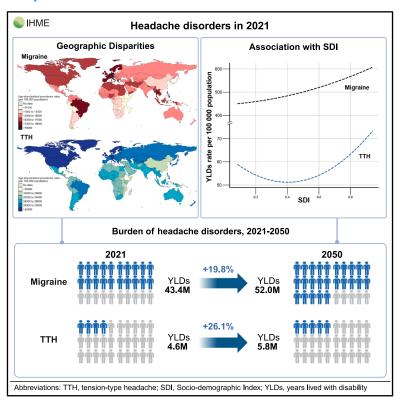
# Global, regional, and national burden of headache disorders, 1990–2021, with forecasts to 2050: A Global Burden of Disease study 2021

#### **Graphical abstract**



- Tension-type headache is more common than migraine in 2021
- Migraine contributes to a more disabling burden than tension-type headaches in 2021
- Headache burden is projected to remain age standardized and stable through 2050
- Females aged 30–44 years experience a disproportionately higher burden in 2021

#### **Authors**

GBD 2021 Headache Collaborators, Tissa Wijeratne, Jiyeon Oh, ..., Tae-Jin Song, Dong Keon Yon, Valery L. Feigin

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#### In brief

Using GBD 2021, Wijeratne et al. present updated global estimates and 2050 forecasts for migraine and tension-type headaches. Despite stable agestandardized rates, the burden remains high, especially among women aged 30–44 years, underscoring the need to prioritize headache disorders in global health policy and resource allocation.



**Highlights** 





**Article** 

# Global, regional, and national burden of headache disorders, 1990–2021, with forecasts to 2050: A Global Burden of Disease study 2021

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#### **SUMMARY**

Headache disorders, especially migraines and tension-type headaches (TTHs), are major global public health concerns, as shown by the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021. We provide updated global estimates of prevalence and years lived with disability (YLDs) from 1990 to 2021 across 204 countries and territories and forecasts through 2050. In 2021, there are 2.0 billion people with TTH and 1.2 billion with migraine. Although TTH is more prevalent, migraine causes higher disability. While crude prevalence and YLDs increased, age-standardized rates remained stable and are projected to continue this trend due to population growth. There is a disproportionately higher burden in women aged 30–44 and countries with higher Socio-demographic Index and Healthcare Access and Quality Index. Despite this, migraines remain underrecognized in health policies and funding. This study emphasizes the urgent need to prioritize headache disorders in global health agendas.

#### **INTRODUCTION**

Migraines and tension-type headaches (TTHs) are prevalent and disabling neurological disorders that contribute significantly to the global headache burden. Migraine, a recurrent condition characterized by moderate to severe headaches, is often accompanied by reversible neurological and systemic conditions, such as photophobia, phonophobia, skin sensitivity, and gastrointestinal disturbances. In contrast, TTH is characterized by mild to moderate pain, often described as a tight band around the head, and presents as a bilateral headache without symptoms such as nausea or vomiting typically seen in migraines.

According to the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021, headache disorders ranked as the second most prevalent condition worldwide, following oral disorders, and the third leading cause of years lived with disability (YLDs), following low back pain, major depressive disorder, and age-related and other hearing loss. 6 Migraines and TTH are the most prevalent among headache disorders, affecting diverse populations globally. However, they are often underdiagnosed and undertreated, imposing a significant burden due to their chronic nature and frequent comorbidities, such as sleep disorders, anxiety, and depression, underscoring their critical role in global health challenges. The COVID-19 pandemic disrupted efforts to reduce the burden of headache disorders, with many individuals experiencing increased triggers, such as stress, reduced access to healthcare, and lifestyle changes. Evidence suggests that SARS-CoV-2 infection caused acute or chronic headaches, while vaccination occasionally triggered transient migraine-like episodes.8-10 However, the duration and generalizability of the impact of the pandemic on headache disorders remain unclear and may take time to fully emerge.

The significance of this study lies in its comprehensive analysis of all currently available GBD data, offering estimates of the disease burden from 1990 to 2021 across different age groups, sexes, geographical regions, Socio-demographic Index (SDI), and the Healthcare Access and Quality (HAQ) Index. In addition, to provide valuable insights into future trends, we also projected YLD counts and rates up to 2050. Understanding the burden estimates can allow healthcare providers, policymakers, and researchers to allocate resources better, priori-

tize interventions, and tailor treatment strategies to reduce the burden of headache disorders. This manuscript was produced as part of the GBD Collaborator Network and following the GBD Protocol.<sup>11</sup>

#### **RESULTS**

#### Overview

In 2021, headache disorders were the second most prevalent disease globally, following oral disorders, affecting an estimated 2.8 billion (95% uncertainty interval [UI], 2.6–3.0) individuals. TTH was the second most common specific condition (2.0 billion [1.8–2.3]), while migraine was the seventh (1.2 billion [95% UI, 1.0–1.3]). Headache disorders were also the third leading cause of YLDs among all conditions in GBD 2021 (48.0 million [95% UI, 9.8–101.0]), following low back pain and depressive disorders. In terms of incidence, there were 809.2 million (95% UI, 717.8–896.0) incident cases in 2021, with an age-standardized rate of 10,084.5 (8,956.5–11,170.8) per 100,000.

### Global, regional, and national burden of migraine, 1990–2021

In 2021, the global prevalence of migraine was estimated at 1.2 billion cases (95% UI, 1.0–1.3), reflecting a 58.1% increase from 732.6 million cases (624.6–847.1) in 1990. While the absolute number of migraine cases has grown significantly, the global age-standardized prevalence rate of migraines experienced a marginal 1.6% (95% UI, 0.3–2.6) increase, from 14,027.7 per 100,000 in 1990 to 14,246.6 per 100,000 in 2021 (Table 1). Similarly, the number of YLDs in 2021 reached 43.4 million (95% UI, 6.7–95.1), representing a 58.2% increase from 1990 (27.4 million [4.1–60.3]). The agestandardized YLD rate for migraines remained stable (526.8 per 100,000 in 1990; 532.7 per 100,000 in 2021; Table 1).

There are geographical differences in age-standardized migraine prevalence (Table S1; Figure 1A), ranging from the lowest in Ethiopia (8,365.4 per 100,000 [95% UI, 7,232.9–9,566.2]) to the highest in Belgium (21,751.5 per 100,000 [18,730.1–25,705.5]), and YLD (Table S1; Figure 1B), ranging from the lowest in Ethiopia (313.6 per 100,000 [64.0–683.8]) to the highest in Belgium (800.4 per 100,000 [92.0–1772.0]). Overall, among 21 GBD regions, Tropical Latin America and Western Europe showed the highest burden of migraine, and Eastern

