BMJ Open Disease composition and epidemiological characteristics of primary care visits in Pudong New Area, Shanghai: a longitudinal study, 2016–2018

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ABSTRACT

Objectives This study aims to analyse the disease composition of primary care visits rather than specialist visits, the former of which had scarcely been studied. We adopted specific disease classification (International Statistical Classification of Diseases and Related Health Problems, 10th Revision), disease system and communicable/non-communicable/injury disease classification, and variations of sex and age were also analysed.

Setting We extracted data from all community health service centres (CHSCs) and community health service stations in Pudong, Shanghai, from 2016 to 2018 using the electronic health record systems of the Pudong health information centre.

Participants Our data included all 46 720 972 primary care visits from 2016 to 2018 in CHSCs in Pudong.

Results We found that the top five diseases in primary care visits continued to be primary hypertension, problems related to medical facilities, chronic ischaemic heart disease, unspecified diabetes mellitus and acute upper respiratory infection. Lipoprotein metabolism disorder visits continued to increase over the study years. The numbers and proportions of patients with hypertension and unspecified diabetes were higher among men than women, and other cerebrovascular diseases were higher among women than men. The top five disease systems were circulatory system diseases, respiratory system diseases, endocrine/nutritional/metabolic diseases, factors influencing health status and digestive system diseases. The rankings of respiratory system and endocrine/nutritional/metabolic diseases rose over time. Non-communicable diseases (NCDs) accounted for approximately 90% of the primary care visits—a much higher percentage than other causes. The top five NCDs in primary care visits were cardiovascular and circulatory diseases, musculoskeletal disorders, diabetes, digestive diseases and urogenital diseases. Compared with women, men suffered from cardiovascular diseases at an earlier age.

Conclusions Different from specialist visits, common diseases, especially NCDs, were the main disease composition of current primary healthcare visits while the former focused on intractable diseases such as tumours, indicating that primary healthcare had played the role of gatekeeper of the healthcare system.

Strengths and limitations of this study

- The study examined the realisation status of hierarchical diagnosis and treatment based on primary care in Shanghai using the electronic medical data of all community health service centres in Pudong region.
- This is the first community-level analysis of the epidemiological disease characteristics of primary care visits in the entire Pudong region.
- Limited by the electronic medical record system, we analysed the disease composition only at the primary care level, rather than including both specialist visits and primary care visits at the same time, and future work should also consider examining the latest data after 2018.

BACKGROUND

Scholars worldwide agree that general practitioners (GPs) have a significant effect on improving population health and controlling medical expenses.^{1–5} Additionally, it is widely accepted that an orderly medical treatment system should be based on GPs. Many scholars argued that it would not be possible to achieve first-contact GPs and ‘GP-specialist’ referrals if GPs could not provide satisfactory primary healthcare, and therefore orderly medical care could not be achieved as well.^{6,7} The World Bank estimated that up to 90% of healthcare demands could potentially be dealt with at the primary care level.⁸ In China, primary healthcare was set as one of five targets in the new round of healthcare reform in 2009. The Chinese government initially intended to improve access to medical care and decrease individual medical costs by implementing a GP system comprising the main body of tier 1 hospitals.⁹ In China, healthcare is provided through a three-tiered system in which all specialists work in secondary and tertiary hospitals,

whereas GPs make up the majority of the staff of tier 1 hospitals—community health service centres (CHSCs) or community health service stations (CHSSs) in cities and medical clinics in rural areas.¹⁰ The family doctor (FD) system was initially established throughout China in 2013.¹¹ A referral system was proposed by the central government in 2015, with the key strategy of strengthening the primary healthcare system.¹² A series of policies have been implemented to encourage people to visit GPs in CHSC for their initial visit; these policies include free health examinations, lower out-of-pocket medical expenses and more personalised health management services.¹³

However, some researchers have argued that patients continue their previous doctor-visiting behaviour, preferring visiting specialists directly, regardless of the severity of their conditions.¹⁴ Li *et al*⁹ explored the primary healthcare system in China thoroughly, pointing out that patients still preferred to go to hospitals for more specialised consultations rather than first-contact FDs in CHSCs; these scholars argued that the reason for this behaviour could be found on the supply side (ie, FDs lacked adequate technical support and appropriate financial incentives to deliver integrated and high-quality care).⁹ Other studies have found that the FD system has played a positive role in achieving orderly doctor-visiting behaviour, reporting that most common diseases were being treated through the primary healthcare system.^{15–17} Li¹⁸ argued that, although the experience in Shanghai City, Zhejiang Province, Qinghai Province and Zhengjiang City in Jiangsu Province had been endorsed by the central government, the policy innovations in Xiamen City had also succeeded in alleviating the overutilization of secondary care with improved outcomes in medical treatment and chronic disease management.¹⁸ Li *et al*¹⁹ demonstrated that local health insurance coverage could help improve the management and control of hypertension in a primary care setting. A longitudinal study conducted by Huang *et al*²⁰ suggested that the percentage of patients preferring to first contact FDs in CHSCs or CHSSs had progressively increased. However, there is still significant controversy regarding the role of FDs in achieving the orderly coordination of medical care through the referral system.

The present study explored a wide disease spectrum. It is generally accepted that the main diseases affecting human health have transitioned from acute and chronic infectious diseases to chronic non-communicable diseases (NCDs).²¹ NCDs is already the main trend of epidemiology, although there will be outbreaks of epidemic diseases from time to time, such as the recent global transmission of COVID-19.²² The WHO has identified NCDs as the leading cause of death globally,²³ and numerous studies in China have also revealed the same dramatic epidemiological shift.²⁴ However, previous studies in China have several limitations. Many of these studies have selected one or a few hospitals to explore epidemiological characteristics and the disease spectrum due to data collection problems,²⁵ and existing studies have tended

to focus on inpatient diseases, neglecting epidemiological characteristics at the primary care level.^{26–29} Huang *et al*³⁰ analysed the existing studies of the disease spectrum and epidemiological characteristics, finding that 39.1% of these studies focused on inpatients, 20.4% on emergency room patients, 9.1% on literature and statistical reports, and 7.2% on medical examinations, with epidemiological surveys accounting for only 6.4% of current studies. No existing studies on this topic have focused on primary care visits or included data on entire regions. We believe that it is significant and necessary to fill this research gap, overcoming the potential bias of investigating a single hospital or tertiary hospitals, exploring the epidemiological characteristics of primary care visits, and contributing to understanding the controversial topic of the role of FDs in the orderly coordination of medical care.

