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Trends in Health Service Use for Dry Eye Disease From 2017 to 2021: A Real-World Analysis of 369,755 Outpatient Visits

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Purpose: We aimed to analyze the trends and patterns in outpatient health service treatment of dry eye disease (DED) using real-world data from Yinzhou District in China.

Methods: The Yinzhou Health Information System is a comprehensive database including electronic medical records from 277 medical institutions representing over 1.64 million residents. We extracted outpatient records from January 1, 2017, to December 31, 2021, that included the first diagnosis of DED according to the *International Classification of Diseases*, 10th Revision (H04.101, H04.103, H11.104, H16.202, or H18.803). We analyzed the trends and patterns of DED outpatient visits using the Mann–Kendall trend test and Cochran–Armitage trend test.

Results: We identified a total of 369,755 outpatient visits from 145,712 patients with DED of all ages (60.37% female; 54.10% 50 years or older). Primary medical institutions had the largest number of DED outpatient visits (42%), followed by tertiary medical institutions (35%). Over the 5-year period, the number of DED outpatient visits increased from 59,260 to 90,807 (53.23%). We observed significant consecutive annual proportion increases in females (from 61.09% to 62.01%; $P = 0.001$), patients 50 years or older (from 55.10% to 60.08%; $P < 0.001$), and outpatient visits in primary medical institutions (from 33.19% to 48.75%; $P < 0.001$).

Conclusions: Our study found an increase in outpatient health service use for DED in Yinzhou from 2017 to 2021, with higher proportions and increases among females, patients 50 years or older, and primary medical institutions.

Translational Relevance: The rapid growth in the prevalence of DED indicates high eye healthcare needs in patients.

Introduction

Dry eye disease (DED) is a kind of ocular surface disease characterized by a loss of homeostasis of the tear film. It is accompanied by ocular signs and symptoms such as red eyes, pain, irritation, and foreign body sensation.[1] The reported prevalence of DED globally has varied greatly from 5% to 50%, but it is increasing over time.[2] As DED is a chronic disease that cannot be completely cured, long-term medical care can help prevent deterioration and recurrence of DED.[2,3] Nearly all DED patients are treated in an outpatient setting. Common outpatient treatments include medication, meibomian gland massage, and intense pulsed-light therapy.[3,4]

Although a large number of epidemiological studies in different countries have examined the prevalence of and risk factors for DED,[2] relatively little is known about health service use by patients with DED. A recent study from 52 hospitals in China showed significant increases in the number of DED patients above 60 years of age and relevant prescriptions from 2013 to 2019, as well as an increase in the cost of treatment.[5] Several studies have reported the characteristics of outpatient ophthalmology utilization[6,7]; however, as far as we know, there has been no specific analysis for patients with DED.

Large regional health databases that integrate electronic medical records (EMRs) across many medical institutions in a region offer a unique opportunity to examine health service use in depth. In China, Yinzhou District, in Ningbo, Zhejiang Province, has 1.64 million residents (as of the 2020 census) and is one of the earliest areas to build such a database. Over 18 years of integration and development, the Yinzhou Health Information System (YHIS) has been regarded as one of the most comprehensive, high-quality, real-world health databases in China. Given the strengths of the YHIS, its database has been used for dozens of policy and health research projects.[8,9]

Due to the increasing prevalence of DED and its health and economic burdens,[2,10,11] we aimed to use the YHIS to fill the knowledge gap in the patterns and temporal trends of outpatient health service use among DED patients. In addition, the YHIS provides real-world evidence regarding an important ocular surface disease that can be applied to health resource allocation and potential eye health improvement at the population level.

Methods

Data Source and Study Population

We selected Yinzhou District, Ningbo, Zhejiang Province, as our study area because of the comprehensive administrative (real-world) database available in this district—the YHIS. Yinzhou District is the largest district of Ningbo, which is a major port city. It has more than 1.64 million long-term residents according to the 2020 census.

The YHIS was the data source for our study. It is a multiple-source health database that is updated daily for over 98% of residents in Yinzhou. This platform was initiated by the Yinzhou Health and Family Planning Commission in 2005. The YHIS database is known for its standardization and consistent structure, the inclusion of many different data sources, individual traceability, and long history. The platform contains EMR data from the majority of health institutes across Ningbo. The outpatient records used in this study were retrieved from 36 medical institutions, including 26 primary medical institutions that provide simple eye examinations by general practitioners (e.g., township health centers, community health service centers), five secondary medical institutions that provide comprehensive eye examinations by ophthalmologists and offer cataract surgery and other minor procedures (e.g., secondary hospitals), and five tertiary medical institutions equipped to provide the entire spectrum of eyecare services (e.g., tertiary hospitals).