	Prevalence		YLDs		
		Percentage change,		Percentage change,	
Location	2021	1990–2021	2021	1990–2021	2050
Migraine					
Global	14,246.55 (12,194.12 to 16,378.70)	0.02 (0.00–0.03)	532.70 (80.57–1,167.71)	0.01 (-0.04 to 0.03)	531.80 (81.05–1,165.38)
SDI levels					
High SDI	15,365.14 (13,250.29 to 17,765.44)	0.01 (-0.01 to 0.02)	573.62 (89.78–1,236.04)	0.00 (-0.02 to 0.02)	601.57 (100.89–1,290.92)
High-middle SDI	13,502.73 (11,610.06 to 15,484.75)	0.02 (0.00-0.03)	517.57 (92.95–1,103.35)	0.01 (-0.08 to 0.04)	512.63 (85.46–1,098.01)
Middle SDI	14,344.23 (12,233.37 to 16,477.29)	0.06 (0.04-0.07)	535.85 (74.81–1,178.27)	0.05 (0.02-0.07)	546.97 (77.11–1,203.26)
Low-middle SDI	14,786.99 (12,677.14 to 16,979.01)	-0.00 (-0.02 to 0.01)	544.25 (73.88–1,201.85)	0.00 (-0.02 to 0.02)	547.01 (76.46–1,206.14)
Low SDI	12,808.97 (10,909.26 to 14,754.40)	-0.00 (-0.01 to 0.01)	475.21 (76.39–1,031.51)	0.01 (-0.01 to 0.02)	457.06 (79.27–985.23)
GBD region					
Southeast Asia, East Asia, and Oceania	13,313.82 (11,492.53 to 15,284.36)	0.07 (0.05–0.09)	500.77 (67.92–1,104.95)	0.07 (0.00–0.10)	517.50 (68.89–1,140.37)
East Asia	11,798.36 (10,162.49 to 13,566.96)	0.07 (0.03-0.11)	444.29 (66.76–971.75)	0.07 (-0.00 to 0.11)	444.77 (67.45-973.60)
Oceania	14,043.19 (11,934.61 to 16,427.13)	0.00 (0.00-0.00)	519.02 (64.65-1,151.04)	0.00 (-0.02 to 0.03)	524.35 (65.47-1,163.51)
South Asia	14,859.95 (12,704.02 to 16,953.54)	0.00 (-0.03 to 0.03)	537.87 (68.02-1,198.33)	0.01 (-0.03 to 0.04)	542.09 (68.05-1,207.38)
Central Europe, Eastern Europe, and Central Asia	13,923.11 (11,992.78 to 16,000.50)	-0.01 (-0.01 to -0.00)	547.23 (133.10–1,174.44)	-0.01 (-0.03 to -0.00)	544.11 (128.43–1,172.78)
Central Asia	13,584.23 (11,538.76 to 15,918.11)	−0.01 (−0.01 to −0.00)	507.35 (90.34-1,144.53)	-0.01 (-0.02 to 0.01)	507.14 (90.23-1,145.20)
Central Europe	13,822.04 (11,854.14 to 15,865.31)	−0.00 (−0.01 to −0.00)	525.24 (109.75–1,158.95)	-0.00 (-0.01 to 0.01)	527.05 (109.96–1,163.21)
Eastern Europe	14,077.09 (12,210.58 to 16,112.04)	−0.00 (−0.00 to −0.00)	574.43 (164.13-1,193.90)	-0.00 (-0.01 to 0.01)	574.95 (164.91–1,196.49)
High-income	15,927.19 (13,797.87 to 18,423.50)	0.00 (-0.01 to 0.02)	592.45 (90.70-1,280.41)	-0.00 (-0.02 to 0.02)	597.87 (90.85-1,291.37)
Australasia	13,433.71 (11,438.78 to 15,621.49)	0.00 (0.00-0.00)	498.64 (86.96-1,100.43)	0.00 (-0.02 to 0.03)	499.53 (87.14-1,102.99)
High-income Asia Pacific	11,072.69 (9,484.03 to 12,800.27)	0.01 (-0.03 to 0.04)	422.48 (85.63-937.71)	0.01 (-0.03 to 0.04)	422.07 (85.95–936.20)
High-income North America	16,709.11 (14,462.52 to 19,276.29)	-0.02 (-0.06 to 0.02)	614.00 (89.37-1,352.42)	-0.03 (-0.07 to 0.01)	613.28 (89.39-1,350.77)
Southern Latin America	11,706.98 (9,960.37 to 13,667.23)	0.03 (-0.01 to 0.08)	442.43 (85.81-974.19)	0.02 (-0.03 to 0.07)	442.72 (85.95–974.29)
Western Europe	18,170.70 (15,724.92 to 21,091.55)	0.01 (-0.01 to 0.02)	676.64 (96.68-1,471.91)	0.01 (-0.01 to 0.03)	675.63 (96.78-1,471.35)
Latin America and Caribbean	15,409.21 (13,263.10 to 17,822.77)	0.01 (-0.01 to 0.03)	570.79 (74.56–1,251.75)	0.01 (-0.01 to 0.03)	571.43 (74.72-1,254.99)
Andean Latin America	10,614.71 (8,993.46 to 12,309.15)	0.06 (0.02-0.13)	401.89 (72.75-893.96)	0.06 (-0.01 to 0.12)	405.56 (72.93-903.75)
Caribbean	14,237.12 (12,004.33 to 16,529.90)	−0.00 (−0.00 to −0.00)	528.99 (72.30-1,148.15)	-0.01 (-0.02 to 0.01)	530.77 (72.61-1,152.78)
Central Latin America	14,178.67 (12,097.70 to 16,441.61)	0.01 (-0.01 to 0.04)	531.67 (76.53-1,159.87)	0.01 (-0.02 to 0.04)	531.60 (76.81-1,161.34)
Tropical Latin America	18,595.34 (16,084.24 to 21,444.51)	0.02 (-0.01 to 0.06)	679.39 (73.91-1,542.87)	0.02 (-0.01 to 0.07)	680.10 (74.00-1,544.60)
Sub-Saharan Africa	12,244.68 (10,486.07 to 14,159.33)	0.01 (0.00-0.02)	459.32 (81.66-994.71)	0.01 (-0.00 to 0.02)	464.92 (82.16-1,007.45)
Central Sub-Saharan Africa	12,396.15 (10,491.24 to 14,511.21)	−0.00 (−0.00 to −0.00)	461.37 (80.99–1,008.48)	0.01 (-0.02 to 0.03)	466.43 (81.92–1,017.87)
Eastern Sub-Saharan Africa	9,084.26 (7,732.97 to 10,507.26)	0.01 (-0.00 to 0.02)	347.19 (77.86–757.55)	0.01 (-0.02 to 0.03)	349.98 (78.59–763.53)
Southern Sub-Saharan Africa	12,876.73 (11,102.68 to 14,843.51)	−0.00 (−0.00 to −0.00)	477.47 (85.49-1,025.39)	-0.01 (-0.03 to -0.00)	478.67 (85.39–1,025.96)
Western Sub-Saharan Africa	14,870.35 (12,715.58 to 17,284.92)	0.00 (-0.02 to 0.02)	554.49 (84.75–1,214.04)	0.01 (-0.01 to 0.03)	558.74 (85.54-1,222.08)
North Africa and Middle East	15,304.13 (13,071.93 to 17,749.48)	0.00 (-0.01 to 0.02)	598.94 (108.94–1,305.73)	0.00 (-0.02 to 0.02)	605.59 (109.46–1,318.88)
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Table 1. Continued					
Table II Commuca	Prevalence		YLDs		
	- Tovalones	Percentage change,	1250	Percentage change,	
Location	2021	1990–2021	2021	1990–2021	2050
Southeast Asia	16,180.66 (13,890.15 to 18,730.39)	-0.02 (-0.03 to -0.01)	607.13 (69.70–1,362.67)	-0.02 (-0.03 to 0.01)	609.13 (70.45–1,365.61)
ттн					
Global	24,764.77 (21,863.62 to 27,954.74)	-0.01 (-0.01 to 0.00)	55.69 (16.13–185.07)	-0.02 (-0.05 to 0.01)	55.36 (16.03–183.65)
SDI levels					
High SDI	30,603.28 (27,152.87 to 34,513.40)	-0.02 ( $-0.03$ to $-0.01$ )	66.79 (18.15–235.79)	-0.02 (-0.07 to 0.01)	71.94 (20.35–247.94)
High-middle SDI	23,862.61 (21,031.88 to 26,904.35)	-0.01 (-0.02 to 0.01)	59.93 (18.33-179.03)	-0.05 ( $-0.10$ to $-0.01$ )	57.20 (16.57-179.34)
Middle SDI	23,378.72 (20,608.16 to 26,365.06)	0.06 (0.05-0.07)	51.54 (14.95–174.76)	0.05 (-0.02 to 0.14)	52.44 (15.20-177.11)
Low-middle SDI	25,022.79 (22,033.70 to 28,284.15)	0.00 (-0.00 to 0.00)	52.99 (14.84-182.64)	0.01 (-0.06 to 0.07)	53.78 (15.23-183.84)
Low SDI	22,780.22 (19,950.88 to 25,943.94)	-0.01 (-0.01 to -0.01)	51.76 (15.45–171.97)	0.00 (-0.05 to 0.05)	51.48 (15.72-167.07)
GBD region					
Southeast Asia, East Asia, and Oceania	20,715.30 (18,205.92 to 23,454.07)	0.08 (0.05–0.10)	45.87 (13.30–153.94)	0.04 (-0.02 to 0.17)	46.64 (13.40–157.30)
East Asia	18,489.51 (16,320.68 to 20,929.50)	0.08 (0.04-0.12)	43.40 (13.06–141.04)	0.04 (-0.03 to 0.19)	43.41 (13.06–141.25)
Oceania	22,142.50 (18,985.45 to 25,544.46)	0.00 (-0.00 to 0.00)	46.21 (13.06–163.83)	0.00 (-0.09 to 0.09)	46.26 (13.14–164.55)
South Asia	25,405.47 (22,430.09 to 28,583.39)	0.00 (-0.00 to 0.00)	50.98 (13.59–180.49)	0.00 (-0.06 to 0.07)	50.81 (13.52-180.51)
Central Europe, Eastern Europe, and Central Asia	30,801.99 (27,185.92 to 34,791.81)	-0.00 (-0.01 to 0.01)	84.31 (26.91–262.98)	-0.02 (-0.05 to 0.01)	82.59 (25.96–259.86)
Central Asia	30,274.55 (26,183.72 to 34,528.86)	-0.00 (-0.00 to 0.00)	66.89 (18.09–236.36)	-0.00 (-0.05 to 0.04)	66.71 (18.02–236.15)
Central Europe	30,488.91 (26,793.28 to 34,697.76)	0.00 (-0.00 to 0.00)	74.70 (22.49–248.04)	0.01 (-0.06 to 0.04)	74.67 (22.43–248.23)
Eastern Europe	31,243.12 (27,766.56 to 34,948.02)	0.00 (-0.02 to 0.02)	96.83 (33.12-286.15)	0.00 (-0.03 to 0.03)	96.81 (33.07-286.63)
High-income	32,202.15 (28,549.08 to 36,321.00)	-0.00 (-0.02 to 0.01)	68.85 (18.18-247.13)	-0.00 (-0.05 to 0.02)	68.81 (18.12-247.70)
Australasia	27,215.52 (23,764.26 to 31,068.68)	-0.00 (-0.00 to 0.00)	60.99 (17.51–200.38)	0.01 (-0.07 to 0.08)	60.92 (17.49–200.55)
High-income Asia Pacific	29,867.61 (26,437.50 to 33,548.63)	0.01 (-0.02 to 0.04)	63.72 (17.35–216.52)	0.00 (-0.04 to 0.05)	63.70 (17.36-217.39)
High-income North America	34,180.26 (30,603.85 to 38,251.42)	-0.02 (-0.05 to 0.00)	70.01 (17.89–257.69)	-0.02 (-0.06 to 0.02)	69.93 (17.83-257.73)
Southern Latin America	26,264.27 (22,771.94 to 30,205.10)	0.01 (-0.00 to 0.02)	59.96 (16.44-196.75)	0.00 (-0.08 to 0.08)	59.83 (16.38-196.27)
Western Europe	32,770.54 (28,999.01 to 37,028.00)	0.00 (-0.01 to 0.01)	71.93 (19.05–261.97)	0.00 (-0.06 to 0.04)	71.74 (18.95–261.72)
Latin America and Caribbean	25,685.02 (22,480.17 to 29,170.88)	-0.00 (-0.01 to 0.01)	53.59 (15.02-185.16)	0.00 (-0.04 to 0.04)	53.44 (14.97-185.27)
Andean Latin America	20,715.91 (17,622.56 to 23,911.58)	0.01 (-0.02 to 0.05)	48.09 (14.42-173.97)	0.01 (-0.08 to 0.11)	47.90 (14.36–173.69)
Caribbean	23,730.24 (20,293.00 to 27,687.86)	-0.00 (-0.00 to 0.00)	51.21 (14.83–177.77)	-0.00 (-0.05 to 0.05)	51.09 (14.78–178.75)
Central Latin America	24,421.55 (21,365.98 to 27,955.62)	-0.00 (-0.00 to 0.00)	53.44 (15.36–180.62)	0.01 (-0.04 to 0.05)	53.39 (15.30-180.96)
Tropical Latin America	29,005.61 (25,648.55 to 32,612.92)	0.00 (-0.02 to 0.02)	55.97 (14.51–205.79)	0.01 (-0.05 to 0.05)	55.73 (14.42-205.01)
Sub-Saharan Africa	22,454.11 (19,657.92 to 25,642.78)	-0.01 ( $-0.01$ to $-0.00$ )	53.56 (16.42-172.25)	0.00 (-0.04 to 0.04)	53.31 (16.34-173.23)
Central Sub-Saharan Africa	23,232.00 (20,084.38 to 27,079.59)	-0.00 (-0.00 to 0.00)	53.98 (16.14-173.91)	0.01 (-0.06 to 0.08)	53.98 (16.15-174.07)
Eastern Sub-Saharan Africa	18,801.27 (16,305.57 to 21,690.09)	-0.02 ( $-0.03$ to $-0.01$ )	48.12 (15.48–151.06)	-0.01 (-0.05 to 0.04)	47.88 (15.42-151.05)
Southern Sub-Saharan Africa	24,193.08 (21,262.85 to 27,462.85)	-0.00 (-0.00 to 0.00)	57.04 (17.38–179.73)	-0.01 (-0.05 to 0.03)	56.75 (17.19–179.38)
Western Sub-Saharan Africa	25,108.38 (22,066.05 to 28,468.24)	0.00 (-0.00 to 0.00)	57.49 (17.21–191.19)	0.02 (-0.04 to 0.06)	57.38 (17.21–191.73)
North Africa and Middle East	24,090.29 (20,941.08 to 27,533.32)	0.01 (-0.00 to 0.02)	67.78 (22.25–202.06)	0.00 (-0.09 to 0.06)	67.63 (22.16–202.16)
Southeast Asia	25,256.68 (22,085.09 to 28,547.33)	0.00 (-0.00 to 0.00)	51.03 (13.89–181.26)	0.01 (-0.04 to 0.06)	51.15 (13.92–181.17)

