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Secular Trends in the Incidence of Migraine in China From 1990 to 2019: a Joinpoint and Age-period-cohort Analysis

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Secular trends in the incidence of migraine in China from 1990 to 2019: A joinpoint and age–period–cohort analysis

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Abstract

Background

Migraine is a common disorder of the nervous system in China, imposing heavy burdens on individuals and societies. Optimal healthcare planning requires understanding the magnitude and changing trend of migraine incidence in China. However, the secular trend of migraine incidence in China remains unclear.

Methods

Data were collected from the Global Burden of Disease Study 2019 in China from 1990 to 2019 to investigate changes in the incidence rate of migraine. The average annual percent change and relative risk were calculated using joinpoint regression and an age–period–cohort model, respectively.

Results

From 1990 to 2019, the age-standardized incidence rates of migraine in China increased by 0.26% (95% CI: 0.22 to 0.31) and 0.23% (95% CI: 0.19 to 0.28) per year in males and females, respectively. The age effect exerted the most significant impact on the incidence of migraine. The period effect showed a slightly decreasing trend in the incidence of migraine. In terms of the cohort effect, people born after the 1960s presented a higher risk of migraine as compared with the total cohort, with the occurrence risk of migraine increasing with birth cohorts.

Conclusion

Migraine incidence shows an overall increasing trend in China, with a significant gender difference. An intensive understanding of the risk characteristics and disease pattern of migraine could allow the early detection of persons with a high risk of developing migraine and promote the development of timely intervention measures to relieve this burden effectively.

Keywords: migraine, incidence, joinpoint regression analysis, age–period–cohort model, secular trend

Introduction

Migraine is a common neurovascular disorder primarily characterized by prolonged headache disorders, with moderate-to-severe pain and connected clinical symptoms, such as sensitivity to light and sound, nausea, and vomiting [1]. Migraine is the second cause of years lived with disability in 2016 in the world, and people living with migraine are immensely influenced by this burden [2]. A study with a large population-based nationwide sample indicated an above 2.4% incidence rate of migraine in Turkey [3]. In China, migraine is also connected with public health. With a population of over 1.3 billion, 20% of the total in the planet, China may have the largest migraine population worldwide [4]. Improving the epidemiological understanding of migraine is the basic requirement to promote the diagnosis and treatment of migraine and the rational allocation of health care resources. Thus, the incidence of migraine and its possible changes could afford assistance to illustrate the risk factors of developing the disease.

At present, studies on migraine involved small sample size, limited localities, and high rates of underdiagnosis and misdiagnosis [5]. Moreover, migraine burden is easily ignored probably because this disease is nonfatal. The long-term changes in migraine incidence are difficult to obtain because migraine is multifaceted and fragmented. The Global Burden of Disease Study (GBD) 2019 employed a normative approach to assess the disease burden of migraine by age, sex, year, and location. GBD data can produce abundant information and up-to-date estimates of migraine burden at the global, regional, and national levels [6,7].

Migraine incidence estimates may be affected by age, sex, race, geography, and socioeconomic status. Age–period–cohort models have an excellent advantage in evaluating the age, period, and cohort effects on the disease burden. Age effects exhibit a various risk of the outcome associated with different age brackets. Time period effects express impacts of an intricate combination of historical events and environmental factors. Moreover, birth cohort effects represent the influence of physical and social exposure that appear earlier in life process and accumulate as time progresses [8]. Age–period–cohort models might provide researchers with significant information to evaluate the pathogenesis of migraine. In this paper, we sought to analyze the secular trend of the incidence of migraine from 1990 to 2019 in China.

Materials and methods

Data source

The GBD study in 2019 integrated literature research, monitoring and investigation information, inpatient and outpatient data, medical insurance situation, and other information to evaluate the incidence, prevalence, mortality, and disability adjusted life years of 369 diseases, injuries, and 87 risk factors in 204 countries and regions from 1990 to 2019. Details of the 2019 GBD data, statistical modeling, and metrics have been reported in previous studies [9-11]. Our studies about secular trends in the incidence of migraine were based on the GBD 2019 data in China. In GBD 2019, migraine was defined according to the International Classification of Headache Disorders. Migraine is a primary headache disorder, typically characterized by recurrent moderate or severe unilateral pulsatile headache disorders. Migraine with and without aura in GBD studies has no distinction because most epidemiological studies only report migraine as a whole. In GBD, the incidence rate is an important indicator of migraine burden. We used the incidence rate as a measurement standard to analyze the impact of the disease burden on the population comprehensively. Age-standardized incidence rates were obtained by quantified secular trends in migraine incidence.