In this study, we tried to map the disease composition of primary care visits by collecting real data for the whole district of Pudong New Area of Shanghai using the ‘big data’ of 46 720 972 visit records, to analyse the epidemiological characteristics at the primary care level, to explore the variation of disease distribution by sex and age over years, and to summarise epidemiological characteristics by comparing with that of specialist visits in China and other countries.

METHODS

Study design and setting

This study was conducted in the Pudong New Area district of Shanghai. As the largest district of Shanghai, Pudong has a permanent population of 5.5 million inhabitants and covers an area of 1210 square kilometres.³¹ Pudong is always the pilot area for healthcare reform in Shanghai and even in China, and many policies have been piloted and implemented initially in Pudong. In Shanghai, only CHSCs and CHSSs provide primary healthcare services, rather than specialists in tier-2 and tier-3 hospitals, and the CHSSs are affiliated to CHSCs. Pudong has the largest number of CHSCs than any other district in Shanghai. The 47 CHSCs and 386 CHSSs in Pudong provide more than 15 million visits per year. All 47 CHSCs and CHSSs belong to the Health Commission of Pudong New Area, and the medical data are managed by the health information centre (HIC) affiliated to the Health Commission. Since 2014, we have cooperated with the HIC to extract the whole data of primary visits in Pudong New Area. Thus, this is a population-based study covering all primary care visits using longitudinal data from 2016 to 2018.

Data collection

Data on primary care visits from 2016 to 2018 were extracted from Pudong HIC’s electronic health records (EHRs) system. We chose 2016 as the starting point because the system was not completely reliable until 2016, even though the EHR system including data of all primary care visits had been launched by the Pudong HIC since 2014. We used data of all 46 720 972

primary care visits recorded from 2016 to 2018 in all 47 CHSCs in Pudong (17 008 874 visits in 2016, 14 670 104 visits in 2017 and 15 041 994 visits in 2018). The data included all outpatient visits from all the 47 CHSCs and the 386 CHSSs in Pudong, regardless of whether they had medical insurance or a type of medical insurance, whether they were permanent residents or not. However, the data didn't include the unofficial care clinics. In Shanghai, there were few unofficial care clinics for GPs and patients rarely visited the unofficial clinics, according to the Shanghai Pudong New Area statistical yearbook.³²

The data from the EHR system consisted of diagnosis information, institution name, visit time, International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) diagnostic codes, sex and age. The physicians diagnosed each patient according to ICD-10 codes. The diagnosis would be problems related to medical facilities (Z75) if the patients only visited for health examination. Original electronic documents were reviewed and audited by the HIC, and the original data were extracted and analysed. We received the data without personal information so that no individual patient could be identified.

Measures

We initially analysed the data using ICD-10 codes, and then classified the diseases by the ICD-10 system according to its 2016 version. We focused on NCDs because NCDs accounted for a large proportion of diseases and also because of the enormous global burden associated with NCDs. The ICD-10 system codes for disease systems and NCDs can be found in online supplemental tables 1–3. The data were analysed separately by sex (male and female) and age groups. The population was divided into five age groups: ≤18 years, 19–39 years, 40–59 years, 60–79 years and ≥80 years.

Statistical analysis

We analysed all data using SAS software V.9.20. The most common disorders and systems and all NCDs were ranked by proportion of primary care visits. First, the disease composition of the overall population was analysed. The sex and age subgroups were then analysed separately. Finally, we conducted a cross analysis of both sex and age to further investigate the disease composition of primary care. No statistical tests were used in our study because this is a descriptive study using longitudinal data from the whole population rather than a sample data.

Patient and public involvement

We use secondhand statistical data, rather than an original individual data set, which was reviewed and processed anonymously by the Health Commission. Thus, patients and the public were not required to be directly involved in this study.

RESULTS

Ranking of disorders in all primary care visits within sex and age groups

The order of the top five diseases did not change over time among the patients who visited CHSCs from 2016 to 2018: The most common diseases were hypertension, problems related to medical facilities, chronic ischaemic heart disease, unspecified diabetes mellitus, and acute upper respiratory infections of multiple and unspecified sites. The proportions of patients with lipoprotein metabolism disorder, conjunctivitis and other arrhythmias continually increased over the three study years (figure 1). In each year, the numbers and proportions of patients with hypertension and unspecified diabetes were higher among men than women. Conversely, the numbers and proportions of patients with chronic ischaemic heart disease, sequelae of cerebrovascular disease and other cerebrovascular diseases were higher among women than men (see figure 2 for details).

Figure 3 presents the disease composition by age groups. In each adult age group, the proportions increased and the rankings rose with age for ischaemic heart disease, cerebrovascular sequelae and other diseases, whereas the proportion decreased and the rankings dropped with age for acute upper respiratory infection. Cross analysis of both sex and age revealed that, in the 19–39 years age group, the proportion for hypertension was much lower among women than men. Among the three oldest age groups, the proportion for ischaemic heart disease increased with age more obviously for women than for men (see online supplemental table 1 for details).

Distribution of disease systems overall and by age and sex groups

As shown in figure 4, circulatory system diseases, factors influencing health status and contact with health services, respiratory system diseases, endocrine diseases/nutrition/metabolism diseases, and digestive system diseases were the top five disease types, accounting for most primary care visits in each study year (77.1% in 2016, 75.51% in 2017 and 76.76% in 2018). The proportions of circulatory system diseases, endocrine diseases, nutrition and metabolism diseases, and urogenital system diseases increased each year. There were some differences between women and men. In each year, the proportions of visits due to circulatory system diseases in men increased and were much higher than those of women (see figure 5 for details).

The analysis by age group (figure 6) showed that the proportion of respiratory system diseases was far higher among patients aged 19–39 years than in the other age groups. In the 60–79 years age group, the proportions of endocrine diseases and nutritional and metabolic diseases were much higher than in other age groups. In addition, among the three oldest age groups, the proportion of diseases of the circulatory system, the most common disease system, increased with age. The difference between men and women was largest in the 19–39 years age group, for example, the top three disease systems for men were

Figure 1 Distribution of the top 20 diseases in primary care visits, 2016–2018.

diseases of the respiratory system, factors influencing health status and contact with health services and diseases of the digestive system while they were factors influencing health status and contact with health services, diseases of the respiratory system and diseases of the genitourinary system for women (see online supplemental table 2 for details on the cross analysis of sex and age).