This study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Wenzhou Medical University Eye Hospital (approval no. 2022-190-K-148). Informed consent was not required because anonymous and de-identified information was used for our analyses.

Definition of Dry Eye Disease and Covariates

Patients with valid information regarding their unique ID, sex, and date of birth and who made visits within the period from January 1, 2017, to December 31, 2021, were included. Diagnosis information was classified according to the *International Classification of Diseases*, 10th Revision (ICD-10). Patients with DED were defined as those who had an admission history with ICD-10 codes of H04.101, H04.103, H11.104, H16.202, or H18.803 as the first diagnostic code. The diagnostic names corresponding to each ICD-10 code are shown in Supplementary Table S1.

Demographic variables included in this study were sex and age. The age at the time of the first visit was calculated if patients visited the medical institutions more than once in a year. The seasons were defined as spring (March to May), summer (June to August), autumn (September to November), and winter (December to February). We also examined health service use by days of the week from Monday to Sunday.

Statistical Analysis

The COVID-19 pandemic had a huge impact on the number of outpatient visits.[12] To isolate the impact and observe the overall trend of outpatient visits, we used long short-term memory (LSTM) networks to predict the number of weekly outpatient visits from 2020 to 2021. Choosing to use LSTM networks was motivated by their ability to effectively process long-term sequential data, which can be attributed to its unique cell state structure.[13,14] In the preprocessing stage, we normalized our data into a format suitable for LSTM networks. Our initial model consisted of a two-layer LSTM network with 200 hidden neurons. Following the LSTM layer, we used a dense layer that maps

LSTM outputs. The LSTM model was trained using backpropagation with an Adam optimizer, and the mean squared error was employed as our loss function. The dataset was divided into three sections: the training dataset (January 1, 2017, to December 31, 2018), the test dataset (January 1, 2019, to December 31, 2019), and the prediction dataset (January 1, 2020, to December 31, 2021). Upon normalizing the input data, the root mean square errors of the training, test, and prediction data were 0.077, 0.132, and 0.141, respectively, indicating that the model exhibited good predictive performance.

Categorical variables were described by frequency and percentage. We used the Shapiro–Wilk test ($N < 2000$) or Kolmogorov–Smirnov test ($N \geq 2000$) to test for normality and Levene's test to analyze the homogeneity of variance. Continuous variables with a normal distribution were described as mean ± SD; otherwise, as median (interquartile range [IQR]). Age was evaluated as both a continuous variable and a categorical variable at 10-year intervals. The proportion of patients 50 years or older was also calculated due to the high incidence of DED in this age group.[2] In each subgroup, the Mann–Kendall trend test was used to assess the trend in the number of patients and visits, and the Cochran–Armitage trend test was used to assess the trend in the proportion of patients and visits. The Jonckheere–Terpstra trend test was used to assess the trend in ages of patients. The two-sided significance levels were set as $P < 0.05$.

The average number of daily visits for each season was compared by the Kruskal–Wallis test, with the significance threshold set at $P < 0.008$ after adjustment by the Bonferroni test. Similarly, the average number of daily visits for each day of the week was compared, with $P < 0.002$ considered statistically significant. In addition, Spearman rank correlation was used to assess the associations of sex and age with levels of medical institutions, seasons, and days of the week. The statistical analysis of this study was performed using SAS 9.2 (SAS Institute, Cary, NC) and R 4.4.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Overall Trend in Outpatient Use

Figure 1 shows the data cleaning process and distribution of outpatient visits and patients by year. Over the 5 years, there were a total of over 30 million outpatient records. After excluding 1.22% records with missing information on study ID, sex, or age, a total of 369,755 DED outpatient visits were identified. We found a significant increase of 53.23% in the number of outpatient visits, rising from 59,260 in 2017 to 90,807 in 2021.

Figure 2 provides a visual representation of the time series distribution of weekly outpatient visits from 2017 to 2021, illustrating an overall upward trend year by year. However, during the early stages of the COVID-19 outbreak (January 2020–March 2020), the number of weekly outpatient visits experienced a sharp decline. By contrast, the LSTM model, which excluded the impact of the COVID-19 pandemic, predicted a relatively consistent pattern of weekly outpatient visits from 2020 to 2021.

