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Background

Heatstroke, the most severe form of heat-related illness, is characterized by an elevated core body temperature and central nervous system dysfunction [1]. As climate change increases the frequency and intensity of heat waves, the global public health burden of heatstroke continues to rise [2,3]. Traditionally regarded as an acute medical emergency, heatstroke is primarily associated with damage to the cardiovascular [4], neurological [5], renal [6] and hepatic systems [7], as well as increased mortality [1]. However, its potential long-term neurological consequences, particularly in relation to primary headache disorders, remain poorly understood.

Among these disorders, migraine, one of the most prevalent recurrent headache disorders worldwide [8,9], substantially reduces quality of life and productivity [10,11]. The aim of this study was to investigate the association between heatstroke and subsequent migraine development.

Methods

This retrospective cohort study used data from the Disease Analyzer database (IQVIA) and included individuals diagnosed with heatstroke, as well as propensity score-matched individuals without heatstroke. Data about these individuals was recorded in 1,216 general practices in Germany between January 2005 and December 2023. Patients with heatstroke were matched and compared with those without the condition to examine the incidence of migraine.

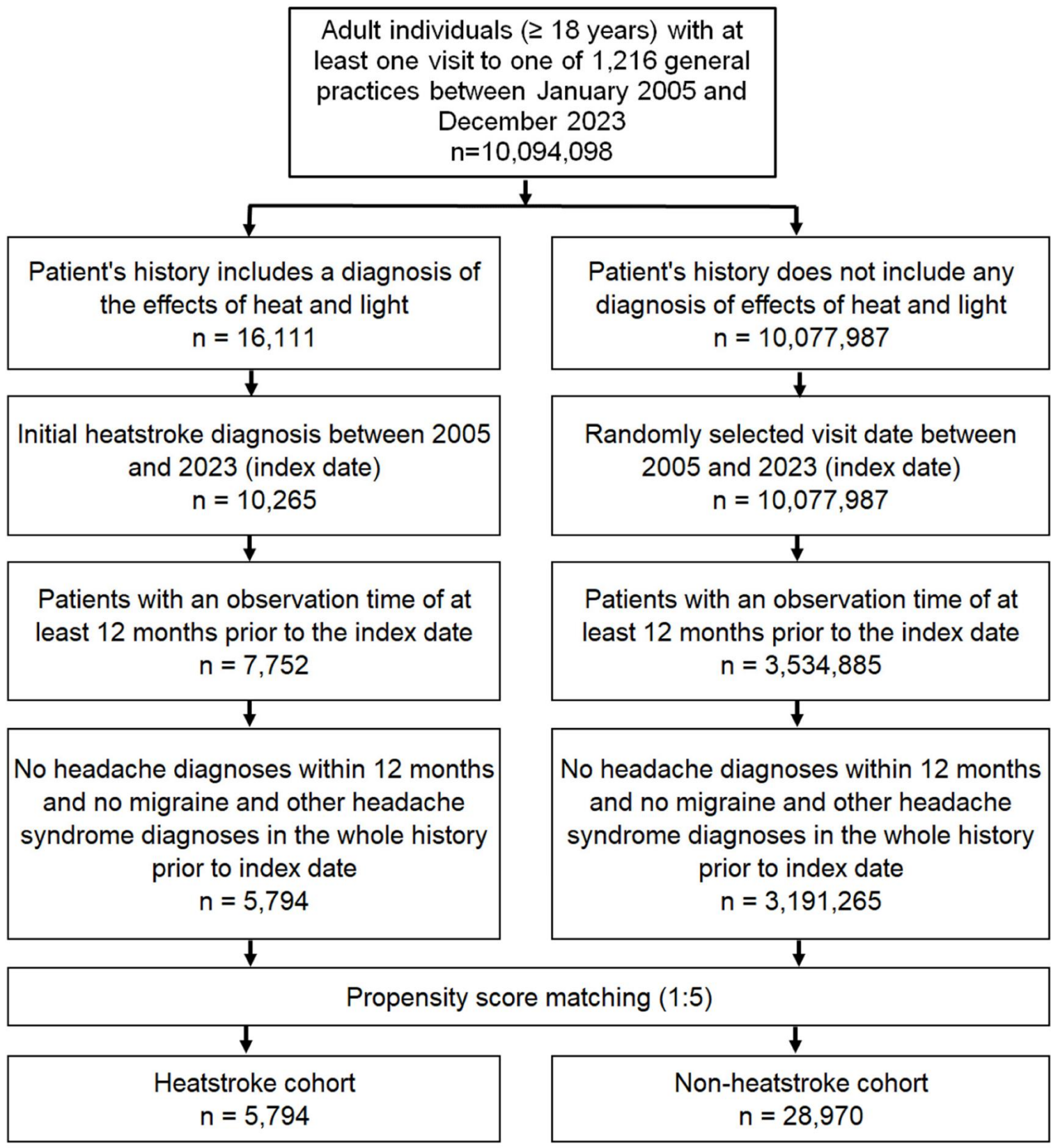


Figure 1. Selection of study patients

- Analysis of 5-year cumulative migraine incidence: Kaplan-Meier curves
- Association between heatstroke and migraine diagnosis: univariable Cox regression (Hazard Ratios, with 95% confidence intervals)
- P-value of <0.05 was considered statistically significant

Key Findings

The study included 5,794 individuals with heatstroke and 28,970 matched controls without heatstroke. Basic characteristics of included patients are displayed in Table 1.

Most heatstroke cases were documented in June (32–34%), followed by July (30%), August (15–17%), and May (13%). Within five years of follow-up, 8.8% of patients with heatstroke and 4.0% of controls were diagnosed with migraine. The regression analysis revealed that heatstroke was significantly associated with an increased risk of migraine in the total population (HR: 2.26; 95% CI: 2.00–2.57), as well as in women (HR: 2.33; 95% CI: 1.96–2.79) and men (HR: 2.26; 95% CI: 1.89–2.70). In analyses restricted to more specific migraine diagnoses, heatstroke remained significantly associated with migraine with aura (HR 3.03; 95% CI: 1.85–4.96) and migraine without aura.