NCDs overall and by age group and sex

From 2016 to 2018, primary care visits for NCDs were much more frequent, compared with visits for other causes, with NCDs accounting for approximately 90% of all visits. This was followed by infectious diseases. Few differences were observed by sex and age groups over years. In 2016 and 2017, the top five NCDs were cardiovascular and

Figure 2 Distribution of the top 20 diseases in primary care visits by sex, 2016–2018.

circulatory system diseases, musculoskeletal disorders, diabetes, digestive diseases and urogenital diseases. In 2018, diabetes replaced musculoskeletal disorders as the NCD with the second-highest number of primary care visits (see figure 7). In sex group analysis, the proportion of musculoskeletal disorders was more among women than among men while the proportion of diabetes was more among men (see table 1 for details).

The analysis by age group showed that the composition of NCDs was quite different for patients aged ≤ 18 years, compared with the other age groups. The visits by patients aged 18 years or younger were commonly caused by respiratory diseases, oral diseases and skin diseases. Among the three oldest age groups (40–59 years, 60–79 years and ≥ 80 years), cardiovascular and circulatory diseases accounted for the largest number of primary care visits, with a proportion far higher than those of the other diseases. Furthermore, in the three oldest age groups, the proportions of cardiovascular and circulatory diseases increased with age. The proportion of diabetes was also higher in the three oldest age groups than in the youngest age group (≤ 18 years; see table 2 for details). The cross analysis of sex and age revealed a difference between men and women in patients aged 19–39 years. In this age group, visits by women were mainly caused by urogenital diseases, whereas cardiovascular and circulatory system diseases ranked first for visits by men. Among the three oldest age groups, the proportion of visits for cardiovascular and circulatory diseases ranked first for

Year	Age	1	2	3	4	5	6	7	8	9	10
2016	<18	medical facilities problems 303694 63.67%	General examination 32867 6.89%	Routine health check-up 26707 5.6%	acute upper respiratory infection 16449 3.44%	health services 13456 2.82%	Fever 8315 1.74%	bronchitis, not specified 7753 1.63%	Disorders of tooth 7000 1.49%	Vitamin D deficiency 4294 0.9%	Acute tonsillitis 3844 0.81%
	19-39	medical facilities problems 128660 17.41%	acute upper respiratory infection 66408 8.99%	Supervision of normal pregnancy 41221 5.58%	hypertension 31375 4.25%	gastroitis and duodenitis 21633 2.93%	inflammation of vagina and vulva 20955 2.84%	Acute pharyngitis 18762 2.54%	bronchitis, not specified 18422 2.49%	local infections of skin 16863 2.28%	Dorsalgia 15120 2.05%
	40-59	hypertension 566098 22.12%	medical facilities problems 323502 12.76%	DM 165618 6.53%	acute upper respiratory infection 146951 5.8%	CHD 90679 3.58%	gastroitis and duodenitis 78496 3.1%	bronchitis, not specified 56332 2.24%	Dorsalgia 50986 2.01%	other arthritis 15955 1.81%	Gingivitis and periodontal diseases 13069 1.54%
	60-79	hypertension 207328 22.05%	medical facilities problems 128189 13.63%	CHD 846321 9%	DM 759234 8.07%	acute upper respiratory infection 346731 3.69%	gastroitis and duodenitis 272743 2.9%	disorders of lipoprotein metabolism 216844 2.3%	other arthritis 193379 2.06%	sequelae of cerebrovascular disease 174311 1.85%	170363 1.81%
	>80	hypertension 730955 19.43%	medical facilities problems 530447 14.1%	CHD 488090 12.97%	DM 232865 6.19%	sequelae of cerebrovascular disease 112584 2.52%	acute upper respiratory infection 99049 2.63%	gastroitis and duodenitis 98275 2.61%	Disorders of tooth 86345 2.14%	Hypertonia of prostate 73405 1.96%	disorders of lipoprotein metabolism 70826 1.88%
2017	<18	medical facilities problems 409097 66.58%	General examination 46199 7.52%	Routine health check-up 31133 5.07%	acute upper respiratory infection 17928 2.92%	health services 12916 2.1%	bronchitis, not specified 8660 1.41%	Fever 8360 1.36%	Disorders of tooth 6953 1.13%	Vitamin D deficiency 6293 1.02%	Other vitamin deficiencies 4342 0.71%
	19-39	medical facilities problems 111890 16.1%	acute upper respiratory infection 68933 9.92%	Supervision of normal pregnancy 41994 6.04%	hypertension 29350 4.22%	gastroitis and duodenitis 20214 2.91%	inflammation of vagina and vulva 18457 2.66%	Acute pharyngitis 18446 2.65%	local infections of skin 17859 2.57%	bronchitis, not specified 16999 2.45%	irregular menstruation 14045 2.02%
	40-59	hypertension 560750 22.38%	medical facilities problems 218827 9.78%	DM 144407 6.45%	acute upper respiratory infection 126746 5.66%	CHD 84979 3.8%	gastroitis and duodenitis 70253 3.14%	bronchitis, not specified 48324 2.17%	disorders of lipoprotein metabolism 41378 1.85%	other arthritis 39066 1.74%	Gingivitis and periodontal diseases 37193 1.66%
	60-79	hypertension 1742982 21.56%	CHD 842958 10.43%	DM 629637 7.79%	medical facilities problems 580043 7.18%	acute upper respiratory infection 287643 3.56%	disorders of lipoprotein metabolism 267207 3.31%	gastroitis and duodenitis 248774 3.08%	sequelae of cerebrovascular disease 199694 2.47%	other arthritis 177399 2.14%	bronchitis, not specified 150393 1.86%
	>80	hypertension 574044 18.91%	CHD 448870 14.78%	DM 199651 6.57%	DM 176186 5.8%	sequelae of cerebrovascular disease 115437 4.46%	gastroitis and duodenitis 85098 2.81%	acute upper respiratory infection 81750 2.69%	disorders of lipoprotein metabolism 78984 2.6%	Hypertonia of prostate 74418 2.43%	other arthritis 68102 2.24%
2018	<18	medical facilities problems 417580 68.68%	General examination 53855 8.86%	Routine health check-up 23134 3.8%	acute upper respiratory infection 16751 2.76%	Disorders of tooth 7523 1.24%	health services 7118 1.2%	Asthma 6616 1.09%	Other vitamin deficiencies 6069 1%	Vitamin D deficiency 5515 0.91%	Acute laryngitis and tracheitis 4637 0.77%
	19-39	medical facilities problems 109213 16.29%	acute upper respiratory infection 72216 10.77%	Pregnant state, incidental 38763 5.77%	hypertension 34488 5.14%	Acute pharyngitis 18125 2.7%	gastroitis and duodenitis 17909 2.67%	bronchitis, not specified 16024 2.39%	local infections of skin 15879 2.37%	inflammation of vagina and vulva 15506 2.31%	Acute bronchitis 15158 2.26%
	40-59	hypertension 592216 24.65%	medical facilities problems 208582 8.68%	DM 159903 6.65%	acute upper respiratory infection 155617 6.48%	CHD 90410 3.76%	gastroitis and duodenitis 68076 2.83%	disorders of lipoprotein metabolism 54478 2.27%	bronchitis, not specified 49962 2.08%	sleep disorders 38609 1.61%	Gingivitis and periodontal diseases 38198 1.59%
	60-79	hypertension 1964428 23.15%	CHD 831425 9.8%	DM 679552 8.01%	medical facilities problems 486271 5.73%	acute upper respiratory infection 355779 4.19%	disorders of lipoprotein metabolism 322888 3.8%	gastroitis and duodenitis 233388 2.75%	sequelae of cerebrovascular disease 193279 2.28%	other arthritis 162584 1.92%	bronchitis, not specified 146454 1.73%
	>80	hypertension 558002 19.96%	CHD 387285 13.85%	DM 167458 5.99%	DM 135753 4.86%	sequelae of cerebrovascular disease 115917 4.15%	acute upper respiratory infection 90689 3.24%	disorders of lipoprotein metabolism 82695 2.96%	Hypertonia of prostate 75443 2.7%	gastroitis and duodenitis 72639 2.6%	Other functional intestinal disorders 64223 2.3%