Abbreviation: GBD, Global Burden of Diseases, Injuries, and Risk Factors; TTH, tension-type headaches; UI, uncertainty interval; YLDs, years lived with disability.





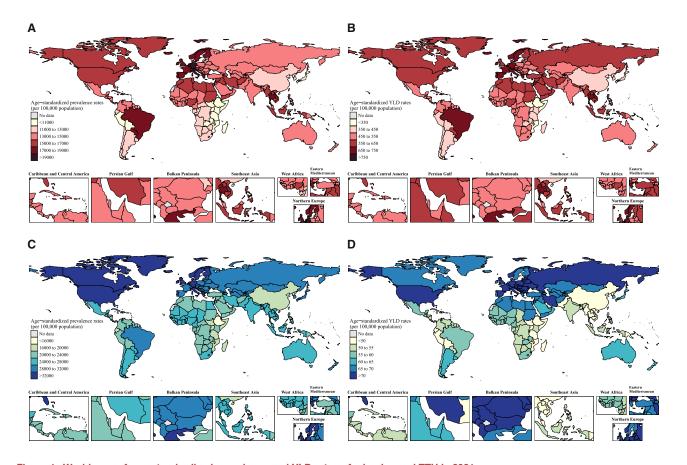


Figure 1. World map of age-standardized prevalence and YLD rates of migraine and TTH in 2021
(A–D) (A) and (B) represent the 2021 values of age-standardized prevalence and YLD rates for migraine, respectively, while (C) and (D) represent the 2021 values of age-standardized prevalence and YLD rates for TTH, respectively. Abbreviation: TTH; tension-type headaches; YLDs, years lived with disability.

Sub-Saharan Africa had the lowest, as measured by age-standardized prevalence and YLD rates. In addition, regional incidence estimates of migraine in 2021 and changes since 1990 are provided in Table S1.

#### Global, regional, and national burden of TTH, 1990-2021

The number of TTH cases in 2021 was 2.0 billion (95% UI, 1.8–2.3) globally, representing a 56.4% rise from 1990 (1.3 billion [1.1–1.5]). However, the global age-standardized prevalence rate of TTH remained stable (24,904.9 per 100,000 in 1990; 24,764.8 per 100,000 in 2021; Table 1). Similarly, the YLD count for TTH in 2021 was 4.6 million (95% UI, 1.3–15.0), representing a 61.4% increase from 1990, when the YLD count was 2.8 million (0.8–9.6). The age-standardized YLD rate remained stable, from 57.0 per 100,000 in 1990 to 55.7 per 100,000 in 2021 (Table 1).

We observed national disparities in the burden of TTH (Table S2; Figures 1C and 1D), with an age-standardized prevalence rate ranging from 15,855.3 per 100,000 (95% UI, 13,637.6–18,206.9) in Ethiopia to 35,492.4 per 100,000 (31,718.0–39,481.9) in Norway and age-standardized YLD rate ranging from 40.3 per 100,000 (13.0–128.5) in Ethiopia to 99.7 per 100,000 (34.8–288.4) in Russian Federation. Regionally, as measured by age-standardized prevalence and YLD rates, the most significant burden was observed in

high-income North America, while the lowest burden was in East Asia. Regional estimates of TTH incidence in 2021, along with the percentage change from 1990 to 2021, are presented in Table S2.

#### Burden of headaches according to age and sex

Figure 2 illustrates age- and sex-specific prevalence and YLD rates for headache disorders in 2021. Migraines and TTH were more prevalent in females than males across all age groups, with TTH showing consistently higher prevalence rates than migraines in all demographic groups. The age-specific prevalence of both conditions was highest during young-to-middle adulthood, peaking between the ages of 30 and 44 years. Notably, while the prevalence of migraines declined steadily with advancing age, TTH showed greater persistence in older age groups, remaining relatively prevalent even among old adults.

The age-specific YLD rates for migraines and TTH largely mirrored the age-specific prevalence patterns, with females experiencing a notably greater disability burden than males across all age groups. The highest age-specific YLD rates for both conditions were observed in the 40–49 age group in both sexes. However, unlike prevalence, migraines consistently exhibited higher YLD rates than TTH across all age and sex groups.