Trends in DED Outpatient Use by Patient Characteristics

Our study included a total of 145,712 patients with DED (39.63% males and 60.37% females). The average number of outpatient visits for DED was 2.46 visits for males and 2.59 visits for females. The Table shows the demographic distribution of patients with DED by year. From 2017 to 2021, the average annual increase in the number of patients was 10.72%. The proportion of females was consistently greater than that of males, representing over 60% of total patients each year. The increase in the proportion of females was significant ($P = 0.001$), but the magnitude of the increase was small, from 61.09% in 2017 to 62.01% in 2021. In addition, patients 50 years or older constituted the majority (over 50% each year) and showed a significant increase over time, from 55.10% in 2017 to 60.08% in 2021 ($P < 0.001$). The distributions of outpatient visits by age group and sex from 2017 to 2021 are shown in Supplementary Table S2.

Outpatient Visits by Different Levels of Medical Institutions

Overall, the number of DED outpatient visits was highest in the primary medical institutions (155,230 visits, 41.98%), followed by tertiary (129,370 visits, 34.99%) and secondary medical (85,155 visits, 23.03%) institutions. Figure 3A shows that the number of DED outpatient visits in primary medical institutions increased the most, from 19,666 in 2017 to 44,272 in 2021, a 125.12% increase with an average annual growth rate of 22.49%. A significant upward trend was also found in the proportion of DED outpatient visits in primary medical institutions ($P < 0.001$) (Fig. 3B, Supplementary Table S3). Figure 3C shows that there appeared to be no sex difference among the three levels of medical institutions, and Figure 3D shows that the proportion of elderly patients (60 years or