Figure 3 Distribution of the top 20 diseases in primary care visits by age group, 2016–2018. CHD, Coronary Heart Disease; DM, Diabetes Mellitus.

both men and women (see online supplemental table 3 for details).

DISCUSSION

We found that the top five diseases in primary care visits were consistently primary hypertension, problems related to medical facilities, chronic ischaemic heart disease, unspecified diabetes mellitus and acute upper respiratory infection. Lipoprotein metabolism disorder was found to increase continually over the study years, possibly because of an increased detection rate and a higher prevalence

caused by changes in diet.³³ The top five disease systems were circulatory system diseases, respiratory system diseases, endocrine/nutritional/metabolic diseases, factors influencing health status and digestive system diseases. Respiratory system and endocrine/nutritional/metabolic diseases moved up in terms of frequency ranking over the study years. More (and more serious) air pollution may have led to the increase in respiratory system diseases.³⁴ Increases of both prevalence and detection rates likely led to the increases in endocrine/nutritional/metabolic diseases and lipoprotein metabolism

Visits	Proportion	Rank in 2016	Visits	Proportion	Rank in 2017	Visits	Proportion	Rank in 2018
5444113	32.01%	1 Diseases of the circulatory system	4888033	33.32%	1 Diseases of the circulatory system	5198248	34.56%	1 Diseases of the circulatory system
2802353	16.48%	2 Factors influencing health status	1742896	11.88%	2 Factors influencing health status	1711014	11.37%	2 Diseases of the respiratory system
1896546	11.15%	3 Diseases of the respiratory system	1608940	10.97%	3 Diseases of the respiratory system	1707278	11.35%	3 Endocrine, nutritional and metabolic diseases
1624835	9.55%	4 Endocrine, nutritional and metabolic diseases	1530219	10.43%	4 Endocrine, nutritional and metabolic diseases	1638513	10.89%	4 Factors influencing health status
1376850	8.09%	5 Diseases of the digestive system	1306600	8.91%	5 Diseases of the digestive system	1291378	8.59%	5 Diseases of the digestive system
1256618	7.39%	6 The musculoskeletal system diseases	1133434	7.73%	6 The musculoskeletal system diseases	1107375	7.36%	6 The musculoskeletal system diseases
677759	3.98%	7 Diseases of the genitourinary system	651190	4.44%	7 Diseases of the genitourinary system	651518	4.33%	7 Diseases of the genitourinary system
532593	3.13%	8 Symptoms and abnormal findings	404614	2.76%	8 Diseases of the skin	393819	2.62%	8 Diseases of the skin
421177	2.48%	9 Diseases of the skin	401698	2.74%	9 Symptoms and abnormal findings	327965	2.18%	9 Diseases of the nervous system
278135	1.64%	10 Diseases of the eye and adnexa	291720	1.99%	10 Diseases of the eye and adnexa	312184	2.08%	10 Diseases of the eye and adnexa
264096	1.55%	11 Diseases of the nervous system	229170	1.56%	11 Diseases of the nervous system	299233	1.99%	11 Symptoms and abnormal findings
146039	0.86%	12 Mental and behavioural disorders	209240	1.43%	12 Mental and behavioural disorders	135325	0.9%	12 Mental and behavioural disorders
113476	0.67%	13 Infectious and parasitic diseases	107823	0.73%	13 Infectious and parasitic diseases	102475	0.68%	13 Infectious and parasitic diseases
65041	0.38%	14 Diseases of ear and mastoid process	70860	0.48%	14 Diseases of ear and mastoid process	75851	0.5%	14 Diseases of ear and mastoid process
36040	0.21%	15 Injury, poisoning	36994	0.25%	15 Diseases of blood and immune mechanism	37635	0.25%	15 Diseases of blood and immune mechanism
35164	0.21%	16 Diseases of blood and immune mechanism	26229	0.18%	16 Injury, poisoning	25587	0.17%	16 Injury, poisoning
15451	0.09%	17 External causes of morbidity and mortality	12928	0.09%	17 Neoplasms	16549	0.11%	17 Neoplasms
14214	0.08%	18 Neoplasms	11334	0.08%	18 External causes of morbidity and mortality	6220	0.04%	18 Pregnancy, childbirth and the puerperium
7235	0.04%	19 Pregnancy, childbirth and the puerperium	5210	0.04%	19 Pregnancy, childbirth and the puerperium	3295	0.02%	19 External causes of morbidity and mortality
1106	0.01%	20 Congenital and chromosomal abnormalities	934	0.01%	20 Congenital and chromosomal abnormalities	518	0.00%	20 Congenital and chromosomal abnormalities
32	0.00%	21 Certain conditions in the perinatal period	38	0.00%	21 Certain conditions in the perinatal period	14	0.00%	21 Certain conditions in the perinatal period
1	0.00%	22 Codes for special purposes	0	0.00%	22 Codes for special purposes	0	0%	22 Codes for special purposes

Figure 4 Distribution of disease systems in primary care visits, 2016–2018.