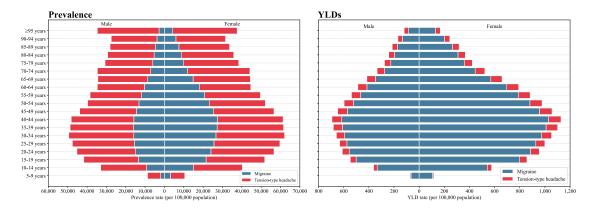


Figure 2. Prevalence and YLD of migraine and TTH by age group and sex in 2021 Abbreviation: TTH, tension-type headaches; YLDs, years lived with disability.

#### Burden of headache according to SDI and HAQ Index

Figure 3 presents age-standardized YLD rates for migraine and TTH according to SDI levels in 2021. Higher age-standardized YLD rates of migraine were observed in countries with higher SDI. However, for TTH, while countries with high SDI had the highest age-standardized YLD rates, the lowest rates were observed in middle SDI. A similar pattern was observed for the HAQ Index (Figures S1 and S2).

When stratified by five SDI levels, high-SDI regions had the highest age-standardized prevalence (15,365.1 per 100,000 [95% UI, 13,250.3–17,765.4]) and YLD rates (573.6 per 100,000 [98.8–1236.0]) for migraines, while low-SDI regions had the lowest age-standardized prevalence (12,809.0 per 100,000 [10,909.3–14,754.4]) and YLD rates (475.2 per 100,000 [76.4–1031.5]; Figure S3). Similarly, for TTH, high-SDI regions had the highest age-standardized prevalence (30,603.3 per 100,000 [95% UI, 27,152.9–34,513.4]) and YLD rates (66.8 per 100,000 [18.1–235.8]). The age-standardized prevalence for TTH was lowest in the low-SDI region (22,780.2 per 100,000 [95% UI, 19,950.9–25,943.9]); however, the YLD rate was lowest in the middle-SDI region (51.5 per 100,000 [15.0–174.8]).

#### Headache burden in the future up to 2050

The global number of YLDs attributable to migraine is projected to increase from 43.4 million (95% UI, 6.7–95.1) in 2021 to 52.0 million (8.7–111.6) by 2050. Despite this increase, the age-standardized YLD rates for migraines are anticipated to remain stable, with estimates of 531.8 per 100,000 (95% UI, 81.1–1,165.4) in 2050 compared to 532.7 per 100,000 (80.6–1,167.7) in 2021 (Table 1). As presented in Figure 4, similar findings are observed across all five SDI levels; the highest age-standardized rates of migraine in 2050, similar to 1990, will be observed in high-SDI countries (601.6 per 100,000 [95% UI, 100.9–1,290.9]), and the lowest in low-SDI countries (457.1 per 100,000 [79.3–985.2]).

Similarly, the number of YLDs due to TTH is expected to rise from 4.6 million (95% UI, 1.3–15.0) in 2021 to 5.8 million YLDs (1.8–18.1) in 2050. However, the age-standardized YLD rates for TTH are also expected to remain stable, with estimates of 531.8 (95% UI, 81.1–1,165.4) per 100,000 in 2050 and 532.7 per 100,000 (80.6–1,167.7) in 2021 (Table 1). In 2050, the highest

age-standardized rates of TTH will be found in high-SDI countries (71.9 per 100,000 [95% UI, 20.4–247.9]), while the lowest will be found in low-SDI countries (51.5 per 100,000 [15.7–167.1]). A detailed depiction of the percentage changes in both age-standardized YLD rates and the number of YLDs for migraine and TTH from 1990 to 2050 is provided in Figure 4. At the regional level, the age-standardized YLD rates for migraine and TTH are expected to change minimally. However, in some regions, the rates are expected to decrease, including Central Europe (–21.4%), high-income Asia Pacific (–19.2%), East Asia (–15.5%), and Eastern Europe (–14.4%). Our decomposition analysis, both regionally and globally, revealed that population growth will be the primary driver of the projected change in the number of YLDs by 2050 (Figure 5), a trend observed across all regions.

#### **DISCUSSION**

This study provides a comprehensive assessment of the global, regional, and national burden of headache disorders, including migraines and TTH, from 1990 to 2021, and the forecasts up to 2050 based on GBD 2021 estimates. In 2021, TTH was the second most common specific condition, while migraine was the seventh. While the absolute number of migraine and TTH cases increased, age-standardized prevalence and YLD rates remained stable or had a minimal increase. We found that the age-standardized disability burden of migraine and TTH is forecasted to remain stable up to 2050, driven by population growth and demographic changes rather than worsening individual outcomes, highlighting the importance of sustained healthcare access and effective management strategies to reduce the burden.

Although TTH was more prevalent than migraine, migraine accounted for a disproportionately higher disability burden, reflecting its greater impact on quality of life. In addition, there were substantial variations in the burden of these conditions across regions and demographic groups in 2021. Countries with higher socioeconomic development and better healthcare access (i.e., countries with high SDI and HAQ Index) tend to have a higher burden of headache disorders, as measured by age-standardized prevalence and YLD rates, which could be due to a combination of better diagnosis and modern lifestyle

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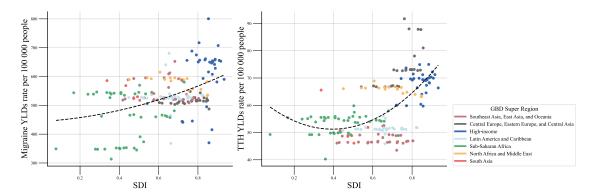


Figure 3. Age-standardized YLD rates of migraine and TTH by SDI level

Abbreviation: GBD, Global Burden of Diseases, Injuries, and Risk Factors; SDI, Socio-demographic Index; TTH, tension-type headaches; YLDs, years lived with disability.

risk factors. In addition, young and middle-aged females will be disproportionately affected by headache disorders, underscoring the significance of addressing the unique needs of females suffering from headache disorders.

The stability of age-standardized estimates for headache disorders, including migraines and TTH, observed in GBD 2021, can be attributed to a combination of persistent risk factors and improvements in healthcare systems. Stress, sedentary lifestyles, caffeinated or alcohol consumption, and poor-quality sleep remain widespread triggers, sustaining the burden of these conditions globally. While advancements in diagnostic tools and treatment

options have improved the recognition and management of headache disorders, they have primarily mitigated underreporting. 

Looking toward 2050, these rates are expected to remain stable due to the enduring influence of these modern risk factors. Furthermore, the limited utilization of professional healthcare for headaches, with many individuals relying on over-the-counter remedies, 

may continue to impede substantial reductions in prevalence and disability. This equilibrium suggests that healthcare advancements balance but do not eliminate the underlying contributors to headache disorders, leaving the burden relatively stable.

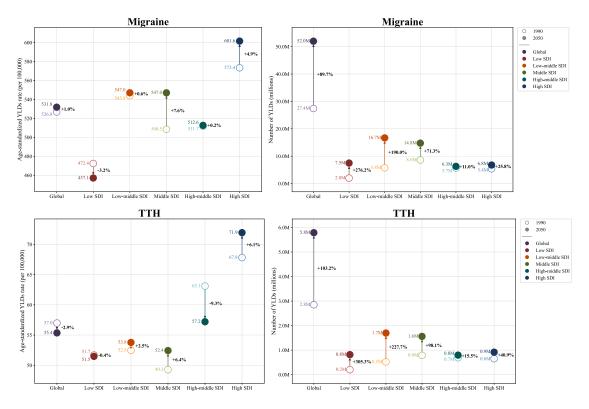


Figure 4. Projected YLD counts and age-standardized rates of migraine and TTH until 2050 by SDI level Abbreviation: SDI, Socio-demographic Index; TTH, tension-type headaches; YLDs, years lived with disability.





Figure 5. Decomposition analysis of percentage change in the number of YLDs due to migraine and TTH between 2021 and 2050, globally and by GBD region

Abbreviation: GBD, Global Burden of Diseases, Injuries, and Risk Factors; TTH, tension-type headaches; YLDs, years lived with disability.

We also found that higher age-standardized prevalence and YLD rates for migraines and TTHs were generally observed in high SDI and HAQ Index, and this trend is expected to continue up to 2050. This may be due to modern lifestyle factors, such as chronic psychosocial stress, high occupational demands, sedentary behavior, higher diagnostic capacity, heightened health literacy, and widespread access to healthcare services. <sup>15</sup> Conversely, low-SDI regions appear to have a lower burden, possibly due to a combination of underdiagnosis, limited access to healthcare professionals trained in headache disorders, and overall underreporting. <sup>16,17</sup> These patterns suggest that tailored approaches are needed—focusing on improving healthcare access and reducing lifestyle-related risk factors in high-SDI regions while addressing healthcare gaps in low-SDI areas.