Joinpoint regression analysis

Analysis of the long-term trend is crucial to the comprehension of disease incidence. Joinpoint Regression Program 4.5.0.1 was used for joinpoint analysis, and a regression model was established to calculate the regression coefficient, annual percent change (APC), average annual percent change (AAPC), and the corresponding 95% confidence intervals (95% CIs) and to conduct a comparative analysis of trend change [12,13]. The basic idea of joinpoint analysis is described to divide a secular trend line into some statistically significant trend sections by model fitting, and each section is described by continuous linear expression.

Age–period–cohort analysis

Age–period–cohort models are commonly used to analyze and estimate the net age, period (year of survey), and cohort (year of birth) effects on incidence trends [14,15]. These models were developed based on Poisson distribution. They require an equal time interval in age, period, and cohort. Otherwise, information in the adjacent queues will overlap. In the GBD 2019 database, the incidence of migraine was not recorded for persons aged under 5 years, and the population after 95 years of age was summarized as one group. The occurrence of migraine in this age group is rare and its age grouping dose not satisfy the data format of the age–period–cohort model. Thus, this age group was excluded in this study. Data for migraine were organized by 5-year periods from 1990 to 2019, 5-year age groups from 5 to 95, and correspondingly consecutive 5-year birth cohort groups starting from 1900–1904 to 2015–2019 in this study. The independent effects of age, period, and birth cohort on disease are difficult to estimate [16, 17]. Therefore, we used the relative ratio (RR) representation to estimate the aggregate effects of age, period, and birth cohort. All analyses and graphics were carried out using STATA 15.0 software (StataCorp, College Station, TX, USA).

Results

Descriptive analysis

Our study indicated that the sex-specific age-standardized incidence rates of migraine maintained an increment from 1990 to 2019. For migraine, the annual age-standardized incidence rates in males were significantly lower than in those in females. The incidence rates of migraine due to age group in China in 2019 are shown in Table 1 and are present in Figure 1. In 2019, the age-standardized incidence rates of migraine in China were 697.27 (95% UI: 608.73 to 787.11) per 100,000 persons in males and 1247.58 (95% UI: 1100.46 to 1400.14) per 100,000 persons in females. The top incidence rates of migraine were surveyed in the 10–14 age group, followed by the 22–44 age group in both sexes. From 1990 to 2019, trends in the sex-specific age-standardized incidence rates of migraine in China are described in Table 1.

Joinpoint regression analysis

From 1990 to 2019, the AAPCs of age–sex-specific rates in migraine are shown in Table 1. The age-standardized incidence rates of migraine from 1990 to 2019 increased by 0.26% (95% CI: 0.22 to 0.31) in males and 0.23% (95% CI: 0.19 to 0.28) in females (Figure 2). Regardless of age groups, remarkable increments in sex-specific incidence rates were also shown in migraine. Joinpoint regression analysis showed that the age-standardized incidence rates of migraine slightly decreased in males (APC = -0.12%, 95% CI: -0.16 to -0.08) and females (APC = -0.09%, 95% CI: -0.12 to -0.05) from 1990 to 2001. However, continuously increasing trends of migraine incidence in China were observed from 2001 to 2019. The joinpoint regression results of sex-specific rates for migraine are presented in Supplementary Table 1.

