

# Association between Periodontitis and Systemic Diseases: Results from the 4th National Oral Health Survey in China

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**Objective:** To evaluate the association between systemic diseases and severity of periodontitis based on Chinese epidemiological data.

**Methods:** Data of dentate subjects (35- to 44-year-old group, 55- to 64-year-old group, and 65- to 74-year-old group) from the Fourth National Oral Health Survey of China were analyzed. Self-report diagnosis of systemic diseases was based on face-to-face interview. Periodontal status was defined by the 2018 classification scheme and periodontal parameters including bleeding on probing (BOP), probing depth (PD) and attachment loss (AL).

**Results:** The prevalence of systemic diseases, was much higher in subjects with advanced periodontitis but similar in subjects with other periodontal status. The association between systemic diseases and advanced periodontitis is stronger in the younger adult group but weakens with age.

**Conclusion:** Periodontitis is a significant associated with systemic diseases, especially hypertension, heart disease, diabetes among Chinese adults based on the data of the Fourth National Oral Health Survey of China. In view of the worsening health burden of periodontitis, it might be necessary for healthcare providers to be more concerned about prevention and treatment of periodontitis in order to enhance systemic health.

**Keywords:** epidemiology, periodontitis, systemic diseases

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In the last 50 years, considerable progress has been made in understanding the aetiology and pathogenesis of periodontal diseases and their interactions with the host. In 2017, periodontal diseases were reclassified at a World Workshop, with periodontitis defined as a chronic multifactorial inflammatory disease associated

with plaque biofilms resulting in chronic destructive inflammatory responses, which progress through periodontal attachment tissue and bone loss.<sup>1</sup> Patients with periodontitis may remain at increased risk of other systemic diseases.

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Severe periodontitis defined by extensive loss of the tooth-supportive apparatus is the sixth most common human disease, estimated to affect 11.2% of the global adult population.<sup>2</sup> If untreated, it results in tooth loss, which in turn can lead to altered speech, nutritional compromise and a poorer overall quality of life, representing a significant health care, economic and social burden.

Since the 1990s, multiple epidemiological, experimental and interventional studies have focused on the possible associations between periodontal diseases and systemic diseases.<sup>3-8</sup> Periodontitis has been showed to be independently associated with the majority of chronic non-communicable diseases of aging and premature mortality.<sup>3</sup> In 2010, the seven leading causes of death in the USA were heart disease, cancer, chronic lower respiratory disease, stroke/cerebrovascular diseases, unintentional accidental injuries, Alzheimer's disease and diabetes, according to the National Centre for Health Statistics of the Centers for Disease Control and Prevention.<sup>4</sup> Except for unintentional accidental injuries, all of these are chronic diseases, which have been associated with periodontitis.

A panel of experts from the USA and Europe reviewed the evidence supporting the associations between periodontal and systemic diseases in 2012 and concluded that periodontitis contributes to the bacterial burden resulting in a significant systemic inflammatory response, which is likely to act as a contributing factor in the pathophysiology of diabetes, cardiovascular diseases and pregnancy complications.<sup>5-7</sup> More recently, other systemic diseases, such as rheumatoid arthritis, cancers, metabolic disease and obesity, respiratory diseases and cognitive disorders including Alzheimer's disease, have been independently associated with periodontitis.<sup>8</sup> A recent systematic review by Monsarrat et al<sup>8</sup> reported that periodontitis is linked to 57 systemic diseases and conditions. The vast population of China showed significant genetic, environmental, and cultural differences from Western populations; however, information on the associations between periodontitis and systemic diseases was lacking in China.

Therefore, the purpose of the present study was to evaluate the associations between periodontitis and systemic diseases based on the data of the Fourth National Oral Health Survey of China.<sup>9-11</sup> The authors sought to determine whether severity of periodontitis, in accordance with the new classification scheme of periodontal diseases proposed at the 2017 World Workshop, was associated with systemic diseases.

## Materials and methods

### *Study design and sample*

This is a cross-sectional study. The data were from the Fourth National Oral Health Survey of China, launched in 2015 by the Chinese Stomatological Association.<sup>10-13</sup> The survey design and sample selection description had been published elsewhere.<sup>14</sup> A multistage cluster sampling method was adopted for this survey. All 31 provinces, autonomous regions and municipalities (including Tibet) in the mainland of China were included. Two urban and two rural districts were selected in each province using probability proportional to size (PPS) sampling.<sup>10</sup> In total, 62 urban and 62 rural districts were selected. Three sub-districts (referred to as streets in urban districts and as townships in rural districts) were then selected using the PPS sampling method in each district.<sup>10</sup> A total of 186 streets and 186 townships were selected. One neighbourhood community from an urban district or one village community from a rural district were selected using a simple random sampling method in each sub-district.<sup>10</sup> Adults (age groups 35 to 44 years, 55 to 64 years and 65 to 74 years) were recruited from neighbourhood or village communities. In each neighbourhood or village community, 36 residents with a male-female ratio of 1:1 (12 for each of the aforementioned age groups) were recruited consecutively using the cluster sampling method. All participants underwent a clinical examination and information regarding their oral health status was recorded. Portable dental chairs were carried to the survey sites and the participants were examined in a supine position. For each age group, participants were given a structured questionnaire covering age, sex, education level, household income per capita, occupation, oral health knowledge and attitude, with their responses recorded in face-to-face interviews by trained interviewers. Data from the oral examination and questionnaire were extracted from the Fourth National Oral Health Survey of China. The sample size was calculated according to the prevalence of periodontal diseases (86%) found in the Third National Oral Health Survey in 2005, with an acceptable margin of error (10%) and an anticipated response rate of 80%.<sup>14</sup> The study protocol was approved by the Ethics Committee of the Chinese Stomatological Association (approval no. 2014-003) and the Biomedical Ethics Committee of Peking University School and Hospital of Stomatology (PKUSSIRB-2024102140). Written informed consent was obtained from participants at enrolment.