Conclusion

Clinical Implications: This study highlights an important, yet previously underrecognized, association between heatstroke and an increased risk of migraine. As global temperatures continue to rise, public health strategies should focus not only on the acute prevention and management of heat-related illnesses, but also on their potential long-term neurological consequences.

Study Limitations: The study's limitations include a potential for misclassification bias as it relies on routinely collected outpatient data. Since heatstroke is a severe, acute condition, many diagnoses may reflect encounters after hospitalization rather than the acute phase itself. Furthermore, as heatstroke is associated with mortality, many patients captured in outpatient records may have experienced milder cases. Information on the severity of heatstroke and hospitalization status was unavailable.

Future Directions: Further research is required to explore the underlying reasons for the observed associations.

References:
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Results

Table 1. Baseline characteristics of the study sample, N (%) after 1:5 propensity score matching

Variable	Patients with Heatstroke (N=5,794)	Patients without Heatstroke (N=28,970)	SMD
Age in years			
Mean (IQR)	30 (22-45)	30 (22-44)	0.003
18 - 22	1,501 (25.9)	7,354 (25.4)	
23 - 30	1,460 (25.2)	7,385 (25.5)	
31 - 45	1,466 (25.3)	7,485 (25.8)	
> 45	1,367 (23.6)	6,746 (23.3)	
Sex			
Female	1,818 (31.4)	9,198 (31.7)	-0.004
Male	3,976 (68.6)	19,772 (68.3)	
Year of study inclusion			
2005-2008	262 (4.5)	1,473 (5.1)	0.001
2009-2012	507 (8.8)	2,487 (8.6)	
2013-2016	1,020 (17.6)	4,995 (17.2)	
2017-2020	1,987 (34.3)	9,651 (33.3)	
2021-2023	2,018 (34.8)	10,364 (35.8)	
Month of diagnosis			
May	756 (13.0)	3,658 (12.6)	-0.017
June	1,994 (34.4)	9,394 (32.4)	
July	1,742 (30.1)	8,612 (29.7)	
August	852 (14.7)	4,972 (17.2)	
Other months	450 (7.8)	2,334 (8.1)	
Comorbidities			
Diabetes mellitus	285 (4.9)	1,302 (4.5)	-0.004
Hypertension	1,030 (17.8)	4,912 (17.0)	-0.008
Sleeping disorders	609 (10.5)	2,888 (10.0)	-0.005
Depression	889 (15.3)	4,277 (14.8)	-0.006
Reaction to severe stress	896 (15.5)	4,289 (14.8)	-0.007
Alcohol addiction	184 (3.1)	768 (2.6)	-0.005