Age–period–cohort analysis

Using age–period–cohort analysis, we calculated the RRs of migraine incidence about net age, period, and cohort effects (Table 2). With the period and cohort effects remained unchanged, the highest RRs of migraine incidence due to age effects were presented in the 10–14 age group with 1.99 (95% CI: 1.93 to 2.05) in males and 1.98 (95% CI:1.93 to 2.03) in females (Figure 3a), followed by the 25–44 age group, and then decreased starting at the 45 age group in both sexes. The RRs of migraine incidence due to period effects indicated a mild decrease from 1.08 (95% CI: 1.06 to 1.10) in 1994 to 0.93 (95% CI: 0.91 to 0.95) in 2019 for males and from 1.08 (95% CI: 1.06 to 1.09) in 1994 to 0.93 (95%CI: 0.92 to 0.95) in 2019 for females (Figure 3b). The RRs of migraine incidence for birth cohort effects continuously increased from 0.66 (95% CI: 0.54 to 0.81) in the 1900–1904 cohort to 1.65 (95% CI: 1.52 to 1.80) in the 2010–2014 cohort for males and from 0.66 (95% CI: 0.55 to 0.78) in the 1900–1904 cohort to 1.61 (95% CI: 1.51 to 1.71) in the 2010–2014 cohort for females (Figure 3c).

Discussion

Prior to this study, no researchers used the age–period–cohort model to explore the secular trends of migraine incidence in China from 1990 and 2019. The burden of migraine is differential with respect to sex and is more common in females than in males [18]. Our study indicated that the evaluation rate of migraine incidence in China is higher in females than in males. Aside from incidence, migraine attacks are more severe in females, leading to greater disability and a longer recovery period than males did [19]. Although the reason for this sex difference in the incidence of migraine is complicated and intricate due to variations in research methodology, females and males undergo pain differently [20]. Females have greater sensitivity to harmful stimuli, higher pain ratings, lower pain thresholds, and tolerance than males. Thus, females are more likely to report pain than males [20]. Moreover, sex difference in migraine incidence may be partly attributable to a combination of psychological, physical, and lifestyle factors [21]. In China, females are more likely to bear a higher psychological and physical burdens than males. For example, females have a higher lifetime risk of mental disorders (e.g., depression and anxiety) than males. These mental disorders are remarkably correlated with an increasing risk of migraine [21]. Concerning the physiological factors, females face special periods, such as puberty and menarche, menstruation, pregnancy, and menopause during their lifetime. The incidence of migraine could be affected by hormonal fluctuations during these women-specific biological periods [23-25]. Lifestyle factors also play a momentous role in migraine. For instance, dietary sodium intake is significantly associated with migraine incidence in females but not in males [26].

The trend of migraine incidence varies with different studies. A large longitudinal study in Germany found no general increase in self-reported migraine incidence over a 15-year period [27]. Another study in Turkey showed above 2.38% increment in migraine incidence during the observation period [3]. Results of joinpoint regression indicated that the incidence rates of migraine increase from 1990 to 2019 in China, regardless of sex and age group. Migraine is associated with a variety of chronic diseases, such as depression or anxiety disorders [28] and epilepsy [29]. Thus, the increasing trend of migraine burden should be paid attention. Clinicians play a crucial role in protecting migraine patients from risk factors. Thus, they must understand modifiable risk factors and migraine progression. Although our understanding of migraine has vastly improved, the epidemiological information for migraine in China is still lacking. Therefore, further study among migraine patients is warranted to understand the true burden of migraine in

China.

According to the age–period–cohort analysis, age effect is a crucial factor for migraine. Our study deemed that males and females aged 10–14 years had the highest RRs of migraine, followed by the 20–44 age group. A study indicated that above 58% of children and adolescents are reported with headache disorders, and 5%–11% of the adolescent population are reported with migraine [30]. Middle-school children are considered high-risk populations for migraine. The way a student exhibits a migraine may be related to many factors, such as genetics, medications, hormones, stress, diet, and dehydration [31]. China requires a 9-year compulsory education, in which junior high school is the most important stage, and then students face an increasing number of courses, exams, and peer competition [32]. These adolescents and students suffering from stress correlate with physical changes, further education, along with mental immaturity, fear of failing in school, fear of peers or teachers, and numerous negative emotions, which increase the risk of migraine. Migraine can cause school problems, behavioral problems, and depression, which substantially impact health and school-related activities, family participation, sport and social activities, and quality of life [33]. Compared with the 10–14 age group, migraine in the 20–44 age group can manifest in ways that are markedly different. Study has indicated that factors that become insignificant with age are consumption alcohol, smoking and neck pain [34]. However, the frequency of variables such as stress as a trigger, pressure, stabbing, and throbbing increases during migraine [35]. In consideration of the higher impact of such conditions among young and adult, we suggest that parents, schools, and societies pay attention to children's mental health and reduce their academic burden appropriately. For adults, a healthy lifestyle should be adopted.