### Data extraction

The following clinical and demographic data were extracted for analysis from the Fourth National Oral Health Survey of China. The diagnoses of periodontitis, periodontal pockets, attachment loss, bleeding gums and calculus through periodontal examinations were ascertained by licensed dental practitioners. Detailed information about the definition of periodontal disease and diagnosis criteria has been provided elsewhere.<sup>14</sup> Briefly, full-mouth periodontal examinations were performed including bleeding on probing (BOP), presence of calculus, periodontal probing depth (PPD) and clinical attachment loss (CAL). For each parameter, the tooth was scored according to the severity of the most severe site.

Data from the oral examinations and questionnaire were extracted from the Fourth National Oral Health Survey of China. The following periodontal examination data were extracted:

- Calculus (defined by visual examination for supragingival calculus and by probing for subgingival calculus: 0 = absence, 1 = presence, 9 = tooth excluded, and X = tooth not present);
- PPD (0 = 1 to 3 mm, 1 = 4 to 5 mm, 2 =  $\geq 6$  mm, 9 = tooth excluded, and X = tooth not present);
- BOP (0 = absence, 1 = presence, 9 = tooth excluded, and X = tooth not present);
- CAL (measured by the distance from the cemento-enamel junction to the bottom of the periodontal pocket: 0 = 0 to 3 mm, 1 = 4 to 5 mm, 2 = 6 to 8 mm, 3 = 9 to 11 mm, 4 =  $\geq 12$  mm, 9 = tooth excluded, and X = tooth not present).

Periodontal disease was diagnosed according to the classification scheme proposed at the 2018 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions as follows:

- periodontally healthy: < 10% BOP-positive sites and PPD  $\leq 3$  mm;
- gingivitis:  $\geq 10\%$  BOP-positive sites and PPD  $\leq 3$  mm;
- periodontitis: staged using the algorithm developed by Graetz et al.<sup>15</sup>

For each tooth, CAL of 1 to 2 mm was defined as stage I, 3 to 4 mm as stage II and  $\geq 5$  mm as stage III. Next, the number of teeth lost was considered (stages I and II, no tooth loss; stage III,  $\leq 4$  teeth lost; and stage IV,  $\geq 5$  teeth lost; it should be noted that reasons for tooth loss were not considered here). The authors also evaluated the complexity of management. Stage II patients were reclassified as stage III if the maximum

PPD was  $\geq 6$  mm, and stage III patients were reclassified as stage IV if there were < 10 opposing pairs of teeth. Severity of periodontitis was then classified based on the results of the algorithm, with stage I indicating mild periodontitis, stage II representing moderate periodontitis and stages III and IV corresponding to advanced periodontitis.

A calibration training programme and quality control procedures were conducted to ensure the reliability of the findings. Prior to the field survey, the calibration training programme was launched to ensure reliability of the results. Two or three examiners selected from each province attended the programme and then conducted all the clinical examinations in their own province. Each examiner was calibrated with a standard examiner in the same setting. Examiners with kappa values higher than 0.6 for PPD were qualified. In the field survey, 5% of the participants were randomly selected for a duplicate examination on each examination day to monitor inter-examiner reproducibility. As measured using Kappa statistics, the inter-examiner reliability for PPD was > 0.6.

In the Fourth National Oral Health Survey, two or three trained investigators acted as interviewers. Furthermore, in districts where the dialect was difficult to understand, a local person acted as an assistant. In the adult age groups, a structured questionnaire covering participants' age, sex, education level, household income per capita, occupation, oral health knowledge and attitude was conducted with responses recorded in face-to-face interviews by trained interviewers. The following information was extracted from the Fourth National Oral Health Survey of China for analysis:

- age (years);
- annual family income (with 10,000 yuan as the unit);
- sex (male versus female);
- highest level of education (no school, primary school, junior high school, high school, technical specialised school, junior college, undergraduate, masters or higher);
- medical history variables including stroke, type 2 diabetes, hypertension, heart disease, chronic obstructive pulmonary disease (COPD) and other systemic diseases;
- smoking status (current smoker, former smoker or non-smoker);
- region (urban versus rural).

The data extraction process was similar to that used in a study that reported the severity of periodontitis in mainland China.<sup>14</sup>

**Table 1** Distribution of systemic diseases with more than 100 patients by age group.

Systemic disease	35–44 y	55–64 y	65–74 y	Total
	n (%)	n (%)	n (%)	n (%)
Hypertension	277 (6.28)	1296 (28.37)	1583 (37.53)	3156 (23.92)
Heart disease	126 (2.86)	526 (11.51)	839 (19.89)	1491 (11.30)
Diabetes	89 (2.02)	473 (10.35)	515 (12.21)	1077 (8.16)
Stroke	21 (0.48)	122 (2.67)	179 (4.24)	322 (2.44)
COPD	23 (0.52)	76 (1.66)	112 (2.66)	211 (1.60)
Chronic gastritis	38 (0.86)	74 (1.62)	79 (1.87)	191 (1.45)
Hyperlipidaemia	11 (0.25)	38 (0.83)	53 (1.26)	102 (0.77)

### Statistical analysis

The primary outcomes, also the dependent variables, were whether a subject had systemic disease(s). The independent variable was periodontal status according to the 2018 new classification. Firstly, descriptive statistics were performed, and distributions of systemic diseases was reported as N and percentage by periodontal status according to different classifying methods:

- six categories: periodontal health, gingivitis and periodontitis stages I to IV;
- three categories: non-periodontitis (periodontal health and gingivitis), mild and moderate periodontitis (periodontitis stage I and II) and advanced periodontitis (periodontitis stages III and IV);
- advanced periodontitis, that is stages III and IV and non-advanced periodontitis, the other four periodontal conditions).