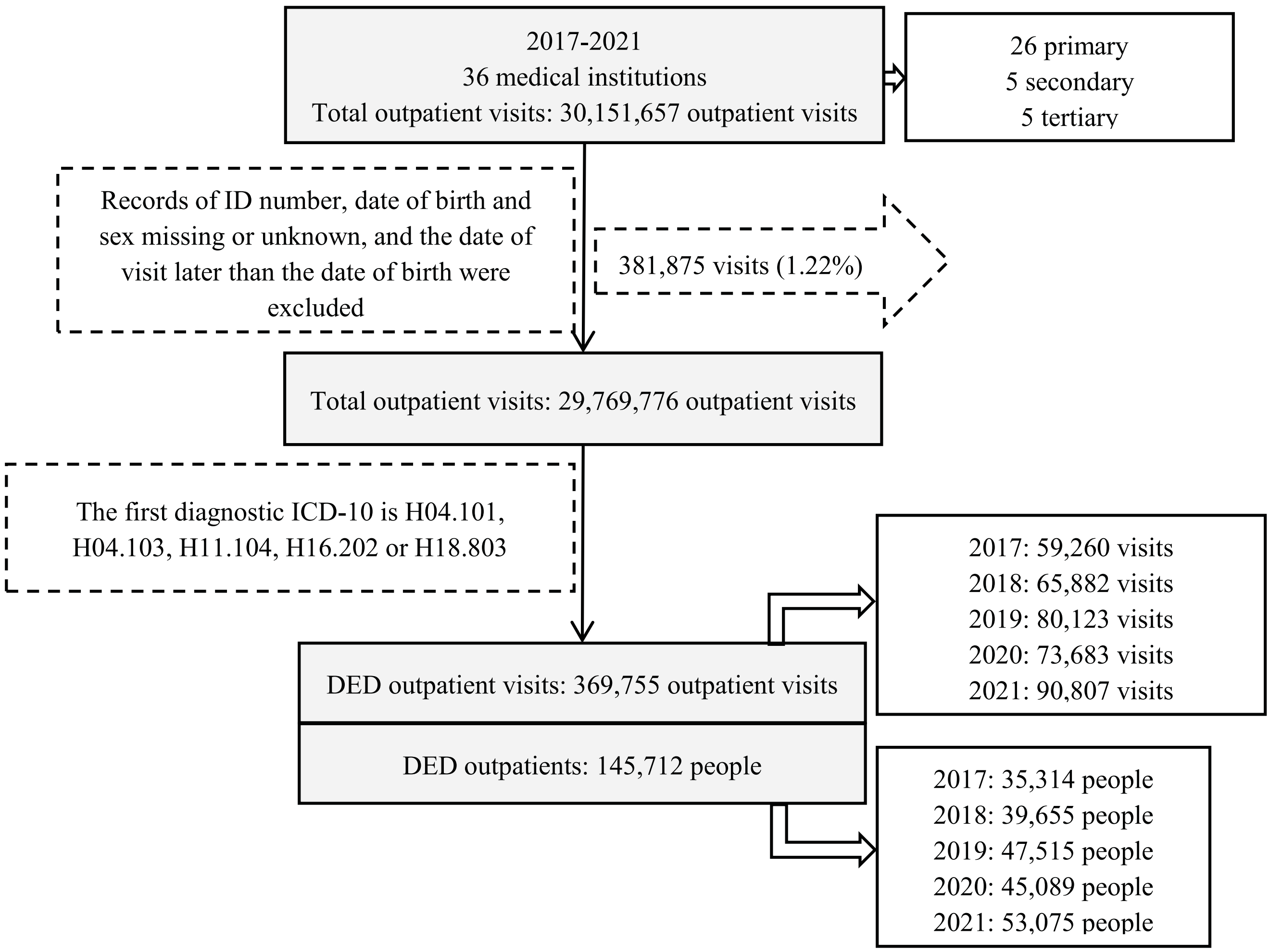

Figure 1. Data cleaning process.

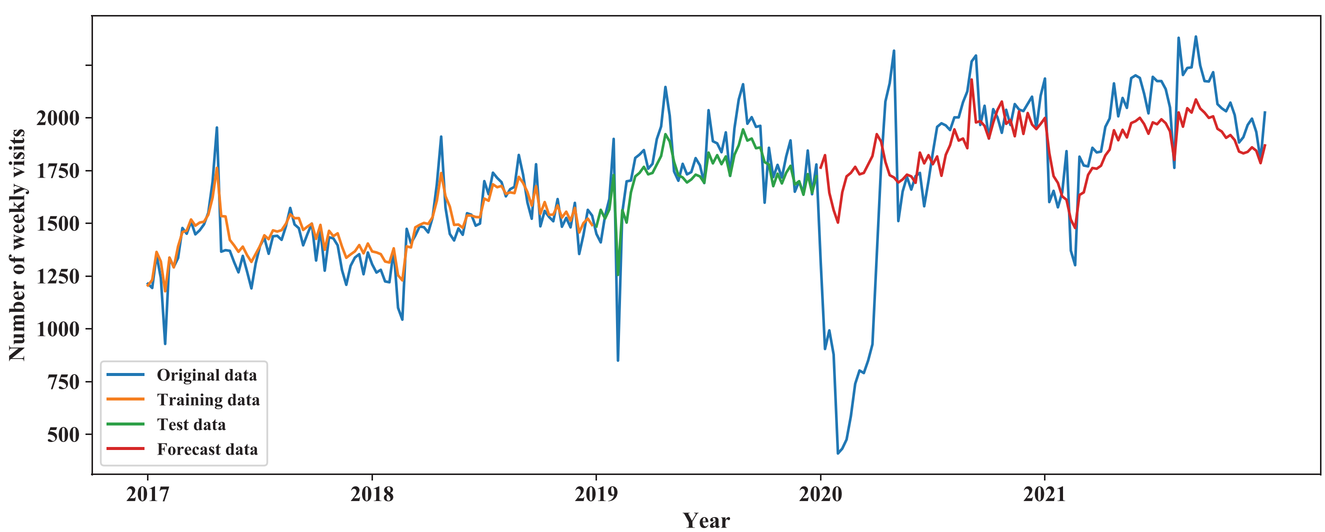

Figure 2. Time series distribution of weekly outpatient visits, stratified by types of datasets. The original dataset was divided into three sections: training dataset (January 1, 2017, to December 31, 2018), test dataset (January 1, 2019, to December 31, 2019), and forecast dataset based on the LSTM model (January 1, 2020, to December 31, 2021).

Table. Demographic Information for Outpatients With DED From 2017 to 2021[a]