Figure 5 Distribution of disease systems in primary care visits by sex, 2016–2018.

disorders. Our findings for the disease composition of primary care visits are very different from those reported by recent studies of specialist visits in large hospitals. According to recent studies conducted in tier 2 or tier 3 hospitals, the most common top diseases among inpatients were neoplasms, circulatory diseases, respiratory diseases, factors affecting health status and nervous system diseases.^{35–39} In our study, we found some differences in the most common diseases for primary healthcare visits and specialist visits. The specific diseases varied more substantially, with CHSCs more often dealing with primary and common diseases. A preliminary conclusion could be drawn that primary care in Shanghai, at least in Pudong district, has played the role of gatekeeper, based on which an ordered treatment and referral system could be established.

Figure 6 Distribution of disease systems in primary care visits by age group, 2016–2018. Note: (1) Factors influencing health status and contact with health services, (2) Diseases of the respiratory system, (3) Diseases of the digestive system, (4) Symptoms, signs and abnormal clinical and laboratory findings, (5) Diseases of the skin and subcutaneous tissue, (6) Endocrine, nutritional and metabolic diseases, (7) Diseases of the eye and adnexa, (8) Diseases of the genitourinary system, (9) Diseases of the musculoskeletal system and connective tissue, (10) Certain infectious and parasitic diseases, (11) Injury, poisoning and certain other consequences of external causes, (12) Diseases of the blood, blood-forming organs and the immune mechanism, (13) Diseases of the circulatory system, (14) Diseases of the ear and mastoid process, (15) Diseases of the nervous system, (16) Diseases of other systems.

We also found that visits for NCDs were dominant in terms of disease composition, accounting for approximately 90% of the primary care visits in our data set, suggesting an ongoing health transition. Recent studies have suggested that China has completed the epidemiological transition from a predominance of infectious diseases and maternal and perinatal conditions to chronic diseases and injury being the main conditions affecting human health.⁴⁰ However, because China, like other developed countries, is facing challenging situations such as the impact of smoking, hypertension, the health effects of environmental pollution and the rise of HIV/AIDS, we prefer to describe the current situation in China as an ongoing ‘health transition’. This designation considers more wide-ranging factors, including cultural, social and environmental determinants of health, rather than focusing only on improvements in medical care and public health. We found that the top five NCDs in our primary healthcare visits were cardiovascular and circulatory diseases, musculoskeletal disorders, diabetes, digestive diseases and urogenital diseases, which differed from recent reports on the disease composition in specialist visits. Shi *et al*⁴¹ collected data from 12 public hospitals in China, finding that the top five NCDs were cardiovascular and circulatory diseases, urogenital diseases, chronic respiratory diseases, cancers and digestive diseases.⁴¹ The emergence of NCDs in China has received significant attention, and the prevalence and burden of NCDs continue to grow. Primary healthcare is thought to be an appropriate strategy to deal with such challenges, as has been strongly recommended by the WHO and implemented globally.⁴² Kane *et al*⁴³ has argued that NCDs can be treated effectively through primary healthcare even in resource-poor settings. Besides, with the increase in the proportion of NCDs, the proportion of communicable diseases (CDs) and injuries had been declining over years. However, the disease composition of CDs, NCDs and injuries may be changed by the outbreak of COVID-19, but we believe that the COVID-19 outbreak is a mutation which will not change the long-term trend of disease composition.

We further analysed disease composition differences by sex and age and found that the numbers and proportions of patients with hypertension and unspecified diabetes were higher among men than women, whereas chronic ischaemic heart disease, sequelae of cerebrovascular disease and other cerebrovascular diseases were higher among women than men. Such sex differences in chronic ischaemic heart disease have been widely observed in current studies, but investigations and data are still lacking. Abbey and Stewart have pointed out that over the last 5 years ischaemic cardiac disease has become the highest cause of mortality for women in most Western countries, but gender difference studies were lacking.⁴⁴ Similar ideas were expressed by Ciambrone and Kaski. They pointed out that despite the relatively high prevalence of coronary artery disease in women, there were little data on the investigation and treatment of ischaemic

Visits	Proportion	Rank in 2016	Visits	Proportion	Rank in 2017	Visits	Proportion	Rank in 2018
544113	44.63%	1 Cardiovascular and circulatory	488803	43.23%	1 Cardiovascular and circulatory	5198248	44.08%	1 Cardiovascular and circulatory
1256618	10.3%	2 Musculoskeletal disorders	1133434	10.02%	2 Musculoskeletal disorders	1128039	9.57%	2 Diabetes
1232252	10.1%	3 Diabetes	1052139	9.31%	3 Diabetes	1107375	9.39%	3 Musculoskeletal disorders
962695	7.89%	4 Digestive diseases	901994	7.98%	4 Digestive diseases	883621	7.49%	4 Digestive diseases
652062	5.35%	5 Urogenital diseases	629993	5.57%	5 Urogenital diseases	631566	5.36%	5 Urogenital diseases
641173	5.26%	6 Chronic respiratory diseases	593480	5.25%	6 Chronic respiratory diseases	597480	5.07%	6 Chronic respiratory diseases
421177	3.45%	7 Skin and subcutaneous diseases	491881	4.35%	7 Endocrine diseases	583751	4.95%	7 Endocrine diseases
414155	3.4%	8 Oral disease	404614	3.58%	8 Skin and subcutaneous diseases	407757	3.46%	8 Oral disease
413011	3.39%	9 Endocrine diseases	404606	3.58%	9 Oral disease	393795	3.34%	9 Skin and subcutaneous diseases
334464	2.74%	10 Sensory organ diseases	354687	3.14%	10 Sensory organ diseases	380102	3.22%	10 Sensory organ diseases
264019	2.16%	11 Neurological disorders	229131	2.03%	11 Neurological disorders	327917	2.78%	11 Neurological disorders
146021	1.2%	12 Mental and behavioural disorders	209206	1.85%	12 Mental and behavioural disorders	135245	1.15%	12 Mental and behavioural disorders
10510	0.09%	13 Other neoplasms	8804	0.08%	13 Other neoplasms	9214	0.08%	13 Other neoplasms
3704	0.03%	14 Cancer	4124	0.04%	14 Cancer	7335	0.06%	14 Cancer
1106	0.01%	15 Congenital anomalies	934	0.01%	15 Congenital anomalies	518	0.00%	15 Congenital anomalies