Then, for univariate analysis, logistic regressions were made with whether a subject had a certain systemic disease (for example hypertension) as the dependent variable and periodontal status (non-advanced periodontitis versus advanced periodontitis) as the dependent variable. In addition, multivariate analysis was conducted to adjust the confounders (sex, smoking status, region, highest level of education and annual family income). Finally, forest plots were created based on the univariate and multivariate logistic regressions. The level of significance was set at  $P \leq 0.05$ .

### Results

Data from 13,195 dentate subjects (6,575 men and 6,620 women) were analysed. The mean age of the subjects was 56 years ( $56.43 \pm 12.40$  years). There were 3,472 non-smokers (26.30%), 8,405 current smokers (63.71%) and 1,318 former smokers (9.99%).

In general, 3,156 subjects (23.92%) had hypertension, 1491 (11.30%) had heart disease, 1,077 (8.16%)

had diabetes, 322 (2.44%) had suffered from a stroke, 211 (1.60%) had COPD, 191 (1.45%) had chronic gastritis and 102 (0.77%) had hyperlipidaemia. The distribution of systemic diseases by age groups is shown in Table 1.

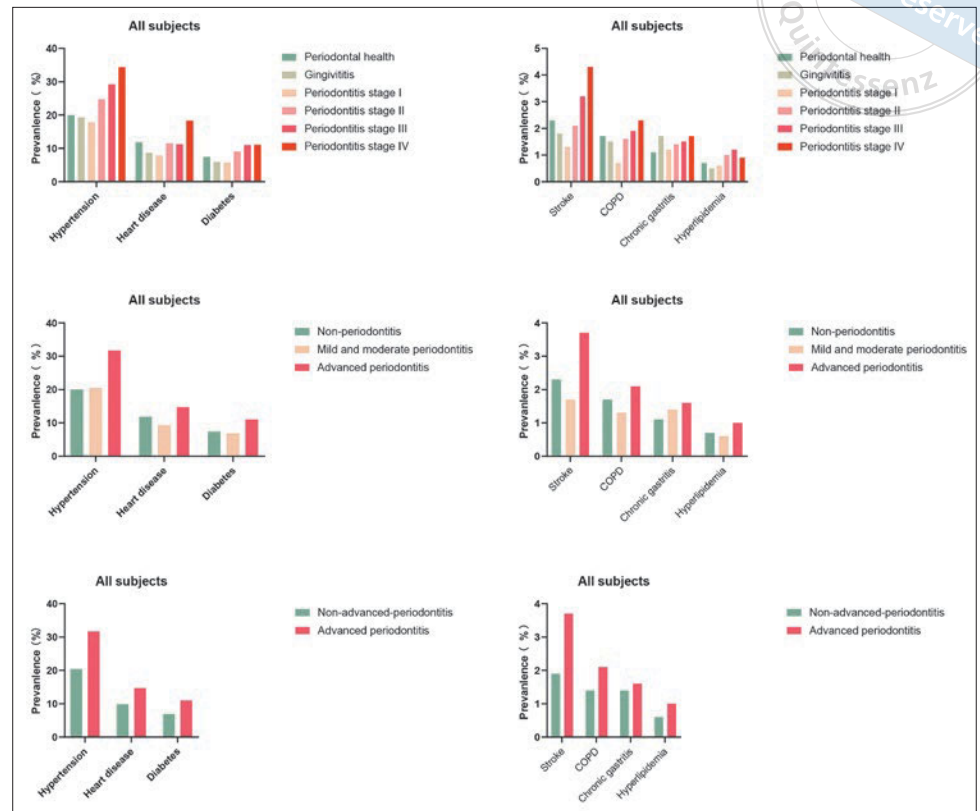
### Systemic diseases and severity of periodontitis

Overall, the prevalence of systemic diseases was much higher in subjects with advanced periodontitis but similar in subjects with non-, mild and moderate periodontitis (Fig 1 and Table 2). The difference became more obvious when the status of periodontitis was combined for analysis. Taking hypertension as an example, the prevalence of hypertension for periodontal health subjects, subjects with gingivitis and subjects with periodontitis stages I to IV was 20.0%, 19.3%, 17.8%, 24.7%, 29.2% and 34.3%, respectively. If periodontal conditions were divided into three categories, that is non-periodontitis (periodontal health and gingivitis), mild and moderate periodontitis (stages I and II) and advanced periodontitis (stages III and IV), the prevalence of hypertension was 19.99%, 20.49% and 31.70%, respectively. If periodontal conditions were divided into only two categories, that is non-advanced periodontitis (all statuses except periodontitis stages III and IV) versus advanced periodontitis, the prevalence of hypertension was 20.39% versus 31.70%.

### Systemic diseases and advanced periodontitis with age

The association between systemic diseases and advanced periodontitis is stronger in the young but weakens with age (Tables 3 to 5 and Fig 2 to 4). Stratification analysis showed that the prevalence of systemic diseases, except for chronic gastritis, in subjects with advanced periodontitis was much higher than subjects with another periodontal status in the 35- to 44-year-old group. In the 55- to 64-year-old group, the prevalence of systemic diseases other than chronic gastritis was still higher in subjects with advanced periodontitis than others; however,

**Fig 1** Prevalence of systemic diseases in subjects with different periodontal statuses according to the 2018 new classification.