Measure	Total[b]	2017	2018	2019	2020	2021	P[c]	P
Total, n (%)	145,712 (100.00)	35,314 (100.00)	39,655 (100.00)	47,515 (100.00)	45,089 (100.00)	53,075 (100.00)	0.09	NA
Sex, n (%)							0.09	0.001[d]
Male	57,740 (39.63)	13,740 (38.91)	15,394 (38.82)	18,292 (38.50)	17,352 (38.48)	20,161 (37.99)		
Female	87,972 (60.37)	21,574 (61.09)	24,261 (61.18)	29,223 (61.50)	27,737 (61.52)	32,914 (62.01)		
Age (y), median (IQR)	52 (27)	52 (26)	52 (26)	53 (26)	54 (26)	55 (25)	NA	<0.001[e]
Age (y), n (%)							0.09	<.001[d]
<50	66,887 (45.90)	15,857 (44.90)	17,512 (44.16)	20,370 (42.87)	18,552 (41.15)	21,187 (39.92)		
≥50	78,852 (54.10)	19,457 (55.10)	22,143 (55.84)	27,145 (57.13)	26,537 (58.85)	31,888 (60.08)		
Age range (y), n (%)								
0–9	7,746 (5.32)	1,554 (4.40)	1,764 (4.45)	2,155 (4.54)	1,849 (4.10)	2,013 (3.79)		
10–19	8,936 (6.13)	2,044 (5.79)	2,476 (6.24)	2,919 (6.14)	2,907 (6.45)	2,749 (5.18)		
20–29	7,644 (5.25)	1,954 (5.53)	2,027 (5.11)	2,117 (4.46)	1,640 (3.64)	1,916 (3.61)		
30–39	17,901 (12.29)	4,114 (11.65)	4,473 (11.28)	5,180 (10.90)	4,768 (10.57)	5,881 (11.08)		
40–49	24,660 (16.92)	6,191 (17.53)	6,772 (17.08)	7,999 (16.83)	7,388 (16.39)	8,628 (16.26)		
50–59	27,852 (19.11)	7,008 (19.84)	7,777 (19.61)	9,111 (19.17)	8,708 (19.31)	10,779 (20.31)		
60–69	30,370 (20.84)	7,736 (21.91)	8,815 (22.23)	10,608 (22.33)	10,085 (22.37)	11,604 (21.86)		
70–79	14,811 (10.16)	3,244 (9.19)	3,951 (9.96)	5,382 (11.33)	5,780 (12.82)	7,194 (13.55)		
≥80	5,792 (3.97)	1,469 (4.16)	1,600 (4.03)	2,044 (4.30)	1,964 (4.36)	2,311 (4.35)		

[a]The demographic distribution was described by year; therefore, outpatients were counted multiple times if they visited medical institutions in different years.
[b]The age was calculated at the time of the first visit from 2017 to 2021.
[c]Based on Mann–Kendall trend test for the trend of the number of patients.
[d]Based on Cochran–Armitage trend test for the trend of the proportion of patients.
[e]Based on Jonckheere–Terpstra trend test for the trend in ages of patients over time.

older) was highest in primary medical institutions. Supplementary Table S4 shows a weak negative association between age and levels of medical institutions ($r = -0.288$, $P < 0.001$). That is, the elderly were more likely to seek care in primary medical institutions. More demographic distributions for the different levels of medical institutions are shown in Supplementary Table S5.

Seasonal and Weekly Patterns

A significant seasonal difference was found in the number of DED outpatient visits (Fig. 4A), and this pattern was essentially consistent across years (Fig. 4B). Winter had an average of 168 ± 72 outpatient visits per day, significantly lower than the other three seasons (all $P < 0.008$), whereas summer had the highest average number of outpatient visits with 221 ± 53 per day (all $P < 0.008$). Given that the annual Spring Festival and the COVID-19 intervention period (January 23, 2020, to March 2, 2020) had a great impact on the number of outpatient visits,[12] we excluded these exceptional periods and conducted a sensitivity analysis to repeat seasonal comparisons of outpatient visits. The final average number of daily outpatient visits in winter was 188 ± 55, which was still significantly lower than that in other seasons. All statistical results are shown in Supplementary Table S6. There appeared to be no difference in sex ratios among seasons (Fig. 4C), but in winter the proportion of patients 60 years or older was slightly lower than in other seasons (Fig. 4D).

Figure 4E shows a Sunday peak with an average of 239 ± 63 outpatient visits, which was significantly higher than other days of the week (all $P < 0.002$). In contrast, the number of outpatient visits on Saturday was the lowest (181 ± 56). All statistical results are shown in Supplementary Table S7. The proportion of patients 60 years or older appeared to be greater on weekends than on weekdays (Fig. 4F).