Figure 7 Distribution of non-communicable diseases in primary care visits, 2016–2018.

heart disease in this population.⁴⁵ Besides, we found that the proportions increased and the rankings rose with age for both men and women for ischaemic heart disease, cerebrovascular sequelae and other diseases, whereas the proportion decreased and the ranking dropped with age for acute upper respiratory infection. The prevalence of upper respiratory infection decreased with age in the study conducted by Zhang and Shi from 2008 to 2012.³⁶ Huang *et al*²⁵ found that tumour was consistently the top inpatient condition for both men and women in specialist visits, and inpatient pregnancy, childbirth and puerperium disorders were the most common conditions for inpatient women. In terms of NCDs and disease systems, Huang *et al*'s study indicated that, as age increased, the number and proportion of visits for NCDs also increased. This finding was degree. Wang *et al*⁴⁶ found that the prevalence of NCDs increased with age and that women had a higher probability of suffering from NCDs. Visits of patients aged younger than 18 years were previously found to be more likely to be caused by respiratory diseases, oral diseases and skin diseases for both male and female patients, and this finding was echoed by a recent study on specialist visits.³⁶ In the present study, the top-ranked NCD in the 19–39 years age group was diseases of the urogenital system for women and cardiovascular system diseases for men. Compared with women, more men suffered from cardiovascular diseases at an earlier age, which is consistent with previous studies.⁴⁶ One study focusing on the disease composition of inpatients in one CHSC also found that women were more likely than men to suffer from diseases of the urogenital system.⁴⁷ Among the three oldest age groups in the present study (40–59 years, 60–79 years and ≥80 years), the proportion of visits for cardiovascular and circulatory diseases ranked highest for both men and women. Cardiovascular and circulatory diseases have also shown to rank highly in the disease composition of specialist visits by people in the middle and older age groups.^{37 38 48}

We compared our findings with those of other countries. Although current research on disease composition does not focus on the field of primary healthcare on a global scale, we still found some similar studies conducted in other countries. Mash *et al*⁴⁹ conducted a morbidity survey of South African primary care, and they found that the top five diagnosed diseases in South Africa were hypertension (12%), upper respiratory tract infection (5.3%), HIV/AIDS (3.9%), type 2 diabetes (3.9%) and TB (3.6%). Another primary care study conducted in Eastern Cape Province of South Africa showed that the most commonly diagnosed category was respiratory diseases (23%).⁵⁰ Malaria was also highlighted as a key prevention and treatment disease for primary care in many African countries such as Kenya.⁵¹ Different to the current findings in China, infectious diseases including HIV/AIDS are still an important disease component of primary healthcare visits. NCDs are currently the main diagnosis and treatment diseases in primary healthcare institutions in Shanghai, China, where HIV/AIDS were scarcely detected. Another interesting finding was that the dominant focus on primary care diseases in developed countries including UK, USA, Australia, even Chile and Brazil were psychiatric morbidity, depression, anxiety or mental health, although we did not find the exact proportion of such diseases at the primary care level nationwide.^{52 53} Martín-Merino *et al*⁵⁴ proposed that the prevalence of anxiety was 7.2% based on a cohort study conducted in UK,⁵⁴ Vazquez-Barquero *et al*⁵⁵ found the prevalence of mental illness (in attenders) was 33.2% in northern Spain while Mari *et al*⁵⁶ insisted that the hidden psychiatric morbidity ranged from 22% to 79% in primary care clinics in the city of Sao Paulo of Brazil. Besides, obesity of the youth was also highlighted in current studies on primary care in advanced countries such as Germany, Canada and Australia, which was less perceived by primary care institutions in China.^{57 58} A further cross-country comparison study is worth conducting, focusing

Table 1 Distribution of non-communicable diseases in primary care visits by sex, 2016–2018

Category	2016						2017						2018					
	Male			Female			Male			Female			Male			Female		
	Visits	%	Rank	Visits	%	Rank	Visits	%	Rank	Visits	%	Rank	Visits	%	Rank	Visits	%	Rank
Communicable, maternal, neonatal and nutritional diseases	599 987	10.33	-	812 493	10.438	-	501 517	9.325	-	678 667	9.53	-	539 426	9.54	-	731 050	9.91	-
Injury	3982	0.07	-	11 316	0.145	-	2610	0.049	-	8723	0.12	-	1258	0.02	-	2033	0.028	-
Non-communicable diseases	5 205 229	89.60	-	6 959 978	89.416	-	4 873 903	90.626	-	6 431 774	90.34	-	5 113 651	90.44	-	6 645 181	90.06	-
Cardiovascular and circulatory diseases	2 370 860	45.55	1	3 069 545	44.10	1	2 147 305	44.06	1	2 740 430	42.61	1	2 292 424	44.83	1	2 898 187	43.61	1
Diabetes	537 163	10.32	2	694 008	9.97	3	475 394	9.75	3	576 657	8.97	3	515 333	10.08	2	611 082	9.20	3
Musculoskeletal disorders	485 835	9.33	3	765 917	11.00	2	434 626	8.92	2	698 642	10.86	2	422 130	8.25	3	680 805	10.25	2
Digestive diseases	402 147	7.73	4	556 987	8.00	4	376 277	7.72	4	525 531	8.17	4	367 717	7.19	4	512 557	7.71	4
Chronic respiratory diseases	295 133	5.67	5	343 372	4.93	6	273 429	5.61	6	319 928	4.97	6	276 691	5.41	6	318 924	4.80	6
Urogenital diseases	284 028	5.46	6	362 554	5.21	5	294 122	6.03	5	335 754	5.22	5	311 845	6.10	5	316 946	4.77	7
Skin and subcutaneous diseases	198 926	3.82	7	217 785	3.13	9	193 708	3.97	9	210 718	3.28	10	184 890	3.62	8	204 234	3.07	10
Oral disease	183 692	3.53	8	227 461	3.27	8	179 717	3.69	8	224 801	3.50	8	180 393	3.53	9	225 030	3.39	9
Endocrine diseases	158 507	3.05	9	253 796	3.65	7	189 553	3.89	7	302 292	4.70	7	228 612	4.47	7	354 100	5.33	5
Sensory organ diseases	125 505	2.41	10	207 559	2.98	10	132 927	2.73	10	221 715	3.45	9	141 877	2.77	10	236 312	3.56	8
Neurological disorders	106 926	2.05	11	156 571	2.25	11	95 119	1.95	11	133 994	2.08	11	138 040	2.70	11	189 074	2.85	11
Mental and behavioural disorders	53 381	1.03	12	92 406	1.33	12	78 414	1.61	12	130 772	2.03	12	48 339	0.95	12	86 329	1.30	12
Cancer	1774	0.03	13	1901	0.03	14	2102	0.04	14	2015	0.03	14	3746	0.07	13	3569	0.05	14
Other neoplasms	976	0.02	14	9393	0.13	13	901	0.02	13	7900	0.12	13	1458	0.03	14	7674	0.12	13
Congenital anomalies	376	0.01	15	723	0.01	15	309	0.01	15	625	0.01	15	156	0.00	15	358	0.01	15