Headache disorders disproportionately affect women, particularly in young and middle-aged groups, which can be explained by a complex interplay of biological, hormonal, environmental, and psychological factors. Hormonal fluctuations, particularly changes in estrogen levels during the menstrual cycle, pregnancy, and menopause, could play an essential role in the pathophysiology of migraines. 18 These fluctuations, combined with the demands of balancing family, career, and social responsibilities, may contribute to the higher prevalence of headache disorders in women. 18 In addition, psychological conditions such as anxiety and depression, which are more common in women, 19 could exacerbate the frequency and severity of migraines and TTH. Furthermore, the larger gap observed in YLD rates compared to prevalence between sexes suggests that these risk factors may not only increase the occurrence of headaches in women but could also intensify their associated disability and impact on daily life.

While TTH is more prevalent than migraines across all demographic groups, migraines consistently exhibited higher YLD rates, highlighting their greater severity and disabling nature. These headaches often impair daily functioning and significantly reduce quality of life. <sup>20,21</sup> Conversely, TTH, although more common, typically results in milder symptoms and a lesser degree of disability. This divergence underscores the need for tailored management strategies: addressing the debilitating effects of migraines through comprehensive treatment and support while implementing preventive measures for the broader but less severe impact of TTH.<sup>4</sup>

While the burden of many fatal and disabling disorders diminished with socioeconomic development, 22,23 that of migraines and TTHs remain persistent, underscoring the need for continued and targeted public health efforts for disproportionated demographic groups. Despite being a major cause of disability, headache disorders are often overlooked in public health strategies, research, and training programs.<sup>24</sup> For instance, less than 30% of primary care physicians in the United States were aware of the American Academy of Neurology's migraine prevention guidelines and important risk factors.<sup>25</sup> Females, particularly in their most productive years, experience the highest prevalence and YLD rates, exacerbating the societal and economic impact of these conditions. This underscores the need for public health initiatives that focus on tailored interventions, such as education, early diagnosis, and sex-sensitive healthcare policies, to reduce the long-term effects on females, especially addressing the unique psychosocial challenges they face.<sup>26</sup>

In addition, disparities between countries with different SDI levels further complicate headache care. High-SDI countries tend to report a higher burden of headaches, with better

#### **Article**



diagnosis but less effective management due to lifestyle factors. In contrast, developing countries often face limited access to healthcare and essential treatments, exacerbating the global disparity. Structured healthcare systems, such as tiered headache services and education regarding the chronic nature of headache disorders, can help bridge these gaps by training primary care providers and ensuring that even underserved populations can receive appropriate diagnosis and management, improving care access across diverse socioeconomic settings. <sup>17</sup>

The COVID-19 pandemic introduced additional challenges for headache management, with acute or chronic headaches after SARS-CoV-2 infection or vaccination adding to the global burden. Some patients with migraines co-infected with SARS-CoV-2 report experiencing more severe pain that is often less responsive to standard analgesics. These new headache issues, combined with increased psychological stress, disrupted healthcare access, and social factors, may have further complicated an already pressing public health issue. Therefore, effective management should address both the biological impacts of the virus and vaccination, as well as the psychological and social factors exacerbating these conditions.

#### Conclusion

Based on the findings of GBD 2021 estimates, headache disorders, including migraines and TTH, remain an immense global health burden, with a disproportionate burden in young to middle-aged females. The burden of headache disorders also substantially varies across SDIs and HAQ Index, with high-SDI and high-HAQ Index regions facing higher prevalence and disability rates due to modern lifestyle factors, while low-SDI regions experience underreporting and limited healthcare access. Region-specific strategies are necessary to address this, focusing on improving healthcare access and affordability of treatment in low-SDI areas. Tailored interventions and resource allocation can reduce the burden of these disorders moving toward 2050.

#### **Limitations of the study**

This study provided updated GBD 2021 analyses of TTH and migraine burden for 1990 to 2021, with the headache disability burden forecasts up to 2050. However, several limitations should be addressed in this study. Our study faces limitations in all GBD works, including the lack of reliable epidemiological data in lowand middle-income countries. Headache disorders are often inadequately represented in national health surveys, and administrative data sources, such as claims or primary care records, frequently fail to capture their prevalence reliably. As a result, country-specific estimates rely on predictive covariates and data from neighboring countries, resulting in greater UIs in these settings. Although the GBD framework employs statistical techniques such as hierarchical modeling and cross-location information borrowing to mitigate data sparsity, region-specific sensitivity analyses or uncertainty decompositions were not conducted. Therefore, residual uncertainty may be underestimated in regions with severely limited input data, and estimates from these areas should be interpreted with caution. Second, limitations in data collection and analysis methods prevented the ability to distinguish between probable and definite diagnoses of migraine based on the International Classification of Headache Disorders (ICHD) criteria. However, it is important to note that probable migraine carries a substantial disease burden and disability similar to that of definite migraine. 28,29 The primary issue leading to a probable rather than definite diagnosis in past studies has often been the duration of the headache. Therefore, the GBD study's approach of categorizing probable migraine within the broader category of migraine may be reasonable. This method may ensure a comprehensive understanding of the disease burden. Third, a similar argument can be made for probable TTH, although the knowledge of this type of headache is significantly less developed. Additionally, the YLDs missed by excluding this headache type are fewer due to the considerably lower disability weight (DW) associated with TTH compared to migraine. Fourth, since the GBD estimates are limited to 2021, we did not conduct secondary analyses to evaluate the impact of the COVID-19 pandemic on headache disorders. The GBD 2021 estimates and forecasts did not account for the effects of the pandemic or recent conflicts on headache burden, as geographically and temporally comprehensive data were unavailable at the time of analysis. We aim to explore the impact of COVID-19 on headaches in future studies as more robust and diverse data become accessible. Fifth, we did not quantify the burden of headache disorders attributable to any risk factors, such as diet, psychological factors, and environmental triggers. 13 Nonetheless, further research is necessary to better understand the impact of these risk factors on headache disorder burden and to refine data collection methods for more accurate assessments in future studies. Finally, our projections were based solely on the SDI as the predictive covariate. While SDI captures broad socioeconomic patterns, it may not adequately account for other influential factors, such as healthcare accessibility, evolving diagnostic practices, and environmental exposures.

#### **RESOURCE AVAILABILITY**

#### Lead contact

Requests for additional information, resources, and reagents should be directed to and will be fulfilled by the lead contact, Dong Keon Yon (yonkkang@gmail.com).

#### **Materials availability**

No new unique materials were generated in this study.

#### **Data and code availability**

- The data used in this study are publicly available through the Global Health Data Exchange (GHDx) GBD 2021 website: https://ghdx. healthdata.org/gbd-2021.
- This study did not generate any original code.
- Any additional information required to reanalyze the data reported in this
  paper is available from the lead contact upon request.

#### **CONSORTIA**

The members of the GBD 2021 Headache Collaborators are Tissa Wijeratne, Jiyeon Oh, Soeun Kim, Yesol Yim, Min Seo Kim, Jae II Shin, Yun-Seo Oh, Raon Jung, Yun Seo Kim, Lee Smith, Hasan Aalruz, Rami Abd-Rabu, Deldar Morad Abdulah, Richard Gyan Aboagye, Meysam Abolmaali, Dariush Abtahi,



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Members of the core research team for this topic area had full access to the underlying data used to generate estimates presented in this study. All other authors had access to and reviewed estimates as part of the research evaluation process, which includes additional stages of formal review. Conceptualization and design: T. Wijeratne, J.O., S. Kim, Y.Y., M.S.K., J.I.S., M.K.C., T.-J. S., D.K.Y., and V.F.; methodology: T. Wijeratne, J.O., S. Kim, Y.Y., M.S.K., J.I. S., M.K.C., T.-J.S., D.K.Y., and V.F.; data acquisition: T. Wijeratne, J.O., S.

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#### **STAR**\*METHODS

Detailed methods are provided in the online version of this paper and include the following:

- KEY RESOURCES TABLE
- EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS
- METHOD DETAILS
  - Case definition and input data
  - Data processing and disease modeling
  - o Classification of geographic locations
- QUANTIFICATION AND STATISTICAL ANALYSIS
  - Association between socio-economic indicators with the migraine and TTH
  - $\,\circ\,$  Estimate projections and decomposition analysis
  - o Data presentation

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#### **REFERENCES**

- GBD 2016 Headache Collaborators (2018). Global, regional, and national burden of migraine and tension-type headache, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 17, 954–976. https://doi.org/10.1016/S1474-4422(18)30322-3.
- Ashina, M., Katsarava, Z., Do, T.P., Buse, D.C., Pozo-Rosich, P., Özge, A., Krymchantowski, A.V., Lebedeva, E.R., Ravishankar, K., Yu, S., et al. (2021). Migraine: epidemiology and systems of care. Lancet 397, 1485–1495. https://doi.org/10.1016/S0140-6736(20)32160-7.
- Singh, G., Chowdhury, D., Wijeratne, T., and Sander, J.W. (2024). Where Does Visual Aura Belong-Epilepsy or Migraine?: A Historical Perspective. Neurol. Clin. Pract. 14, e200343. https://doi.org/10.1212/cpj.000000000 0200343.
- Fumal, A., and Schoenen, J. (2008). Tension-type headache: current research and clinical management. Lancet Neurol. 7, 70–83. https://doi. org/10.1016/S1474-4422(07)70325-3.