Discussion

From 2017 to 2021, we analyzed 369,755 outpatient records from 145,712 patients with DED in Yinzhou. Our findings revealed a rising trend in the use of outpatient health services for DED. This increase was more pronounced among females, among patients 50 years or older, and at primary medical institutions. The upward trend in DED outpatient use was significant, consistent with previous research demonstrating an increase in DED incidence and prevalence globally and in China.[2] These increases have important implications for our understanding of health service use and future

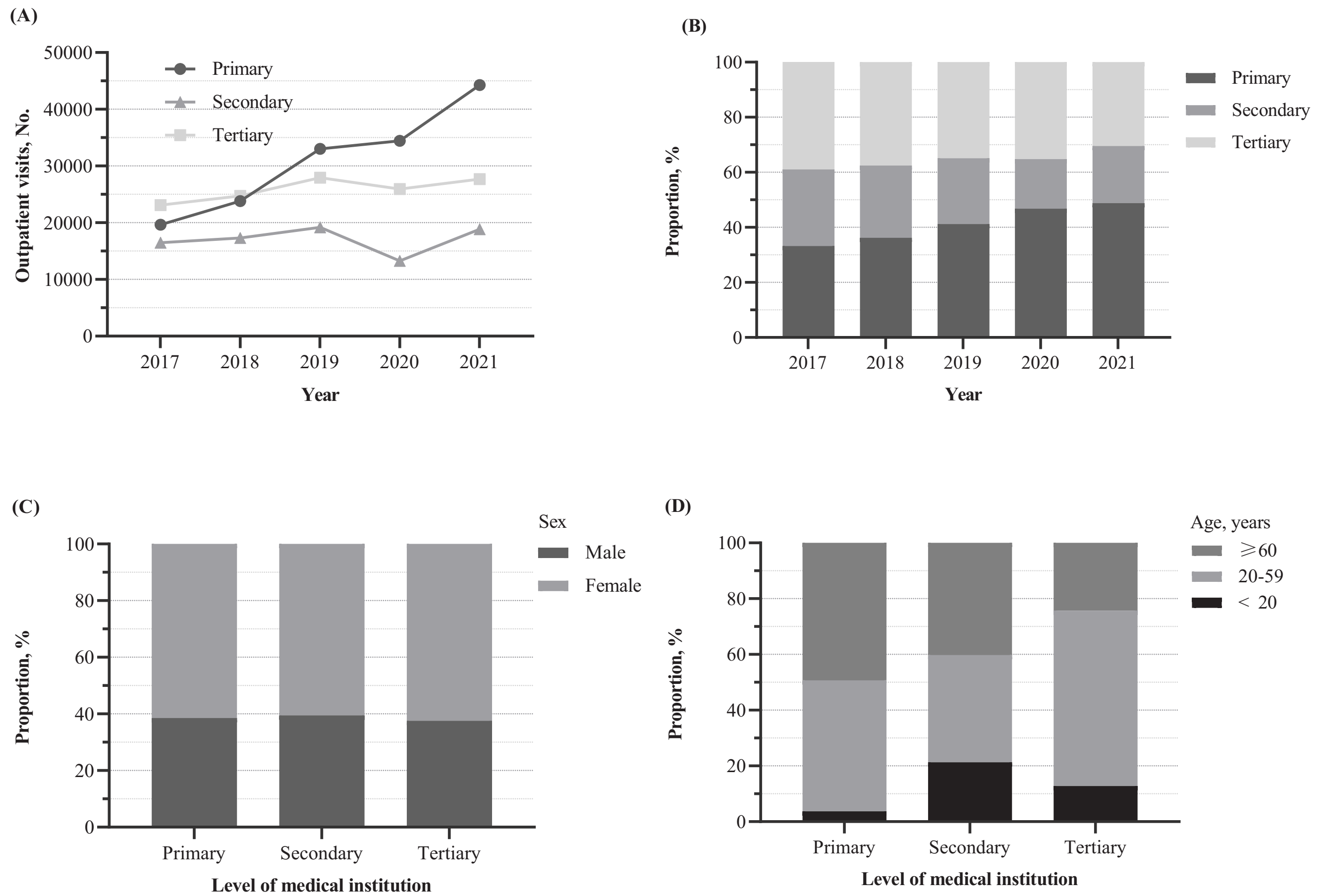

Figure 3. Distribution of outpatient visits for DED at different levels of medical institutions. The number (**A**) and proportion (**B**) of outpatient visits at the different levels of medical institutions by year are shown, in addition to the sex (**C**) and age (**D**) distributions of the outpatient visits.

medical resource allocations. Of note, the number of DED outpatient visits plummeted from January to March 2020, when Zhejiang Province launched its first-level response to major public health emergencies. The decline may be attributable to the cessation of many eye outpatient clinics at the time. Our modeling that adjusted for such an interruption showed a consistent trend based on pre- and post-COVID data.