Table 2 Distribution of non-communicable diseases in primary care visits by age group, 2016–2018

Systems	≥80			60–79			40–59			19–39			≤18		
	Visits	%	Rank	Visits	%	Rank	Visits	%	Rank	Visits	%	Rank	Visits	%	Rank
2016															
Communicable, maternal, neonatal and nutritional diseases	213 498	6.85	-	707 049	9.07	-	307 858	14.75	-	149 015	29.19	-	35 422	42.21	-
Injury	1801	0.06	-	7684	0.10	-	2189	0.10	-	3573	0.70	-	54	0.06	-
Non-communicable diseases	2 900 727	93.09	-	7 082 456	90.83	-	1 777 075	85.14	-	357 933	70.11	-	48 444	57.73	-
Cardiovascular and circulatory diseases	1 441 379	49.69	1	3 262 589	46.07	1	691 974	38.94	1	44 475	12.43	4	628	1.30	9
Musculoskeletal disorders	281 196	9.69	2	716 641	10.12	3	203 224	11.44	2	49 307	13.78	2	1508	3.11	7
Diabetes	248 668	8.57	3	800 304	11.30	2	171 793	9.67	3	10 506	2.94	9	61	0.13	12
Digestive diseases	221 679	7.64	4	536 744	7.58	4	151 493	8.52	4	44 492	12.43	3	4855	10.02	4
Chronic respiratory diseases	157 968	5.45	5	338 516	4.78	5	97 710	5.50	6	32 945	9.20	7	11 487	23.71	2
Urogenital diseases	153 266	5.28	6	317 254	4.48	6	114 518	6.44	5	58 510	16.35	1	3109	6.42	6
Endocrine diseases	85 605	2.95	7	263 190	3.72	7	52 447	2.95	9	10 275	2.87	10	817	1.69	8
Sensory organ diseases	81 186	2.80	8	190 033	2.68	10	44 598	2.51	10	13 621	3.81	8	3648	7.53	5
Skin and subcutaneous diseases	80 174	2.76	9	201 301	2.84	9	85 080	4.79	8	42 748	11.94	5	7454	15.39	3
Neurological disorders	74 034	2.55	10	145 629	2.06	11	35 674	2.01	11	8070	2.25	11	97	0.20	10
Oral disease	43 493	1.50	11	219 677	3.10	8	97 277	5.47	7	36 144	10.10	6	14 618	30.18	1
Mental and behavioural disorders	30 720	1.06	12	84 602	1.19	12	24 743	1.39	12	5639	1.58	12	95	0.20	11
Cancer	735	0.03	13	2140	0.03	14	644	0.04	14	136	0.04	14	19	0.04	14
Other neoplasms	360	0.01	14	3186	0.04	13	5790	0.33	13	1020	0.28	13	18	0.04	15
Congenital anomalies	264	0.01	15	650	0.01	15	110	0.01	15	45	0.01	15	30	0.06	13
2017															
Communicable, maternal, neonatal and nutritional diseases	165 809	6.03	-	573 699	7.92	-	256 451	13.38	-	143 163	29.06	-	41 594	42.58	-
Injury	944	0.03	-	4611	0.06	-	1646	0.09	-	4097	0.83	-	39	0.04	-
Non-communicable diseases	2 583 648	93.94	-	6 663 433	92.01	-	1 658 830	86.54	-	345 323	70.1	-	56 054	57.38	-
Cardiovascular and circulatory diseases	1 249 868	48.38	1	2 970 046	44.57	1	627 415	37.82	1	40 647	11.77	5	448	0.8	9
Musculoskeletal disorders	241 985	9.37	2	654 894	9.83	3	187 189	11.28	2	47 582	13.78	2	1775	3.17	7
Digestive diseases	205 951	7.97	3	509 937	7.65	4	137 535	8.29	4	42 832	12.4	3	5695	10.16	4
Diabetes	196 639	7.61	4	691 205	10.37	2	154 663	9.32	3	9677	2.8	10	31	0.06	14
Urogenital diseases	145 251	5.62	5	320 175	4.8	6	106 167	6.4	5	54 721	15.85	1	3626	6.47	6
Chronic respiratory diseases	142 821	5.53	6	319 588	4.8	7	85 997	5.18	7	29 419	8.52	7	15 716	28.04	1