**Table 2** Distribution of systemic diseases by periodontal status according to the 2018 new classification.

Systemic disease	Periodontal health (n = 1,691)	Gingivitis (n = 3,113)	Periodontitis stage I (n = 2,081)	Periodontitis stage II (n = 2,196)	Periodontitis stage III (n = 2,111)	Periodontitis stage IV (n = 2,003)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Hypertension	338 (20.0)	601 (19.3)	370 (17.8)	543 (24.7)	617 (29.2)	687 (34.3)
Heart disease	200 (11.8)	272 (8.7)	164 (7.9)	252 (11.5)	236 (11.2)	367 (18.3)
Diabetes	125 (7.4)	183 (5.9)	118 (5.7)	200 (9.1)	231 (10.9)	220 (11.0)
Stroke	39 (2.3)	55 (1.8)	27 (1.3)	47 (2.1)	67 (3.2)	87 (4.3)
COPD	28 (1.7)	48 (1.5)	14 (0.7)	35 (1.6)	40 (1.9)	46 (2.3)
Chronic gastritis	18 (1.1)	53 (1.7)	24 (1.2)	30 (1.4)	31 (1.5)	35 (1.7)
Hyperlipidaemia	11 (0.7)	15 (0.5)	13 (0.6)	21 (1.0)	25 (1.2)	18 (0.9)

**Table 3** Distribution of systemic diseases by periodontal status of subjects in 35- to 44-year-old group according to the 2018 new classification.

Systemic disease	Periodontal health (n = 698)	Gingivitis (n = 1,385)	Periodontitis stage I (n = 1,203)	Periodontitis stage II (n = 656)	Periodontitis stage III (n = 400)	Periodontitis stage IV (n = 67)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Hypertension	40 (5.7)	73 (5.3)	70 (5.8)	44 (6.7)	40 (10.0)	10 (14.9)
Heart disease	21 (3.0)	34 (2.5)	26 (2.2)	21 (3.2)	17 (4.3)	7 (10.4)
Diabetes	10 (1.4)	20 (1.4)	18 (1.5)	17 (2.6)	15 (3.8)	9 (13.4)
Stroke	1 (0.1)	5 (0.4)	7 (0.6)	4 (0.6)	4 (1.0)	0 (0.0)
COPD	2 (0.3)	7 (0.5)	3 (0.2)	6 (0.9)	4 (1.0)	1 (1.5)
Chronic gastritis	4 (0.6)	15 (1.1)	10 (0.8)	7 (1.1)	1 (0.3)	1 (1.5)
Hyperlipidaemia	1 (0.1)	1 (0.1)	3 (0.2)	3 (0.5)	3 (0.8)	0 (0.0)

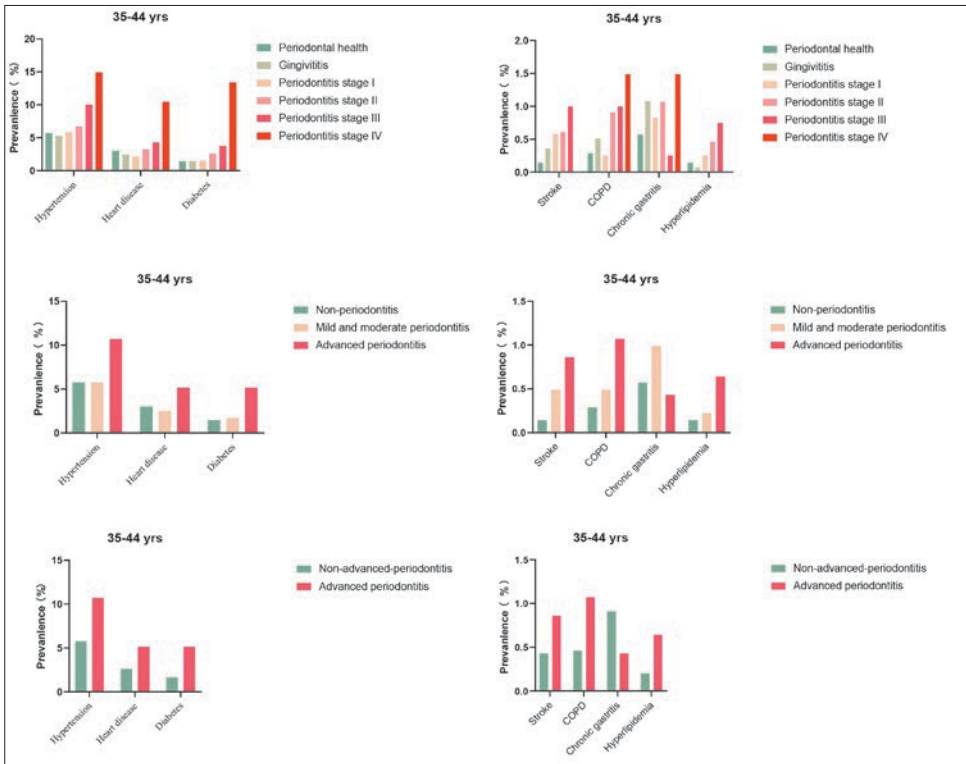


**Table 4** Distribution of systemic diseases by periodontal status of subjects in 55- to 64-year-old group according to the 2018 new classification.

Systemic disease	Periodontal health (n = 463)	Gingivitis (n = 900)	Periodontitis stage I (n = 577)	Periodontitis stage II (n = 905)	Periodontitis stage III (n = 932)	Periodontitis stage IV (n = 791)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Hypertension	116 (25.1)	239 (26.6)	174 (30.2)	247 (27.3)	273 (29.3)	247 (31.2)
Heart disease	70 (15.1)	93 (10.3)	68 (11.8)	91 (10.1)	93 (10.0)	111 (14.0)
Diabetes	49 (10.6)	74 (8.2)	55 (9.5)	98 (10.8)	114 (12.2)	83 (10.5)
Stroke	11 (2.4)	21 (2.3)	10 (1.7)	19 (2.1)	27 (2.9)	34 (4.3)
COPD	11 (2.4)	18 (2.0)	5 (0.9)	9 (1.0)	12 (1.3)	21 (2.7)
Chronic gastritis	6 (1.3)	17 (1.9)	8 (1.4)	15 (1.7)	16 (1.7)	12 (1.5)
Hyperlipidaemia	5 (1.1)	3 (0.3)	6 (1.0)	9 (1.0)	9 (1.0)	7 (0.9)