Sex is a major risk factor for DED.[2] In this study, the number of female patients was around 1.5 times that of male patients, which was consistent with the sex ratios reported in most larger epidemiological studies in Asian countries.[15–19] Sex differences, such as more severe symptoms in females, may affect treatment needs and healthcare-seeking behavior among patients.[20,21] Age is another risk factor for DED,[2] but only a few epidemiological studies have reported the results of all age groups. Consistent with previous studies,[22–25] our study also found that the number of patients increased with age, reaching a peak between 60 and 69 years. In addition, the median age of patients with DED showed an increasing trend over time. There is a great demand for more medical services and products that cater to female and senior patients.

Surprisingly, we found that nearly half of the patients with DED visited primary medical institutions, and this proportion increased year by year. We also found that elderly patients were more common in primary medical institutions (vs. secondary or tertiary). Gabrani et al.[26] found that people 60 years or older were more likely to use primary healthcare services to initiate care when facing health problems, compared to those 18 to 59 years of age (56% vs. 49%; $P < 0.001$). However, primary medical institutions often lack ophthalmic professionals and examination equipment.[27,28] Thus, it is of great importance to strengthen the provision and quality of primary eye care in an aging society.

Summer and winter are regarded as two seasons with a high incidence of DED. In a large community-based study in Hangzhou, China, Yu et al.[29] reported a significant predominance of DED cases in summer

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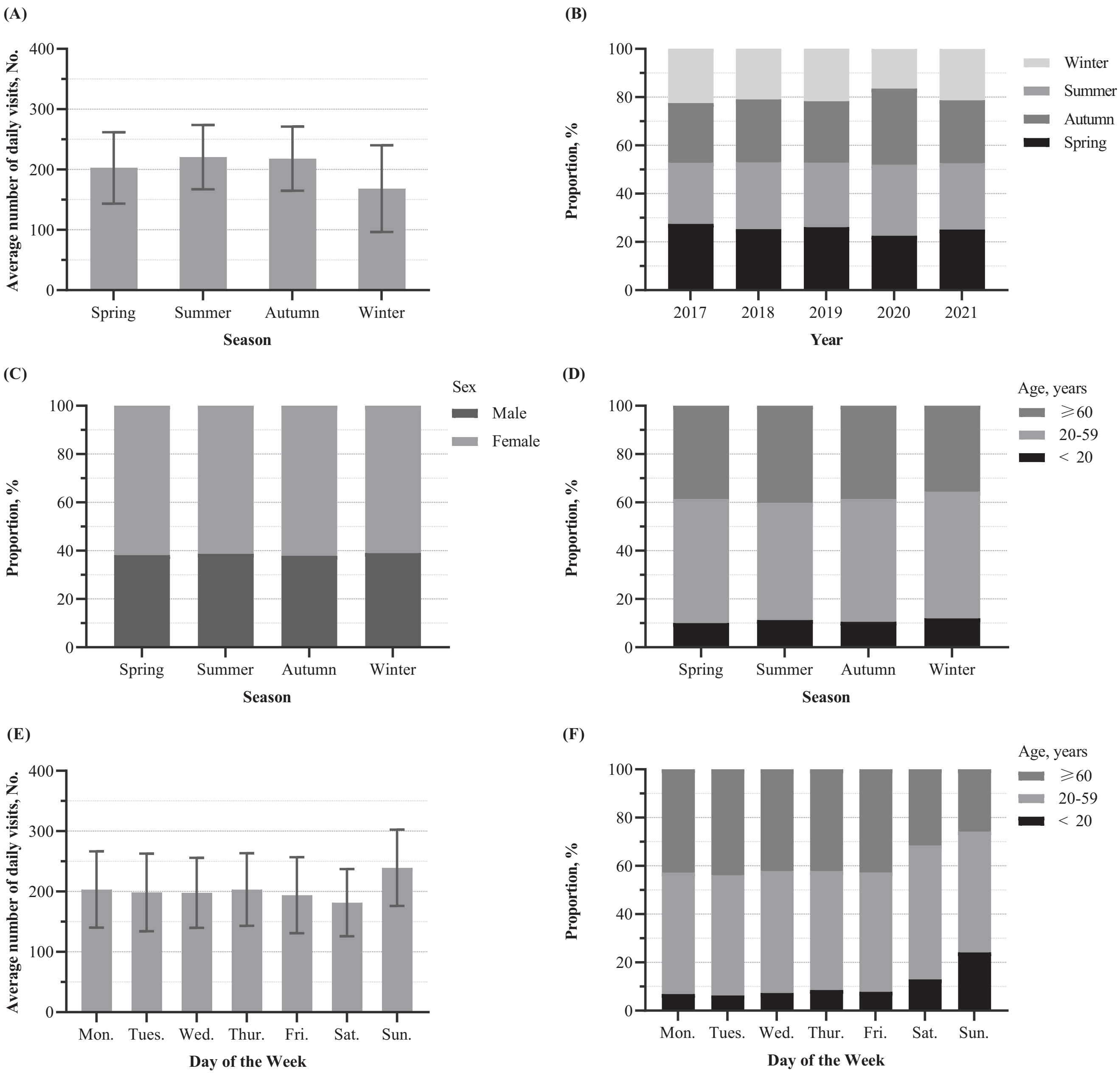