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- Headache Classification Committee of the International Headache Society (IHS) (2018). The International Classification of Headache Disorders, 3rd edition. Cephalalgia 38, 1–211. https://doi.org/10.1177/0333102417 738202.
- GBD 2021 Diseases and Injuries Collaborators (2024). Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet 403, 2133–2161. https://doi.org/10.1016/s0140-6736(24)00757-8.
- Buse, D.C., Gerstein, M.T., Houts, C.R., McGinley, J.S., Uzumcu, A.A., McCarrier, K.P., Cooke, A., Touba, N.M., Nishida, T.K., Wirth, R.J., and Lipton, R.B. (2022). Impact of the COVID-19 pandemic on people living with migraine: Results of the MiCOAS qualitative study. Headache 62, 284–293. https://doi.org/10.1111/head.14274.
- Al-Hashel, J.Y., Abokalawa, F., Alenzi, M., Alroughani, R., and Ahmed, S.F. (2021). Coronavirus disease-19 and headache; impact on pre-existing and characteristics of de novo: a cross-sectional study. J. Headache Pain 22, 97. https://doi.org/10.1186/s10194-021-01314-7.
- Sampaio Rocha-Filho, P.A. (2022). Headache associated with COVID-19: Epidemiology, characteristics, pathophysiology, and management. Headache 62, 650–656. https://doi.org/10.1111/head.14319.
- Tana, C., Bentivegna, E., Cho, S.J., Harriott, A.M., García-Azorín, D., Lab-astida-Ramirez, A., Ornello, R., Raffaelli, B., Beltrán, E.R., Ruscheweyh, R., and Martelletti, P. (2022). Long COVID headache. J. Headache Pain 23, 93. https://doi.org/10.1186/s10194-022-01450-8.
- Institute for Health Metrics and Evaluation (2015). Protocol for the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD). Version 2.0. IHME Seattle (WA). https://www.healthdata.org/research-analysis/about-gbd/protocol
- Seng, E.K., Martin, P.R., and Houle, T.T. (2022). Lifestyle factors and migraine. Lancet Neurol. 21, 911–921. https://doi.org/10.1016/S1474-4422(22)00211-3.
- Robbins, M.S. (2021). Diagnosis and Management of Headache: A Review. JAMA 325, 1874–1885. https://doi.org/10.1001/jama.2021.1640.
- VanderPluym, J.H., Halker Singh, R.B., Urtecho, M., Morrow, A.S., Nayfeh, T., Torres Roldan, V.D., Farah, M.H., Hasan, B., Saadi, S., Shah, S., et al. (2021). Acute Treatments for Episodic Migraine in Adults: A Systematic Review and Meta-analysis. JAMA 325, 2357–2369. https://doi.org/10.1001/jama.2021.7939.
- Liu, H., Dong, M., Liu, K., Jia, Z., Gui, W., Cheng, Y., Lv, Y., Qu, K., Zhao, H., Chen, J., et al. (2023). Status of diagnosis and preventative treatment for primary headache disorders: real-world data of unmet needs in China.
   J. Headache Pain 24, 119. https://doi.org/10.1186/s10194-023-01654-6.
- Stovner, L.J., Nichols, E., Steiner, T.J., Abd-Allah, F., Abdelalim, A., Al-Raddadi, R.M., Ansha, M.G., Barac, A., Bensenor, I.M., Doan, L.P., et al. (2018). Global, regional, and national burden of migraine and tension-type headache, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 17, 954–976. https://doi.org/10.1016/S1474-4422(18)30322-3.
- Mortel, D., Kawatu, N., Steiner, T.J., and Saylor, D. (2022). Barriers to headache care in low- and middle-income countries. eNeurological. Sci. 29, 100427. https://doi.org/10.1016/j.ensci.2022.100427.
- Sacco, S., Ricci, S., Degan, D., and Carolei, A. (2012). Migraine in women: the role of hormones and their impact on vascular diseases. J. Headache Pain 13, 177–189. https://doi.org/10.1007/s10194-012-0424-y.
- Santomauro, D.F., Mantilla Herrera, A.M., Shadid, J., Zheng, P., Ashbaugh, C., Pigott, D.M., Abbafati, C., Adolph, C., Amlag, J.O., Aravkin, A.Y., et al. (2021). Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. Lancet 398, 1700–1712. https://doi.org/10.1016/S0140-6736 (21)02143-7.

- Dalkara, T., Nozari, A., and Moskowitz, M.A. (2010). Migraine aura pathophysiology: the role of blood vessels and microembolisation. Lancet Neurol. 9, 309–317. https://doi.org/10.1016/S1474-4422(09)70358-8.
- Ornello, R., Andreou, A.P., De Matteis, E., Jürgens, T.P., Minen, M.T., and Sacco, S. (2024). Resistant and refractory migraine: clinical presentation, pathophysiology, and management. EBioMedicine 99, 104943. https:// doi.org/10.1016/j.ebiom.2023.104943.
- Naghavi, M., Ong, K.L., Aali, A., Ababneh, H.S., Abate, Y.H., Abbafati, C., Abbasgholizadeh, R., Abbasian, M., Abbasi-Kangevari, M., Abbastabar, H., et al. (2024). Global burden of 288 causes of death and life expectancy decomposition in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet 403, 2100–2132. https://doi.org/10.1016/S0140-6736 (24)00367-2.
- Ferrari, A.J., Santomauro, D.F., Aali, A., Abate, Y.H., Abbafati, C., Abbastabar, H., Abd ElHafeez, S., Abdelmasseh, M., Abd-Elsalam, S., Abdollahi, A., et al. (2024). Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet 403, 2133–2161. https://doi.org/10.1016/S0140-6736(24)00757-8.
- Minen, M.T., Robbins, M.S., Loder, E., Nahas, S., Gautreaux, J., Litin, S., Barch, C., Cook, C., Smith, T., Powers, S.W., et al. (2020). Addressing the Crisis of Diagnosis and Management of Migraine in Primary Care: A Summary of the American Headache Society FrontLine Primary Care Advisory Board. Headache 60, 1000–1004. https://doi.org/10.1111/head.13797.
- Minen, M.T., Loder, E., Tishler, L., and Silbersweig, D. (2016). Migraine diagnosis and treatment: A knowledge and needs assessment among primary care providers. Cephalalgia 36, 358–370. https://doi.org/10.1177/ 0333102415593086
- Pistoia, F., Salfi, F., Saporito, G., Ornello, R., Frattale, I., D'Aurizio, G., Tempesta, D., Ferrara, M., and Sacco, S. (2022). Behavioral and psychological factors in individuals with migraine without psychiatric comorbidities. J. Headache Pain 23, 110. https://doi.org/10.1186/s10194-022-01485.xx
- Chang, Y., and Song, T.-J. (2024). COVID-19 Infection-related Headache:
   A Narrative Review. Headache Pain Res. 25, 24–33. https://doi.org/10.62087/hpr.2024.0008.
- Lanteri-Minet, M., Valade, D., Geraud, G., Chautard, M.H., and Lucas, C. (2005). Migraine and probable migraine–results of FRAMIG 3, a French nationwide survey carried out according to the 2004 IHS classification. Cephalalgia 25, 1146–1158. https://doi.org/10.1111/j.1468-2982.2005.00977.x.
- Patel, N.V., Bigal, M.E., Kolodner, K.B., Leotta, C., Lafata, J.E., and Lipton, R.B. (2004). Prevalence and impact of migraine and probable migraine in a health plan. Neurology 63, 1432–1438. https://doi.org/10.1212/01.wnl. 0000142044.22226.54.
- Kim, S., Lee, H., Woo, S., Lee, H., Park, J., Kim, T., Fond, G., Boyer, L., Rahmati, M., Smith, L., et al. (2025). Global, regional, and national trends in drug use disorder mortality rates across 73 countries from 1990 to 2021, with projections up to 2040: a global time-series analysis and modelling study. eClinicalMedicine 79, 102985. https://doi.org/10.1016/j.eclinm. 2024.102985.
- Global Burden of Disease Study 2021 Autism Spectrum Collaborators (2025). The global epidemiology and health burden of the autism spectrum: findings from the Global Burden of Disease Study 2021. Lancet Psychiatry 12, 111–121. https://doi.org/10.1016/s2215-0366(24)00363-8.
- Rasmussen, B.K., Jensen, R., and Olesen, J. (1991). A population-based analysis of the diagnostic criteria of the International Headache Society. Cephalalgia 11, 129–134. https://doi.org/10.1046/j.1468-2982.1991. 1103129.x.
- 33. Fendrich, K., Vennemann, M., Pfaffenrath, V., Evers, S., May, A., Berger, K., and Hoffmann, W. (2007). Headache prevalence among



