R is statistically significant at the 0.01 level and 0.05 level, respectively. URI: Upper respiratory infection, LRI: Lower respiratory infection.

Table 6. Spearman's correlation between circulatory morbidity and meteorological variables, the annual cycles of all series were filtered out.

		Total	CVD	CHD	Hypertension	CBD	CI	ICH
			R	P	R	P	R	P
Mean temperature (°C)	R	0.084**	0.084**	0.073**	0.037	0.046	0.057*	-0.026
	P	0.000	0.000	0.002	0.117	0.051	0.014	0.264
Maximum temperature (°C)	R	0.091**	0.098**	0.085**	0.035	0.044	0.060*	-0.033
	P	0.000	0.000	0.000	0.135	0.059	0.011	0.154
Minimum temperature (°C)	R	0.037	0.036	0.026	0.001	0.024	0.030	-0.006
	P	0.114	0.123	0.262	0.963	0.306	0.202	0.782
Air pressure (hPa)	R	0.018	0.016	0.026	0.084**	-0.005	0.002	0.001
	P	0.436	0.483	0.264	0.000	0.847	0.943	0.970
Relative humidity (%)	R	-0.045	-0.028	-0.036	-0.049*	-0.037	-0.024	-0.017
	P	0.053	0.240	0.129	0.034	0.111	0.296	0.463
Wind speed (m/s)	R	-0.051*	-0.053*	-0.041	-0.036	-0.022	-0.021	0.030
	P	0.030	0.022	0.079	0.121	0.337	0.377	0.194
Solar duration (hour)	R	0.065**	0.050*	0.055*	0.060**	0.047*	0.042	0.011
	P	0.006	0.034	0.018	0.010	0.045	0.075	0.649

CVD: cardiovascular disease, CHD: coronary heart disease, CBD: cerebrovascular disease, CI: cerebral infarction, ICH: intra-cerebral hemorrhage. ** and * are the same as in Table 5.

Declarations

Author contribution statement

Pan Ma: Conceived and designed the experiments; Performed the experiments; Wrote the paper.

Shigong Wang: Conceived and designed the experiments; Analyzed and interpreted the data.

Ji Zhou: Conceived and designed the experiments; Performed the experiments.

Tanshi Li: Contributed reagents, materials, analysis tools or data.

Xingang Fan, Siyi Wang: Analyzed and interpreted the data; Wrote the paper.

Jin Fan: Performed the experiments; Wrote the paper.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

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