Figure 4. Distribution of outpatient visits for DED in different seasons and on different days of the week. (**A**) Average number of daily outpatient visits (mean ± SD) in different seasons. (**B**) Seasonal distribution of outpatient visits by year. (**C**, **D**) Sex (**C**) and age (**D**) distributions of outpatient visits in different seasons. (**E**) Average number of outpatient visits (mean ± SD) on different days of the week. (**F**) Age distribution of outpatient visits on different days of the week.

(62.8%) followed by winter (23.1%). Similarly, van Setten et al.[30] found that both summer and winter had the greatest impact on DED, with 51% and 43% of patients, respectively, experiencing symptoms during these seasons. Sunlight and heat in the summer were likely to increase dry eye discomfort, as reported by 60% and 42% of patients, respectively.[30] Another factor contributing to the high prevalence in summer may be the increased amount of time people spend in air-conditioned environments. Our results on summer were consistent with these studies. Winter, on the other hand, is characterized by relatively cold temperatures and low humidity, which are unfavorable for the normal function of meibomian gland and stability of tears,[31,32] leading to a higher incidence of DED. Contrary to previous studies,[29,30] our study found that the number of outpatient visits was lowest in winter. In addition, seasonal variations in our study (summer, 27.44%; winter, 20.52%) were not as large as those previously reported.[29,30] These differences in study results may be attributable to differences in study locations. Our study was conducted in coastal Yinzhou District, which has a subtropical monsoon and marine climate, with generally abundant rainfall throughout the year and less extreme weather. Thus, DED may not be as severe a problem in winter as compared to colder and drier places.

A study from Zhongshan Ophthalmic Center reported a Monday peak in outpatient visits and significantly higher outpatient visits on weekdays than that on weekends (2507.9 ± 791.9 vs. 942.8 ± 293.3 visits per day, respectively; $P < 0.001$).[33] In contrast, our study showed that more patients visited on Sunday, with a higher proportion of patients being under 60 years. This phenomenon may be due to people in the working age group being preoccupied with work or study on weekdays and choosing to seek medical care on weekends when possible. Of note, non-emergency outpatient care in Ningbo remains available on weekends and holidays, making it one of most patient-friendly cities in China.

Our study has several limitations. First, we relied exclusively on the ICD-10 code for identification of DED, but the diagnosis of DED in primary-level medical institutions may not be as rigorous as in higher-level facilities. Nevertheless, the increasing use of primary care by patients with DED that we observed is noteworthy and warrants future verification and action by local governments to strengthen the quality of primary eye care if confirmed. Second, our study utilized data from a district in Ningbo, thereby limiting its generalizability to other districts or cities. Nonetheless, our study pioneers the use of regional real-world data to examine DED outpatient service use, and the amount of data available on DED in the YHIS is much larger than that for traditional epidemiological or clinical-based studies. As more high-quality, real-world data become available in the future, we call for future research from other areas to examine this important issue. Finally, we were not able to include analyses on medical costs or other important patient-level factors, such as education or income, due to lack of data or resources. We hope that such analyses will be possible in the future.

In conclusion, our study showed a significant increase in DED outpatient health service use. Both the proportion and the increase were higher for females (vs. males), people 50 years or older (vs. <50 years), and primary medical institutions (vs. secondary or tertiary). Our results suggest potential areas for improvement in the allocation of healthcare resources, such as strengthening primary health services and building female- and elderly-friendly care models. We call for the further development of real-world data, as well as future research making full use of the vast amounts of data obtained, to improve the quality of clinical care, policy-making, and population health.

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