- adolescents-the German DMKG headache study. Cephalalgia 27, 347-354. https://doi.org/10.1111/j.1468-2982.2007.01289.x.
- Pfaffenrath, V., Fendrich, K., Vennemann, M., Meisinger, C., Ladwig, K.H., Evers, S., Straube, A., Hoffmann, W., and Berger, K. (2009). Regional variations in the prevalence of migraine and tension-type headache applying the new IHS criteria: the German DMKG Headache Study. Cephalalgia 29, 48–57. https://doi.org/10.1111/j.1468-2982.2008.01699.x.
- Kim, B.K., Chung, Y.K., Kim, J.M., Lee, K.S., and Chu, M.K. (2013). Prevalence, clinical characteristics and disability of migraine and probable migraine: a nationwide population-based survey in Korea. Cephalalgia 33, 1106–1116. https://doi.org/10.1177/0333102413484990.
- GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018). Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 392, 1789–1858. https://doi.org/10.1016/s0140-6736 (18)32279-7.
- Force, L.M., Abdollahpour, I., Advani, S.M., Agius, D., Ahmadian, E., Alahdab, F., Alam, T., Alebel, A., Alipour, V., Allen, C.A., et al. (2019). The global burden of childhood and adolescent cancer in 2017: an analysis of the Global Burden of Disease Study 2017. Lancet Oncol. 20, 1211–1225. https://doi.org/10.1016/S1470-2045(19)30339-0.
- Vollset, S.E., Ababneh, H.S., Abate, Y.H., Abbafati, C., Abbasgholizadeh, R., Abbasian, M., Abbastabar, H., Abd Al Magied, A.H.A., Abd ElHafeez, S., Abdelkader, A., et al. (2024). Burden of disease scenarios for 204 countries and territories, 2022–2050: a forecasting analysis for the Global Burden of Disease Study 2021. Lancet 403, 2204–2256. https://doi.org/ 10.1016/S0140-6736(24)00685-8.
- Nichols, E., Steinmetz, J.D., Vollset, S.E., Fukutaki, K., Chalek, J., Abd-Allah, F., Abdoli, A., Abualhasan, A., Abu-Gharbieh, E., Akram, T.T.,

- et al. (2022). Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. Lancet Public Health 7, e105–e125. https://doi.org/10.1016/S2468-2667(21)00249-8.
- Wu, A.-M., Cross, M., Elliott, J.M., Culbreth, G.T., Haile, L.M., Steinmetz, J.D., Hagins, H., Kopec, J.A., Brooks, P.M., Woolf, A.D., et al. (2024). Global, regional, and national burden of neck pain, 1990–2020, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021. Lancet Rheumatol. 6, e142–e155. https://doi.org/10.1016/S2665-9913(23)00321-1.
- 41. Hahn, J.W., Woo, S., Park, J., Lee, H., Kim, H.J., Ko, J.S., Moon, J.S., Rahmati, M., Smith, L., Kang, J., et al. (2024). Global, Regional, and National Trends in Liver Disease-Related Mortality Across 112 Countries From 1990 to 2021, With Projections to 2050: Comprehensive Analysis of the WHO Mortality Database. J. Korean Med. Sci. 39, e292.
- Schumacher, A.E., Kyu, H.H., Aali, A., Abbafati, C., Abbas, J., Abbasgholizadeh, R., Abbasi, M.A., Abbasian, M., Abd ElHafeez, S., Abdelmasseh, M., et al. (2024). Global age-sex-specific mortality, life expectancy, and population estimates in 204 countries and territories and 811 subnational locations, 1950–2021, and the impact of the COVID-19 pandemic: a comprehensive demographic analysis for the Global Burden of Disease Study 2021. Lancet 403, 1989–2056. https://doi.org/10.1016/S0140-6736(24)00476-8.
- 43. Oh, J., Kim, S., Kim, M.S., Abate, Y.H., Abd ElHafeez, S., Abdelkader, A., Abdi, P., Abdulah, D.M., Aboagye, R.G., Abolhassani, H., et al. (2025). Global, regional, and national burden of asthma and atopic dermatitis, 1990–2021, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021. Lancet Respir. Med. 13, 425–446. https://doi.org/10.1016/S2213-2600(25)00003-7.

#### **Article**



#### **STAR**\*METHODS

#### **KEY RESOURCES TABLE**

REAGENT or RESOURCE	SOURCE	IDENTIFIER	
Deposited data			
Data source of this paper	Global Burden of Diseases 2021. Available at https://vizhub.healthdata.org/gbd-results/	GBD 2021 is publicly available as of the date of publication.	
Software and algorithms			
Python (version 3.12.8)	https://www.python.org/	Python software (version 3.12.8)	
R (version 4.4.2)	https://www.r-project.org/	R (version 4.4.2)	
Adobe Illustrator CC 2025	https://www.adobe.com/products/ illustrator.html	Adobe company	

#### **EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS**

The GBD 2021 provides comprehensive estimates of the burden of 371 diseases and injuries across 204 countries and territories from 1990 to 2021.<sup>23</sup> It also offers estimates for seven GBD super-regions and 21 GBD regions, categorized by various health metrics such as prevalence and YLD. The data are disaggregated by sex, age, year, and location; however, stratification by gender, race, ethnicity, or ancestry was not available. This study adheres to the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement (Table S3).<sup>30,31</sup> Comprehensive descriptions of the methodology used for GBD estimation are available in prior publications.<sup>23</sup> This research was conducted as part of the GBD Collaborator Network under the established GBD protocol.<sup>11</sup>

#### **METHOD DETAILS**

#### **Case definition and input data**

GBD 2021 provides estimates for headaches categorized into specific subtypes, including migraine and TTH. These estimates are derived from survey data and literature sources related to migraine, TTH, and medication-overuse headaches (MOH).<sup>23</sup> Detailed descriptions of all data sources, including PubMed search strategies, inclusion criteria for systematic reviews, and the number of sources used, are provided in the Figure S4.

Migraine is a disabling primary headache disorder typically characterized by recurrent, moderate to severe, unilateral, pulsatile headaches. Migraine is classified into two major types, with and without aura (transient neurological symptoms); however, GBD does not differentiate between them as most epidemiological studies report only on overall migraine. The reference diagnostic criteria for migraine are based on the ICHD-3.<sup>23</sup> Estimates for migraine are derived from representative, population-based surveys and studies reporting on migraine. 16 Systematic reviews for migraine input data were last conducted for GBD 2017, covering publications up to September 2017; studies based on medical claims were excluded due to their limited comparability with populationrepresentative data. According to ICHD-3, a diagnosis of definite migraine requires fulfillment of five criteria, including attack duration of 4-72 h, specific headache characteristics (e.g., unilateral location, pulsating quality), and associated symptoms such as nausea or photophobia. Cases that meet all but one criterion-most commonly the duration requirement-are classified as probable migraine. 26,32-35 Since GBD 2017, estimates have accounted for both definite and probable migraine by incorporating differences in case definitions across studies. Additionally, TTH is characterized by dull, non-pulsatile, diffuse, band-like (or vice-like) pain of mild to moderate intensity in the head or neck. The reference diagnostic criteria for TTH are also based on the ICHD-3. TTH estimates, like those for migraine, are derived from representative, population-based surveys and studies. 16,23 A systematic review for TTH was also completed for GBD 2017 using identical inclusion criteria, with age- and sex-specific prevalence estimated or split using withinstudy ratios or pooled meta-analytic models. Migraine and TTH are treated as mutually exclusive in GBD analyses to prevent double counting. Each data point for migraine or TTH was labeled "definite" when all ICHD criteria were met and "probable" when exactly one was not; observations coded with earlier editions (ICHD-1 or ICHD-2) were converted to the ICHD-3 standard using version-specific cross-walk coefficients. According to ICHD-3, a diagnosis of definite TTH requires at least 10 episodes of headache lasting from 30 min to 7 days, accompanied by at least two of four features: bilateral location, pressing or tightening quality, mild to moderate intensity, and no aggravation by routine physical activity. Additionally, nausea or vomiting must be absent, and photophobia or phonophobia may be present but not both. As with migraine, a headache fulfilling all criteria is classified as definite TTH, and one that meets all but one criterion is classified as probable TTH.<sup>23</sup> Prior to GBD 2017, estimates did not differentiate between probable



and definite TTH; however, starting with GBD 2017, case definitions used across studies were incorporated to improve the accuracy and consistency of burden estimates.<sup>23</sup> MOH was ascertained in two steps. First, respondents were screened for chronic headache (≥15 headache days per month for ≥3 months); second, follow-up questions captured regular over-use of acute headache medication as specified by ICHD-3.<sup>5,23</sup> While MOH was included in the analysis to address the overlap between migraine and tension-type headaches, individual results for MOH are not presented separately.<sup>16,23</sup> Input data for MOH were extracted from population-based prevalence studies. A meta-analysis was used to estimate the proportion of cases attributable to migraine and to TTH, allowing MOH to be classified into MOH-migraine and MOH-TTH.