Concerning the birth cohort effect, we revealed that people born after the 1960s had a noteworthy higher risk of migraine (RRs > 1) compared with the whole birth cohort. China experienced the Great Leap Forward Famine in 1959–1961, which was evaluated to be the worst famine in human history, with more than 15–43 million deaths [36]. Evidence suggests a link between early life exposure to famine and adult physical and psychological health, and famine is partly responsible for the fleetly increasing burden of chronic disease in China [37]. Today, a crowd of older Chinese experienced famine at the same time in their early life. Early energy and nutritional deficiencies affect physical health, and people born in famine years are more likely to be overweight and suffer from metabolic syndrome than people born in other years [37]. Aside from nutrient deficiencies [38], conditions such as overweight [39] and metabolic syndrome [40] have also been linked to migraine. Over the past 40 years of reform and opening up, The Chinese economic has acquired conspicuous performances, but the problem of environmental pollution is increasingly serious. According to statistics, the burden of disease due to environmental pollution in China accounts for approximately 21% of the total burden of disease and causes huge economic loss [41]. Air pollution is a potential risk factor among patients with migraine. An association has been established between exposure to high levels of air pollution and an increment in the number of outpatient and inpatient visits due to migraine [42]. Until now, a crowd of risk factors has been connected with the onset of migraine. Considering environmental factors, a high level of electromagnetic radiation exposure predicts a high risk of migraine. In the recent decade, with the popularization of intelligent devices such as computers and mobile phones, the harmful effects of electromagnetic radiation to human body have been a cause of concern. A growing body of research manifests a strong connection between excessive computer and mobile phone use and migraine [43]. In terms of lifestyle, the rapid pace of life in modern times has increased the

pressure of social competition, and sleep disorders and psychiatric disease are prevalent. Many people lack physical exercise, leading to obesity. In addition, high consumption of caffeine or alcohol, regular smoking, and frequent use of abortive migraine drugs have been linked to migraine [44,45]. Single-center studies based on small samples have several limitations. Hence, further research is needed to verify the mechanisms of these risk factors.

Risks of migraine persistently decline for all populations in period effects. On the one hand, the decreasing trend of migraine has been attributed to improved treatment of migraine [46]. Physical and behavioral therapy, acupuncture, massage, and physical exercise may be used as effective methods to treat migraine. Acupuncture is a new form used to accomplish a therapeutic effect. It also was used to treat numerous diseases, especially headache disorders and migraine. Another study found that acupuncture could play a momentous function in alleviating pain for persons with migraine [47]. In addition, with the improvement of China's medical insurance system, many people have better access to health care, and through effective health education and other intervention measures, more and more people no longer ignore migraine and voluntarily seek treatment, thus reducing the frequency and duration of migraine attacks [2].

Despite the GBD evaluates filled in the gap in the general population of China, numerous limitations still consist in GBD 2019. First, the estimates from GBD may be inconsistent with the actual data because of the lack of epidemiological survey data in China and the large heterogeneity among studies. Although GBD collected as much published and unpublished data as it can, the quantity and quality of data on migraine remain limited, which may impact the accuracy of the estimated burden. Second, even though the methods used in this study are characterized by unbiased, effective, asymptotic, and superior estimation, the theoretical basis is complex and the practical significance of parameter estimation cannot be explained. Third, the GBD 2019 database only provided the migraine incidence rate and lacked a crowd of risk factors that are closely related to migraine, such as lifestyle, living environment, and educational level. Finally, age–period–cohort analysis might lead to ecological fallacies. Hence, based on available information and resource, a scientific hypothesis about the causal relationship of temporal trends has been supported.

Conclusion

Migraine incidence showed an overall increasing trend from 1990 to 2019 in China. A significant gender difference was found in migraine incidence, which is higher in females than in males. The risk was the highest among adolescents and youths, suggesting that age is a crucial factor in migraine incidence. The period effect showed that the risk of migraine continued to decrease over time. Concerning the cohort effect, people born after the 1960s presented a higher risk of migraine as compared with the whole cohort. The risk characteristics and disease patterns of migraine warrant further investigation to provide early diagnosis, timely interventions, and burden reduction for migraine sufferers.