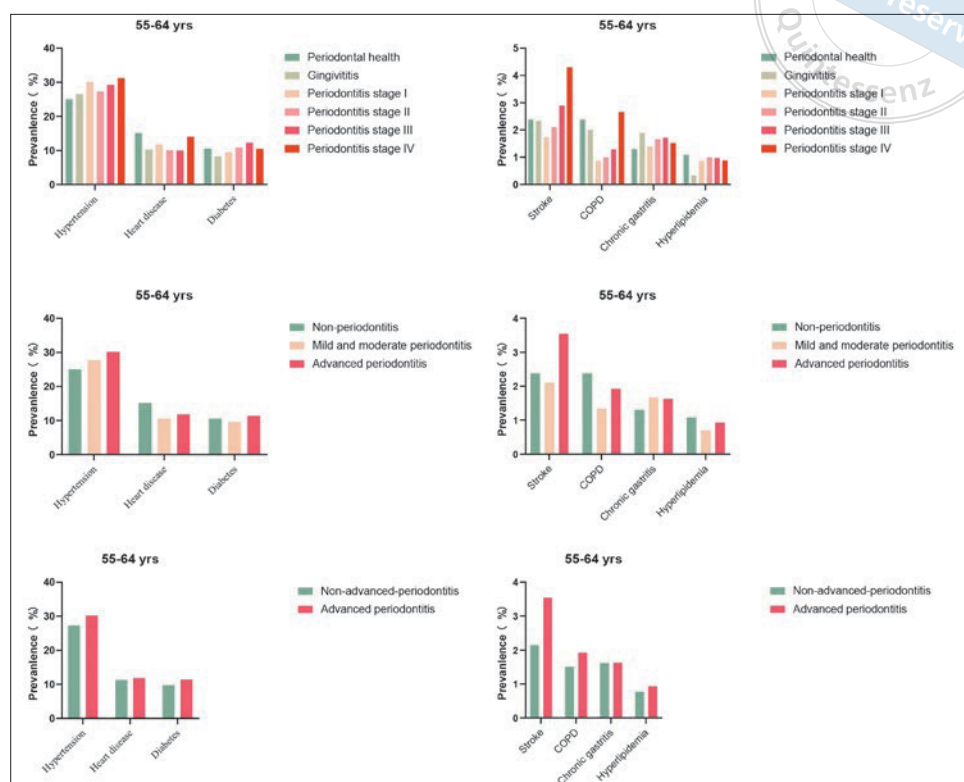
**Table 5** Distribution of systemic diseases by periodontal status of subjects in 65- to 74-year-old group according to the 2018 new classification.

Systemic disease	Periodontal health (n = 530)	Gingivitis (n = 828)	Periodontitis stage I (n = 301)	Periodontitis stage II (n = 635)	Periodontitis stage III (n = 779)	Periodontitis stage IV (n = 1,145)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Hypertension	182 (34.3)	289 (34.9)	126 (41.9)	252 (39.7)	304 (39.0)	430 (37.6)
Heart disease	109 (20.6)	145 (17.5)	70 (23.3)	140 (22.0)	126 (16.2)	249 (21.7)
Diabetes	66 (12.5)	89 (10.7)	45 (15.0)	85 (13.4)	102 (13.1)	128 (11.2)
Stroke	27 (5.1)	29 (3.5)	10 (3.3)	24 (3.8)	36 (4.6)	53 (4.6)
COPD	15 (2.8)	23 (2.8)	6 (2.0)	20 (3.1)	24 (3.1)	24 (2.1)
Chronic gastritis	8 (1.5)	21 (2.5)	6 (2.0)	8 (1.3)	14 (1.8)	22 (1.9)
Hyperlipidaemia	5 (0.9)	11 (1.3)	4 (1.3)	9 (1.4)	13 (1.7)	11 (1.0)