#### Data processing and disease modeling

Both migraine and TTH were modeled in GBD 2021 with standard DisMod-MR settings. Excess mortality was set to zero, and it was assumed that there was no incidence or prevalence before the age of five. Each condition was categorized into probable, definite, and total, and separate DisMod-MR models were executed for each category. The results were then scaled to the total category to ensure consistency across estimates. For migraine, earlier data, particularly from before the adoption of the ICHD criteria, primarily reported on definite migraine.<sup>23</sup> These data were adjusted to the total migraine category to improve modeling accuracy. Migraine and TTH were modeled separately using DisMod-MR 2.1, with estimates stratified into definite, probable, and total categories. Historical data predating the ICHD adoption were adjusted to align with the total envelope. Using MR-BRT regression, the proportion of symptomatic time was estimated at 9.3% for definite migraine and 6.6% for probable migraine. For TTH, unrealistic age patterns were observed in sex-specific regression models, necessitating the implementation of an age-based adjustment model for both sexes. Initially, sex-specific regression models were applied, but they produced unrealistic age patterns for females. To address this, a unified age-based adjustment was applied to both sexes, ensuring more accurate representation across age groups. MR-BRT regression estimated the symptomatic time proportion to be 2.9% for definite TTH and 2.1% for probable TTH. 16,23 MOH was modeled separately in DisMod-MR (remission cap 0.4). Using meta-analytic data, 53.2% of the year was deemed symptomatic, and prevalence was split into MOH-migraine (73.2%) and MOH-TTH (26.8%). Prevalence was divided into MOH-migraine and MOH-TTH, with each subtype inheriting the DW of its respective parent condition (migraine or TTH). As MOH is defined as mutually exclusive from both migraine and TTH, no additional overlap adjustment was necessary; standard GBD comorbidity methods were applied.

The GBD 2021 estimation process addresses data sparsity through hierarchical modeling and statistical borrowing across time, geography, and age. These adjustments help mitigate bias and enable robust estimation even in regions with limited input data. <sup>23</sup> Furthermore, YLD is a quantitative measure of health loss caused by specific diseases or disabilities and plays a critical role in comparing disease burdens and prioritizing public health policies in GBD studies. YLD is calculated as the product of prevalence and DW, where prevalence is estimated using Bayesian modeling tools such as DisMod-MR, and DWs are derived from global surveys that measure disease severity on a scale from 0 (perfect health) to 1 (death). <sup>31</sup> In calculating YLD, GBD stratifies data by sex, age, region, and year while independently evaluating the effects of comorbid conditions to avoid double counting. The calculation of YLD in GBD serves as an essential tool for global comparisons of disease burdens and for addressing regional health disparities.

#### Classification of geographic locations

GBD produced estimates for 204 countries and territories, organized into 21 regions and 7 super-regions. The seven super-regions are: Central Europe, Eastern Europe, and Central Asia, High-income, Latin America and the Caribbean, North Africa and the Middle East, South Asia, Southeast Asia, East Asia, and Oceania, and Sub-Saharan Africa. A full list of GBD regions is provided in Table S4. Similar to GBD 2019, GBD 2021 classifies areas as standard or non-standard. Standard GBD locations include all subnational areas from countries with populations exceeding 200 million and high-quality data. Subnational data for China, India, the US, and Brazil are considered standard locations, whereas Indonesia is not. China, India, the US, and Brazil are also included at the national level. All other countries with subnational estimations are classified as non-standard locations.

#### **QUANTIFICATION AND STATISTICAL ANALYSIS**

#### Association between socio-economic indicators with the migraine and TTH

We used the SDI and the HAQ Index to examine the relationship between migraine, TTH, and socio-economic indicators. The SDI is a composite measure that reflects the social and economic conditions affecting health outcomes in each region. It is calculated as the geometric mean of three indices: the total fertility rate under age 25 years (TFU25), the average educational attainment of individuals aged 15 years and older (EDU15+), and the lagged distributive income per capita. The HAQ Index measures healthcare access and quality based on the mortality rates of conditions that should not result in death given effective medical care, providing insight into the performance of healthcare systems across regions. Both SDI and HAQ Index range from 0 to 1, where 0 indicates the lowest level of socio-demographic development and minimal healthcare access, respectively.

We examined the associations between the national SDI and HAQ Index and the age-standardized prevalence and YLD rates for migraine and TTH in 2021. Polynomial regression models were applied to capture the nonlinear relationships between these socio-economic indicators and health outcomes.<sup>37</sup>

#### **Article**



#### **Estimate projections and decomposition analysis**

We utilized the GBD 2021 forecasting framework to estimate the age-standardized YLD rates and all-age YLD numbers for migraine and TTH from 2022 to 2050. Non-fatal disease burden was forecasted using mixed-effects models, which were employed to directly model prevalence and incidence or to model the mortality-incidence ratio and mortality-prevalence ratio, converting forecasted mortality into incidence and prevalence. However, due to the lack of mortality data for migraine and TTH, the prevalence was directly modeled following the equation below:

$$logit(G_{l,a,s,y}) = \beta_0 + \beta_1 SDI_{l,y} + \pi_{0:l,a,s} + \epsilon_{l,a,s,y}$$

where  $G_{I,a,s,y}$  represents the age-sex-location-year-specific prevalence,  $\pi_{0:I,a,s}$  if the random intercept for age-sex-location, and  $\epsilon_{I,a,s,y}$  is the residual term. <sup>38</sup> From the modeled prevalence, YLDs were calculated by multiplying the estimated prevalence by the recent average DW. This approach assumes that DW remains constant over time, recognizing that future shifts in medical technologies and societal factors may introduce variability. <sup>38</sup> The projected long-term trends through 2050 were generated using the internally optimized GBD forecasting framework, which applies scenario-based smoothing and calibration techniques to align with historical data patterns. Although formal back-testing procedures were not implemented, this approach is designed to produce reliable projections based on historical burden trajectories and demonstrated consistency across multiple disease domains. <sup>39</sup>

To examine the relative contributions of population growth, population aging, and changes in YLD rates for migraine and TTH between 2021 and 2050, the Das Gupta decomposition method was applied. <sup>40</sup> To achieve this, we employed the decomposition methodology developed by Das Gupta, a widely recognized approach in demographic research for analyzing the impact of population structure and age distribution on health outcomes. This method enables a detailed quantitative evaluation of the contribution of each factor to variations in YLDs over time. <sup>30</sup>

The formula utilized in this analysis disaggregates the total YLDs into components attributable to population aging, overall population growth, and epidemiological changes. This approach provides critical insights into the underlying dynamics driving the burden of disease. The decomposition formula is expressed as follows:

$$YLDs_{ay,py,ey} = \sum_{i=1}^{i=20} (a_{i,y} * p_y * e_{i,y})$$

The total YLDs for migraine and TTH, denoted as  $YLDs_{ay,py,ey}$ , are calculated as a function of age distribution, total population size, and age-specific YLD rates. In this formulation, i represents discrete age groups, and y denotes the observation year ranging from 2021 to 2050. The term  $a_{i,y}$  indicates the proportion of the population,  $p_y$  refers to the total population size, and  $e_{i,y}$  corresponds to the YLD rate for the specific condition (migraine or TTH) within. This formulation enables the decomposition of total YLDs into components attributable to demographic structure—specifically population growth and aging—and epidemiological changes. By algebraically disaggregating these standardized effects, the analysis quantifies the relative contribution of each factor to the overall change in disease burden.  $^{41}$ 

#### **Data presentation**

The age-standardized rates for prevalence and YLD of headache disorders were calculated using the GBD world population age standard. Unless stated as an age-specific rate, all rates are presented in age-standardized rates. To evaluate temporal changes (e.g., 1990 to 2021), we determined the percentage change, with the difference between the end and start rates divided by the start rate. Final point estimates are reported with 95% UIs. The UIs represent the range within which the true value is expected to fall. They were calculated as the 2.5th and 97.5th percentile of the distribution of 500 draws at each step in the migraine and TTH estimation process. These 500 draws were used to propagate uncertainty arising from multiple sources, including variability in input data, model parameters, and DWs. Uncertainty was systematically incorporated and propagated throughout the modeling process in accordance with the standard GBD estimation framework. All analyses were conducted using Python software (version 3.12.8; Python Software Foundation, Wilmington, DE, USA) and R (version 4.4.2; R Foundation, Vienna, Austria). The full affiliations of the GBD 2021 Headache Collaborators are provided in Data S1.