Conflicts of interest

The authors have indicated that they have no conflicts of interest about the content of this article.

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Figures

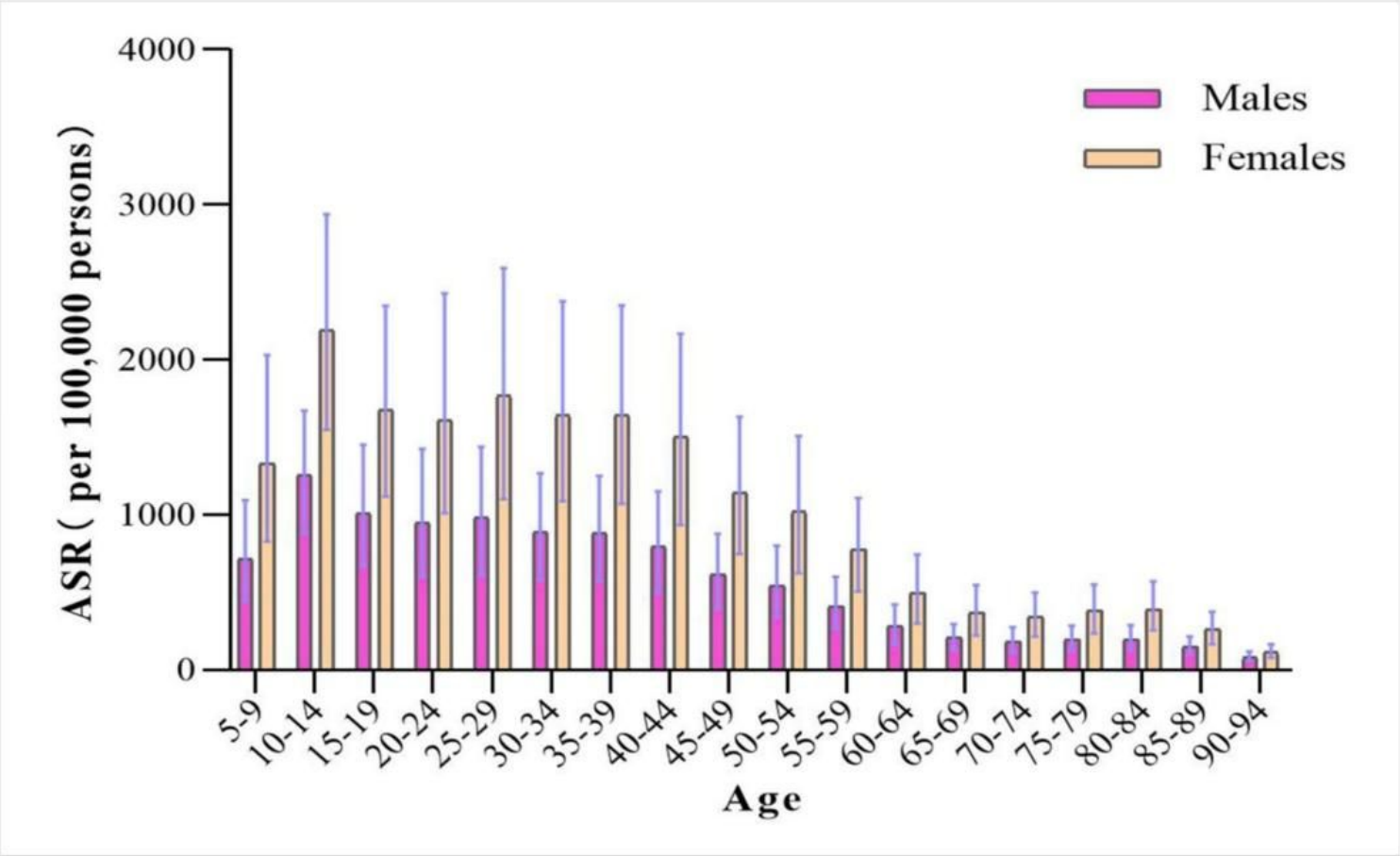

Figure 1

Age-sex-specific rates of migraine in China in 2019.