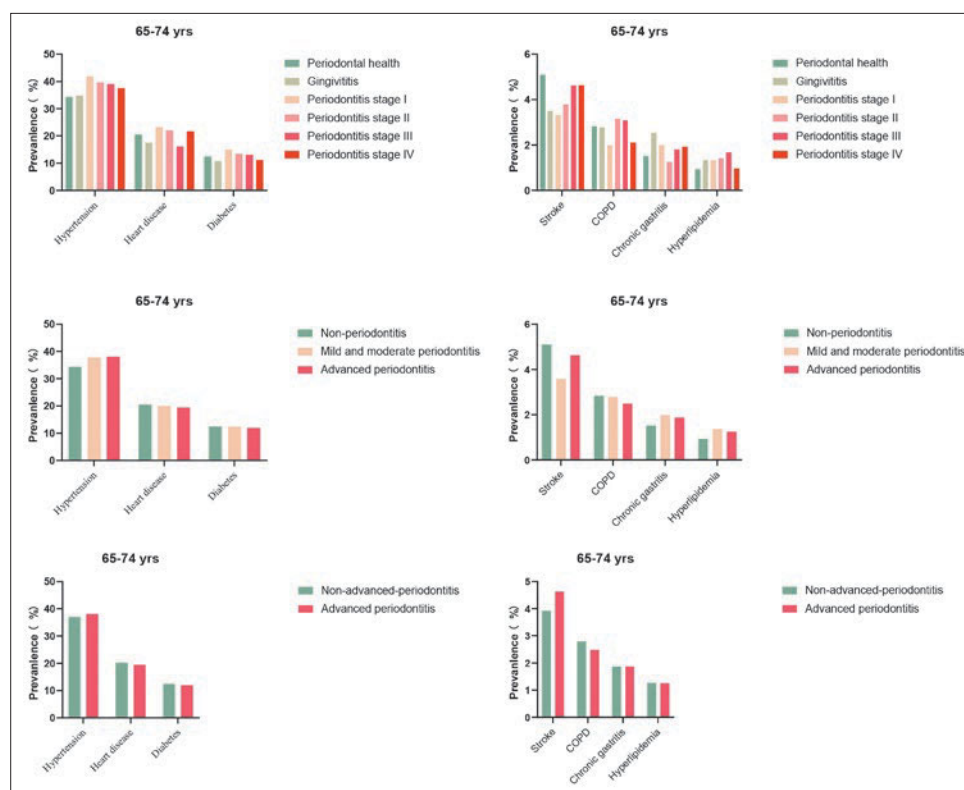


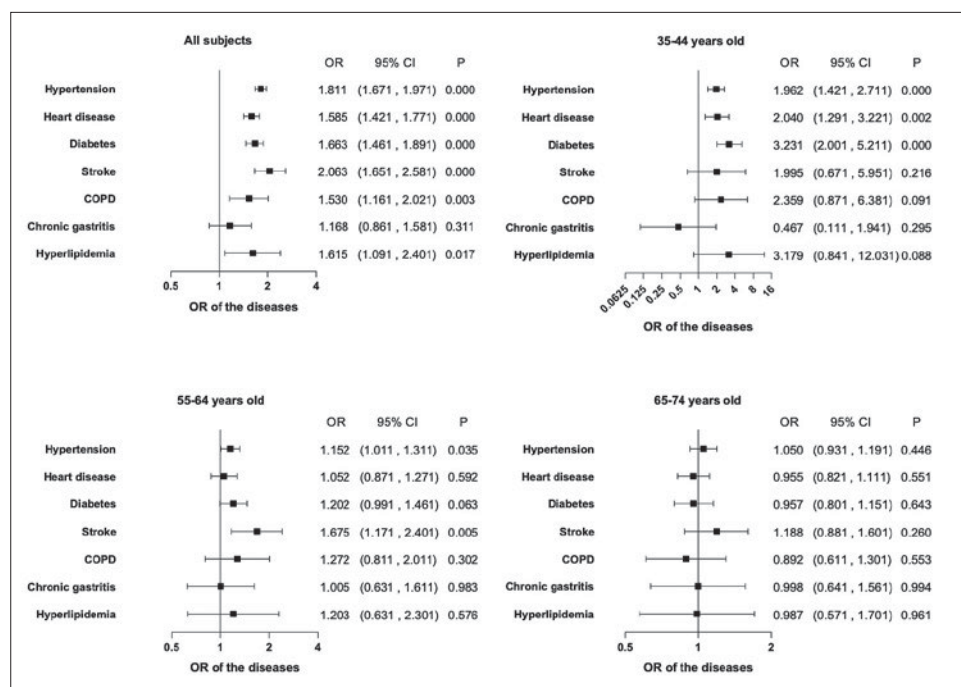
**Fig 2** Prevalence of systemic diseases in subjects with different periodontal statuses in the 35- to 44-year old group according to the 2018 new classification.

**Fig 3** Prevalence of systemic diseases in subjects with different periodontal statuses in the 55- to 64-year-old group according to the 2018 new classification.



**Fig 4** Prevalence of systemic diseases in subjects with different periodontal statuses in the 65- to 74-year-old group according to the 2018 new classification.





**Fig 5** Forest plots of odds ratios of systemic diseases of subjects with advanced periodontitis (stages III and IV), by age group, based on the univariate logistic regressions.

the gap between the subjects with advanced periodontitis and the others narrowed compared to in the 35- to 44-year-old group. In the 65- to 74-year-old group, the prevalence of systemic diseases was similar in subjects with advanced periodontitis and other subjects.

### *Systemic diseases and advanced periodontitis*

In general, univariate analysis based on logistic regressions, illustrated by the forest plots, showed that advanced periodontitis (versus non-advanced periodontitis) increased the risk of systemic diseases except for chronic gastritis (Fig 5). The odds ratios (ORs) for hypertension, heart disease, diabetes, stroke, COPD and hyperlipidaemia ranged from 1.530 to 2.063 and the associations between the diseases and advanced periodontitis were statistically significant. However, the trend of associations between systemic diseases and advanced periodontitis differed among the age groups. Generally, both the number of systemic diseases and the strength of the associations decreased with age. For example, three systemic diseases (hypertension, heart disease and diabetes) and two diseases (hypertension and stroke) were significantly associated with advanced periodontitis in the 35 to 44-year-old group and the 55 to 64-year-old group, respectively. However, no systemic disease was significantly associated with advanced periodontitis in the 65 to 74-year-old group and the ORs, from 0.892 to 1.188, also decreased.

Similar trends whereby the associations between systemic diseases and advanced periodontitis and the number of associated diseases and their strength of the associations decreased with age still exist in multivariate analysis (Fig 6). The association between advanced periodontitis and diabetes was strengthened after confounders (sex, smoking status, region, education and income) were adjusted in the 55 to 64-year-old group, which was insignificant by univariate analysis.