Continued

Table 2 Continued

Systems	≥80			60–79			40–59			19–39			≤18		
	Visits	%	Rank	Visits	%	Rank	Visits	%	Rank	Visits	%	Rank	Visits	%	Rank
Endocrine diseases	94 139	3.64	7	321 470	4.82	5	63 805	3.85	9	11 478	3.32	9	1002	1.79	8
Sensory organ diseases	83 539	3.23	8	204 404	3.07	9	47 834	2.88	10	14 891	4.31	8	3997	7.13	5
Skin and subcutaneous diseases	77 603	3	9	196 922	2.96	10	79 516	4.79	8	41 855	12.12	4	8576	15.3	3
Neurological disorders	61 200	2.37	10	128 769	1.93	11	32 088	1.93	12	6967	2.02	12	117	0.21	11
Mental and behavioural disorders	43 581	1.69	11	120 916	1.81	12	36 176	2.18	11	8356	2.42	11	168	0.3	10
Oral disease	39 951	1.55	12	219 420	3.29	8	94 591	5.7	6	35 802	10.37	6	14 802	26.41	2
Cancer	585	0.02	13	2527	0.04	14	808	0.05	14	154	0.04	14	45	0.08	12
Other neoplasms	325	0.01	14	2634	0.04	13	4936	0.3	13	890	0.26	13	20	0.04	15
Congenital anomalies	210	0.01	15	526	0.01	15	110	0.01	15	52	0.02	15	36	0.06	13
2018															
Communicable, maternal, neonatal and nutritional diseases	163 042	6.28	-	636 200	8.19	-	284 291	13.55	-	140 933	29.89	-	45 994	45.99	-
Injury	390	0.02	-	1942	0.02	-	678	0.03	-	258	0.05	-	23	0.02	-
Non-communicable diseases	2 430 877	93.7	-	7 129 972	91.79	-	1 813 560	86.42	-	330 347	70.06	-	54 000	53.99	-
Cardiovascular and circulatory diseases	1 174 223	48.3	1	3 239 599	45.44	1	730 887	40.3	1	45 470	13.76	2	411	0.76	9
Musculoskeletal disorders	216 657	8.91	2	654 105	9.17	3	186 798	10.3	2	43 814	13.26	3	1553	2.88	7
Diabetes	188 388	7.75	3	752 933	10.56	2	174 310	9.61	3	10 714	3.24	10	61	0.11	13
Digestive diseases	186 641	7.68	4	512 371	7.19	4	137 753	7.6	4	38 184	11.56	4	5316	9.84	4
Urogenital diseases	138 788	5.71	5	334 581	4.69	6	105 013	5.79	5	46 718	14.14	1	3690	6.83	6
Chronic respiratory diseases	130 510	5.37	6	328 878	4.61	7	92 365	5.09	7	29 360	8.89	7	14 502	26.86	1
Endocrine diseases	97 591	4.01	7	387 217	5.43	5	83 329	4.59	8	13 130	3.97	9	1443	2.67	8
Sensory organ diseases	84 755	3.49	8	222 136	3.12	9	52 279	2.88	10	14 823	4.49	8	4192	7.76	5
Neurological disorders	77 601	3.19	9	190 956	2.68	11	48 526	2.68	11	9859	2.98	11	160	0.3	10
Skin and subcutaneous diseases	70 795	2.91	10	195 407	2.74	10	76 828	4.24	9	37 770	11.43	5	8315	15.4	3
Oral disease	36 713	1.51	11	223 921	3.14	8	96 242	5.31	6	34 389	10.41	6	14 158	26.22	2
Mental and behavioural disorders	26 813	1.1	12	80 237	1.13	12	22 711	1.25	12	4804	1.45	12	103	0.19	11
Cancer	980	0.04	13	4509	0.06	13	1434	0.08	14	318	0.1	14	74	0.14	12
Other neoplasms	381	0.02	14	2834	0.04	14	4947	0.27	13	960	0.29	13	9	0.02	15
Congenital anomalies	41	0	15	288	0	15	138	0.01	15	34	0.01	15	13	0.02	14

on detailed disease morbidity and its various factors in primary care.

In addition, there are two points worth noting. First, you might have noticed the unusual name of the Z-ICD code. Problems related to medical facilities is one of the Z-ICD diseases, accounting for a large proportion, from around 9% to 15%. We learnt about the disease diagnosis content included in this code by consulting the information technology section of the Health Commission. Problems related to medical facilities mainly refer to health examination (including occupational exam, child exam, student exam, age ≥ 60 years exam) and some other problems, and factors influencing health status and contact with health services is a health system category—the proportion of which dropped from around 16% to 10%—which is mainly composed of problems related to medical facilities and some other health consultations. These two classifications have a certain impact on our analysis of disease composition. However, as disease diagnosis becomes more precise and standardised, the proportions of these two categories are gradually decreasing. We insist that the decline of these two categories will improve the accuracy of analysis of disease composition, but we also believe that these two categories cannot be zero, as there are health examination cases and undiagnosable cases. Second, NCD-oriented disease intervention is currently the main task of CHSCs in China, at least at the survey site. So, we believe that the current health system matches the morbidity of primary care. However, a problem that cannot be ignored is that mental illnesses are rarely diagnosed in CHSCs. This does not mean that our residents are mentally healthy. On the contrary, stigma prevents residents from taking any measures until their mental health conditions have deteriorated. Psychological problems of residents have been exposed during the COVID-19 outbreak and transmission period, and obviously the FDs of CHSCs still cannot offer psychological consultation, diagnosis and treatment.

CONCLUSION

There are four main findings of this study. First, primary care mostly covered circulatory system diseases, respiratory system diseases, endocrine/nutritional/metabolic diseases, factors influencing health status and digestive system diseases, indicating the cross-coverage of disease systems with specialised hospitals. Second, the top causes for primary care visits were consistently found to be primary hypertension, chronic ischaemic heart disease, unspecified diabetes mellitus and acute upper respiratory tract infection; this finding differed significantly from previous findings for tertiary hospitals, suggesting an initial functional differentiation between CHSCs and large hospitals. Third, there is an ongoing health transition in China, with NCDs accounting for 90% of all CHSC visits, underscoring the importance of a well-functioning FD system to deal with future NCD management burden. Fourth, there is significant variation by sex and age,

indicating that life-cycle-specific health services—rather than homogenised services—should be provided.

Limitations

First, all our data were from a single district, although this district is the largest one in Shanghai, with a permanent population of 5.5 million. Second, to include high-quality data from all 47 CHSCs in the district, we were only able to extract data since 2016, so the study lacked comparison with earlier data, and reliable regression models were also impossible to perform. Third, COVID-19 has not yet occurred during our research period, which might change our results to some degree, thus it is necessary to further explore the epidemiological characteristics of primary care visits especially during 2019 and 2020, or even longer. Finally, the data extracted from the EHR were lacking in factors such as education, occupation, income and some regional variables, thus we only analysed the data by age and sex.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study was approved by the ethics committees of Shanghai Tenth People's Hospital (ref: 2019-K173-02). The research presented minimal risk of harm to participants, and the study only included primary care visits data collected anonymously.

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Data availability statement The data generated and analysed during the present study are only for academic use and are not publicly available because of patient privacy protection. However, they are available from the corresponding author (supercell002@sina.com) for researchers who meet the criteria for access to confidential data.

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