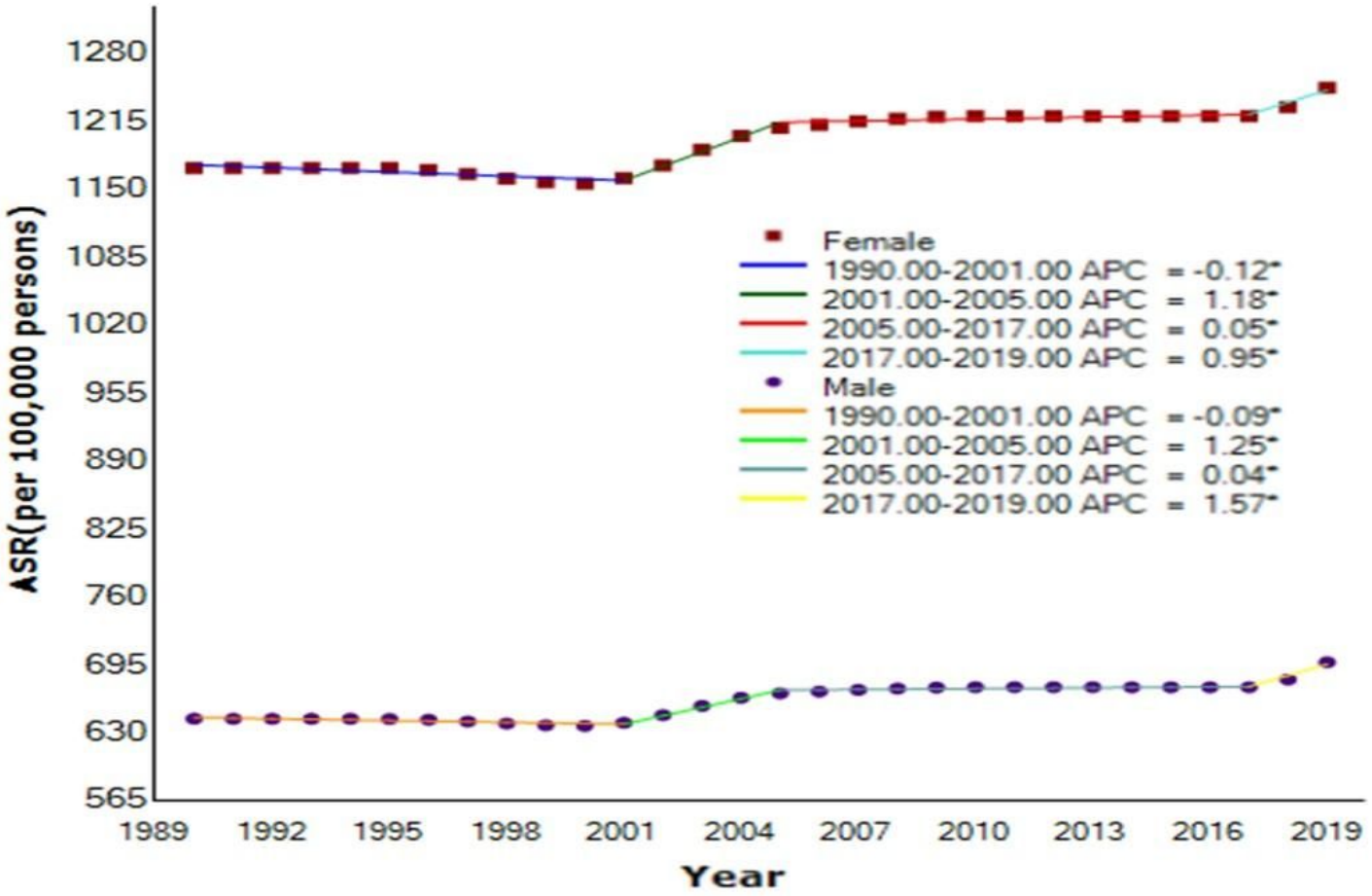

Figure 2

Joinpoint regression analysis in sex-specific age-standardized incidence rates of migraine in China from 1990 to 2019. Notes: an asterisk indicates that the annual percent change is statistically significantly different from zero at the α= 0.05 level.