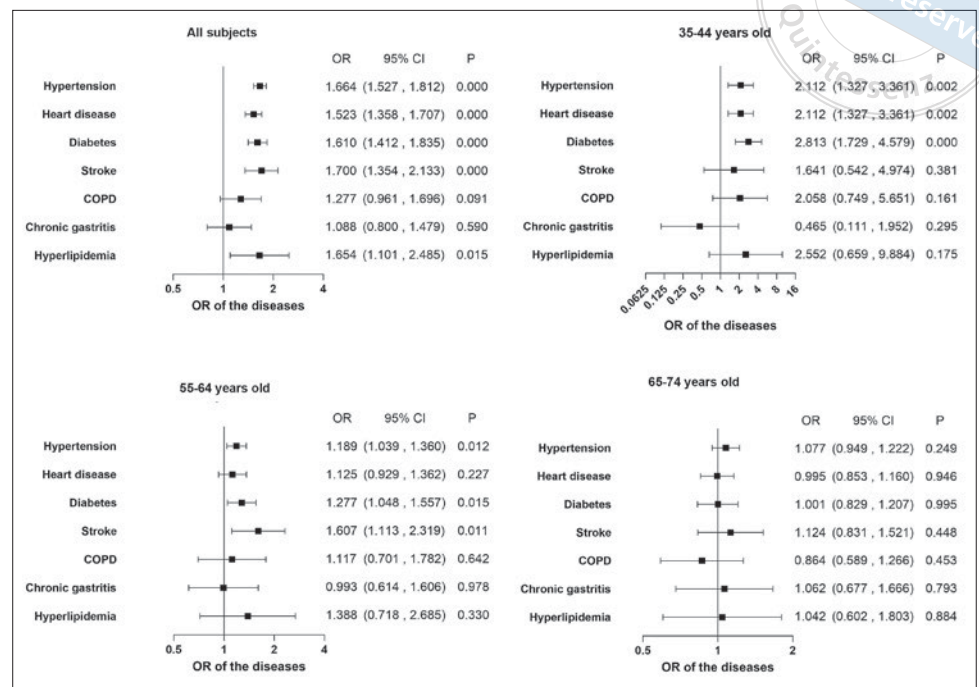
### **Discussion**

In this study, the epidemiological data used were from a large-scale national survey of a representative Chinese population. The association of periodontitis with systemic diseases was assessed by age group and disease-stratified analyses. The present epidemiological data indicate the age of distribution of periodontitis with systemic diseases. The result demonstrated that severe periodontitis increased the risk of hypertension, heart disease, diabetes, and stroke in Chinese adults based on the data of the Fourth National Oral Health Survey of China.

Interestingly, the risk of developing hypertension, heart disease, diabetes, stroke and hyperlipidaemia increased with the severity of periodontitis. In addition, the increased risk of developing hypertension, heart disease and diabetes was significant in the younger age



**Fig 6** Forest plots of odds ratios of systemic diseases of subjects with advanced periodontitis (stages III and IV), by age groups, based on the multivariate logistic regressions.



group (35 to 45-year-old group). The characteristics of chronic periodontitis and chronic systemic diseases mean that a certain period of time is required for the risk factors, such as smoking, to contribute to their development. The exposure time to risk factors in younger individuals is considerably shorter than that in the older groups. This may be because as people age, the influence of other complex factors on systemic diseases gradually increases, masking the association between periodontitis and systemic diseases. As such, the longer exposure time to the common risk factors for periodontitis and systemic diseases in older subjects means that the contribution of periodontitis to the development of systemic diseases could be masked by the influence of these common risk factors. Thus, severe periodontitis in younger subjects may have played a more significant role in developing systemic diseases than in older subjects. The higher susceptibility of severe periodontitis to developing hypertension, heart disease and diabetes in younger subjects could be attributed to periodontal inflammation.

Smoking, sex, region, years of education and annual family income are well-known confounders of the relationship between periodontitis and systemic diseases.<sup>16</sup> Since periodontitis and systemic diseases were affected by multiple factors, when the confounding effects of the risk factors were removed, the link between severe periodontitis and hypertension, heart disease, diabetes, stroke and hyperlipidaemia was observed. The

increased risk of developing hypertension, heart disease and diabetes in patients with severe periodontitis was also significant in younger subjects. Besides cellular and molecular specificity in the acute and chronic setting that can uniquely contribute to the observed association, it is also possible that local bacterial in the course of active periodontitis exert additional immunological and metabolic systemic effects, similar to what has been described for gut dysbiosis and several systemic diseases.<sup>17-19</sup> The present findings regarding the association between systemic diseases and severe periodontal inflammation are in line with previous results.<sup>20,21</sup> Although the causality of the observed association remains unclear, several hypotheses have been proposed to explain the periodontal and systemic interplay.<sup>22</sup>

The term periodontal medicine, as first suggested by Offenbacher,<sup>23</sup> is a broad term that defined a rapidly emerging branch of periodontology focusing on the wealth of new data establishing a strong relationship between periodontal disease and systemic diseases. The main mechanism in periodontal tissue and alveolar bone breakdown is an aberrant immune response to the bacterial challenge. The current knowledge supports a key pathogenic role for non-resolving chronic inflammation triggered by the dysbiotic changes occurring in the subgingival biofilm.<sup>24</sup> The systemic translocation of these local immune responses to distinct distant organs, together with the presence of common

genetic factors favouring a hyper-inflammatory response, may help explain the complex associations between periodontitis and other comorbidities such as hypertension and diabetes.<sup>25</sup> The population of China showed significant genetic, environmental and cultural differences compared to Western populations. Genetic variations could alter susceptibility to inflammation and disease.<sup>25,26</sup> Environmental factors, such as diet and pollution, may impact periodontal health and systemic disease risk.<sup>26</sup> Cultural practices, including oral hygiene habits and health awareness, also play a role.<sup>26</sup> The results of the present study should be considered to better understand the interactions between periodontitis and systemic diseases in the Chinese population.

In summary, the current epidemiological data show an association between periodontitis and systemic diseases. The impact of severity of periodontitis, using new classification systems, on systemic health are described and discussed. The primary limitation of this study was that the cross-sectional design inherently limited the authors with regard to establishing whether a causal relationship exists. Future studies should be conducted to yield better understanding of the mechanisms and interactions between periodontitis and systemic diseases, which will further strengthen the involvement between dental and medical community. Second, the limitation of this study related to using self-reported diagnoses of systemic diseases rather than clinical measurements or medical records. Although recall and reporting bias could not be excluded, the self-reported diagnosis was based on a face-to-face interview and diagnosis from a hospital to ensure validity and accuracy of the information. Further investigations with an improved study design are needed to resolve the limitations of this study such as reporting bias and recall bias, and unmeasured confounders should be addressed.