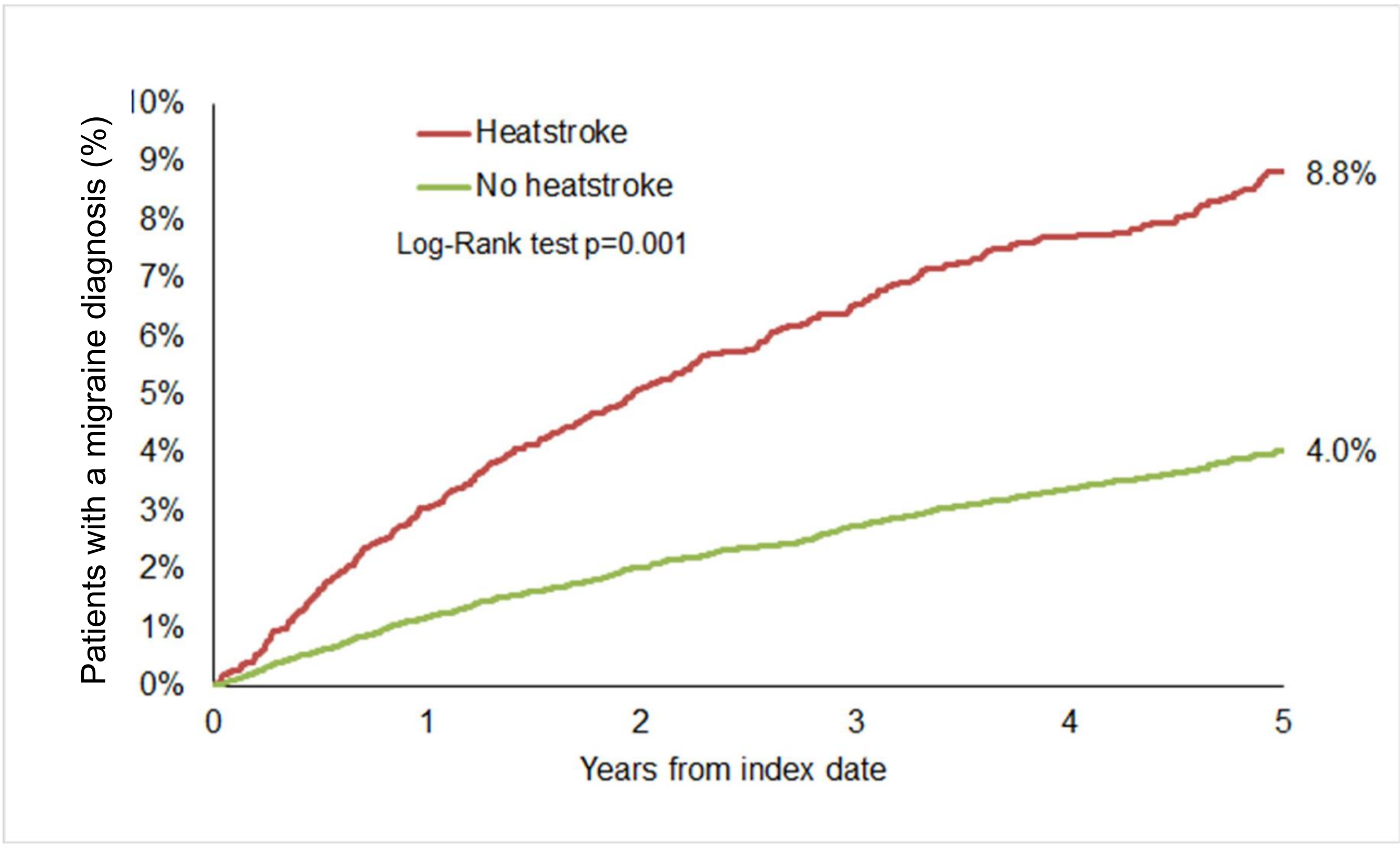


Figure 2. Cumulative incidence of migraine in patients with and without heatstroke