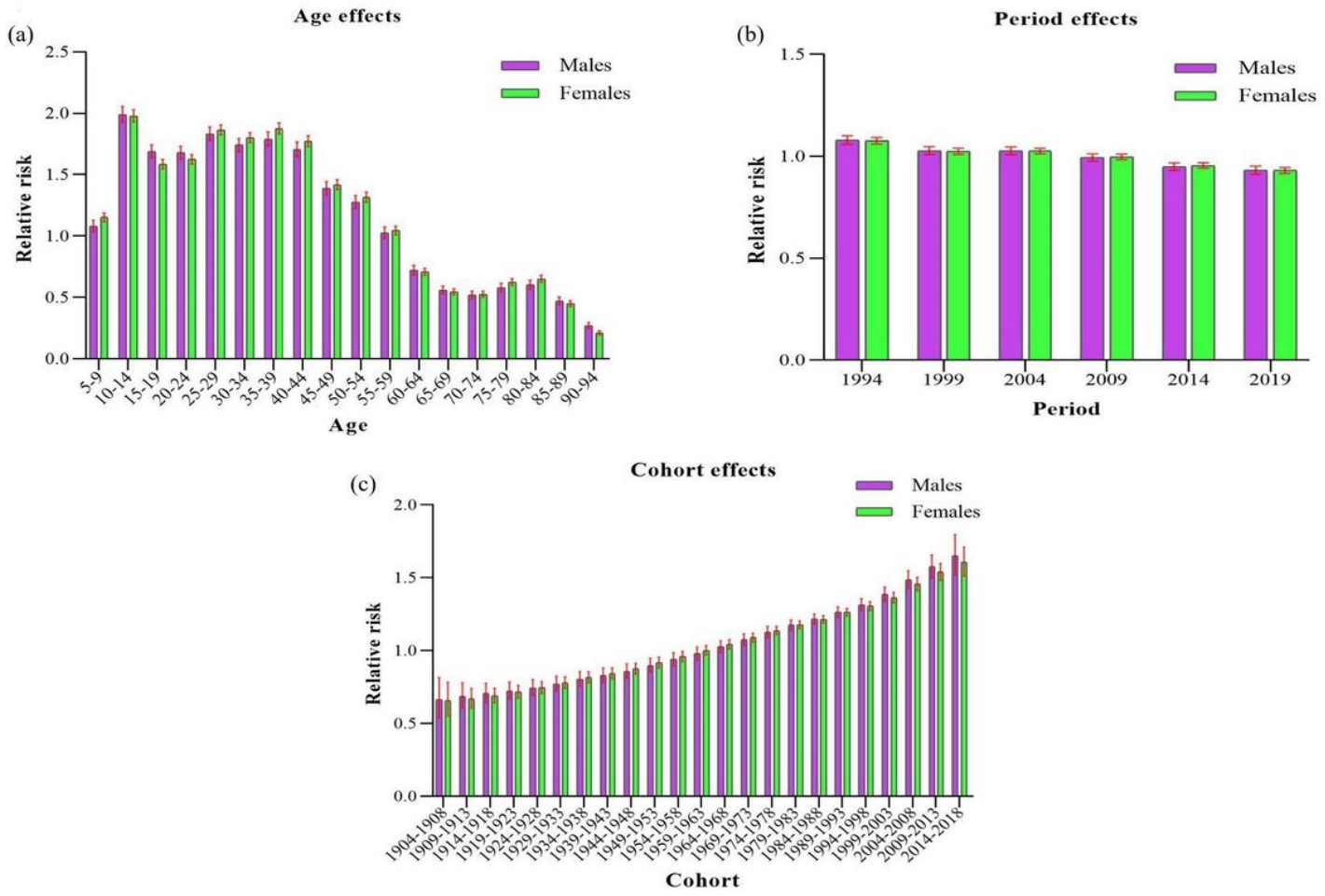

Figure 3

Relative risks of migraine in China from 1990 to 2019 due to age (a), period(b), and cohort (c) effects.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table.pdf
- Supplementtable1.pdf