## Conclusion

Severe periodontitis increases the risk of hypertension, heart disease, diabetes and stroke in Chinese adults. The risk was highlighted in the younger age group. Prevention and treatment of periodontitis in oral health promotion programmes should be emphasised in order to enhance systemic health, particularly in the younger adult population.

## Conflicts of interest

The authors declare no conflicts of interest related to this study.

## Author contribution

Dr Ya Lin ZHAN was the major contributor in writing the manuscript and participated in the data analysis and collation; Dr Jian JIAO participated in the data analysis and collation; Dr Wu Di JING participated in writing the manuscript; Drs Xi Ping FENG, Bao Jun TAI, De Yu HU, Huan Cai LIN, Bo WANG, Chun Xiao WANG, Shu Guo ZHENG, Xue Nan LIU, Wen Sheng RONG, Wei Jian WANG, Xing WANG and Yan SI conceived the study design and drafted the protocol; Dr Huan Xin MENG conceived the study design, drafted the protocol, and revised the manuscript. The manuscript has been read and approved by all the authors.

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## References

1. Caton JG, Armitage G, Berglundh T, et al. A new classification scheme for periodontal and peri-implant diseases and conditions - Introduction and key changes from the 1999 classification. *J Periodontol* 2018;89(suppl 1):S1–S8.
2. Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;386:743–800.
3. Söder B, Jin LJ, Klinge B, Söder PO. Periodontitis and premature death: A 16-year longitudinal study in a Swedish urban population. *J Periodontol* 2007;42:361–366.
4. Murphy SL, Xu J, Kochanek KD. Deaths: Final data for 2010. *Natl Vital Stat Rep* 2013;61:1–117.
5. Chapple IL, Genco R; working group 2 of the joint EFP/AAP workshop. Diabetes and periodontal diseases: Consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *J Periodontol* 2013;84(4 suppl):S106–S112.
6. Sanz M, Kornman K; working group 3 of the joint EFP/AAP workshop. Periodontitis and adverse pregnancy outcomes: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *J Periodontol* 2013;84(4 Suppl):S164–S169.
7. Tonetti MS, Van Dyke TE; working group 1 of the joint EFP/AAP workshop. Periodontitis and atherosclerotic cardiovascular disease: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *J Periodontol* 2013;84(suppl 4S):S24–S29.
8. Monsarrat P, Blaizot A, Kémoun P, et al. Clinical research activity in periodontal medicine: A systematic mapping of trial registers. *J Clin Periodontol* 2016;43:390–400.
9. Cheng ML, Xu MR, Xie YY, et al. Utilisation of oral health services and economic burden of oral diseases in China. *Chin J Dent Res* 2018;21:275–284.
10. Lu HX, Tao DY, Lo ECM, et al. The 4th National Oral Health Survey in the Mainland of China: Background and Methodology. *Chin J Dent Res* 2018;21:161–165.
11. Sun HY, Jiang H, Du MQ, et al. The prevalence and associated factors of periodontal disease among 35 to 44-year-old Chinese adults in the 4th National Oral Health Survey. *Chin J Dent Res* 2018;21:241–247.

12. Sun XY, Yuan C, Wang XZ, et al. Report of the National Investigation of Resources for Oral Health in China. *Chin J Dent Res* 2018;21:285–297.
13. Wang CX, Ma LL, Yang Y, et al. Oral health knowledge, attitudes, behaviour and oral health status of Chinese diabetic patients aged 55 to 74 Years. *Chin J Dent Res* 2018;21:267–273.
14. Jiao J, Jing W, Si Y, et al. The prevalence and severity of periodontal disease in Mainland China: Data from the Fourth National Oral Health Survey (2015–2016). *J Clin Periodontol* 2021;48:168–179.
15. Graetz C, Mann L, Krois J, et al. Comparison of periodontitis patients' classification in the 2018 versus 1999 classification. *J Clin Periodontol* 2019;46:908–917.
16. Tsioufis C, Kasiakogias A, Thomopoulos C, Stefanadis C. Periodontitis and blood pressure: The concept of dental hypertension. *Atherosclerosis* 2011;219:1–9.
17. Del Pinto R, Ferri C, Cominelli F. Vitamin D Axis in inflammatory bowel diseases: Role, current uses and future perspectives. *Int J Mol Sci* 2017;18:2360.
18. Lamont RJ, Koo H, Hajishengallis G. The oral microbiota: Dynamic communities and host interactions. *Nat Rev Microbiol* 2018;16:745–759.
19. Kourtzelis I, Li X, Mitroulis I, et al. DEL-1 promotes macrophage efferocytosis and clearance of inflammation. *Nat Immunol* 2019;20:40–49.
20. Martin-Cabezas R, Seelam N, Petit C, et al. Association between periodontitis and arterial hypertension: A systematic review and meta-analysis. *Am Heart J* 2016;180:98–112.
21. Pietropaoli D, Del Pinto R, Ferri C, et al. Poor oral health and blood pressure control among US hypertensive adults. *Hypertension* 2018;72:1365–1373.
22. Macedo Paizan ML, Vilela-Martin JF. Is there an association between periodontitis and hypertension? *Curr Cardiol Rev* 2014;10:355–361.
23. Offenbacher S. Periodontal diseases: Pathogenesis. *Ann Periodontol* 1996;1:821–878.
24. Curtis MA, Diaz PI, Van Dyke TE. The role of the microbiota in periodontal disease. *Periodontol 2000* 2020;83:14–25.
25. Loos BG, Van Dyke TE. The role of inflammation and genetics in periodontal disease. *Periodontol 2000* 2020;83:26–39.
26. Kapila YL. Oral health's inextricable connection to systemic health: Special populations bring to bear multimodal relationships and factors connecting periodontal disease to systemic diseases and conditions. *Periodontol 2000* 2021;87:11–16.