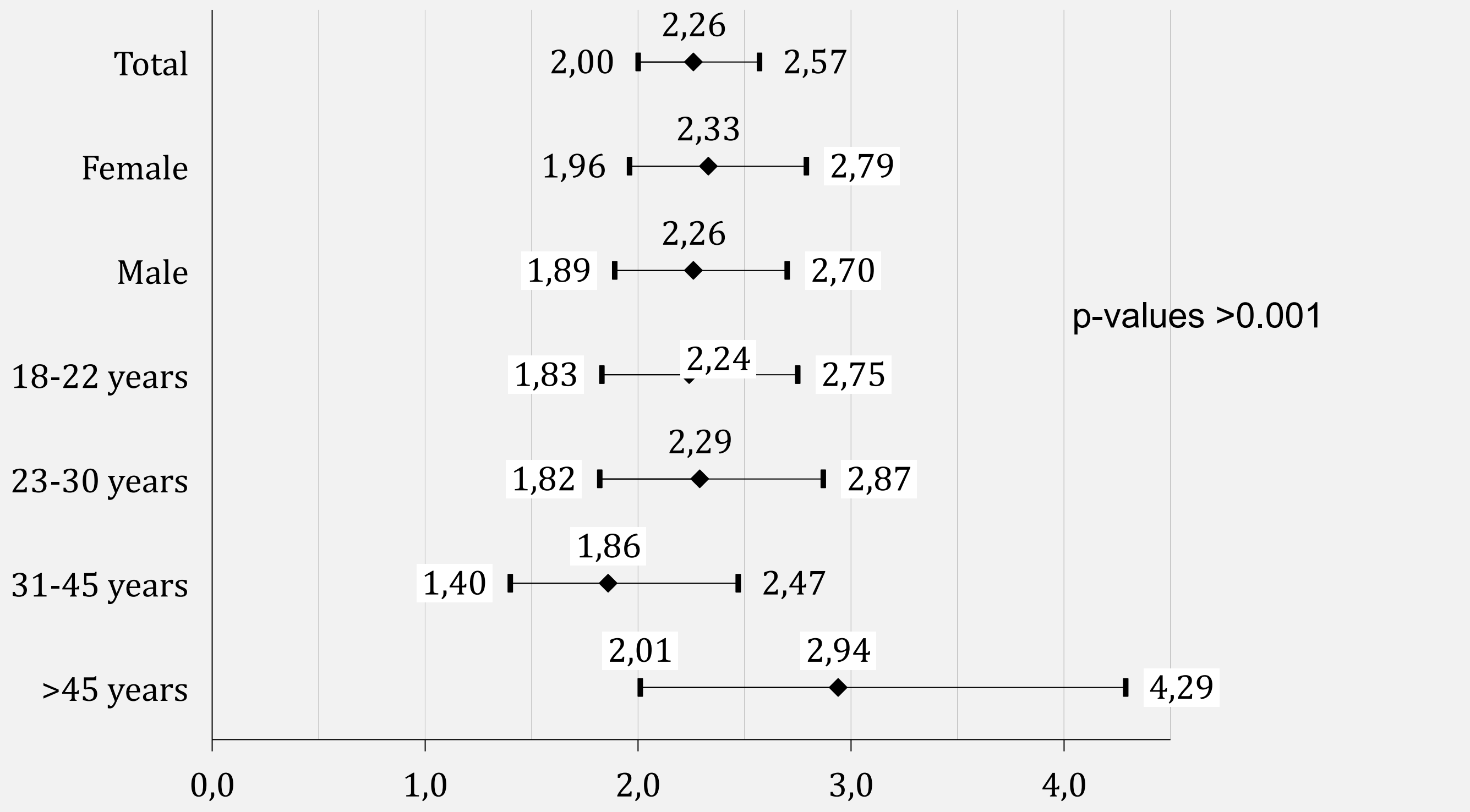


Figure 3. Association between heatstroke and subsequent migraine diagnosis (Hazard Ratios with Confidence Intervals) in patients followed in general practices in Germany