Clinical Orthopaedics, 2026, Volume 1, Issue 1
https://ojs.bbwpublisher.com/index.php/CO
Online ISSN: 3083-1520
Print ISSN: 3083-1539

Global, Regional and National Burdens of Gout in People Aged 20 - 54 Years from 1990 to 2021: An Analysis Based on the 2021 Global Burden of Disease Study

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Abstract: *Objective*: To describe the epidemiology of gout in people aged 20 - 54 years at global, regional, and national levels using data from the 2021 GBD study, and evaluate the impact of BMI and renal dysfunction on the burden of gout in this age group. *Methods*: Incidence, prevalence, and DALYs of gout were extracted from GBD 2021. Descriptive analysis was performed at global, regional, and national levels. Trends were analyzed using estimated annual percentage change (EAPC) and joinpoint regression analysis. Proportional attributable fractions of risk factors (high BMI and impaired kidney function) were calculated. *Results*: Globally, from 1990 to 2021, the rates of incidence, prevalence, and DALYs of gout in people aged 20 - 54 years increased. Regionally, the United States, China, and East Asia had significant increases. By SDI quintiles, the highest increases in prevalence and DALYs were in the High SDI quintile, and in incidence in the High-middle SDI quintile. Males had higher values than females. The fastest increasing periods for incidence (1996 - 2004), prevalence (1996 - 2004), and DALYs (1996 - 2003) were identified. Globally in 2021, high BMI and impaired kidney function accounted for certain proportions of DALYs, with regional and national variations. *Conclusion*: The burden of gout in people aged 20 - 54 years has increased significantly worldwide, with differences across various factors. Prevention strategies, improved management, and further research on gout in this age group are crucial, especially regarding its relationship with high BMI and impaired renal function.

Keywords: Gout; GBD 2021; High BMI; Impaired kidney function

Online publication: August 14, 2026

1. Introduction

Gout is the most common inflammatory arthritis, which manifests as an acute attack of one or more joints with pain, swelling, redness, and fever, leading to decreased mobility and impaired physical function, and

progressing to chronic destructive arthritis [1-2]. Chronic gout leads to tophi formation, chronic joint pain, and joint erosion and damage. It is a common cause of activity limitation in adults, resulting in increased morbidity and disability-adjusted life years (DALYs) [3-5]. Recent studies have used prevalence, incidence and disability-adjusted life years (YLDs) data from the 2021 Global Burden of Disease Study to assess the burden of gout in individuals aged ≥55 years in 204 countries and its changing trends from 1990 to 2021 at global, regional and country levels [6]. Previous studies have also used data from the 2019 Global Burden of Disease (GBD) study to report global, regional and national annual incidence, point prevalence and disability-adjusted life years (YLD) rates and trends for gout among adolescents and young adults aged 15-39 years [7]. The burden of gout varies among different populations, and quantifying the burden and patterns of gout cases by age and sex, and making future projections, is necessary to effectively meet the needs of the current and future populations [8]. To our knowledge, there are no detailed GBD studies examining the global burden and trends of gout in people aged 20-54 years.

The aim of this study was to conduct a descriptive and trend analysis of the prevalence, incidence and disability-adjusted life years (DALYs) epidemiology of gout at global, regional and country levels using data from the 2021 GBD study. The impact of body mass index (BMI) and renal dysfunction as risk factors on the burden of gout in people aged 20-54 years was also evaluated.

2. Methods

2.1. Data source

GBD 2021 used the latest available epidemiological data and improved standardized methods to comprehensively assess the health loss across 288 causes of death, 371 diseases and injuries, and 88 risk factors in 204 countries and territories, including subnational estimates for 21 countries and territories and years from 1990 to 2021.

In this study, the estimates and their 95 % uncertainty intervals (UIs) for incidence, prevalence, and disability-adjusted life-years (DALYs) of Gout were extracted from GBD 2021. All rates were reported per 100,000 population. Developed by GBD researchers and used to help produce these estimates, the Socio-demographic Index (SDI) is a composite indicator of development status strongly correlated with health outcomes. It is the geometric mean of 0 to 1 indices of total fertility rate under the age of 25 (TFU25), mean education for those ages 15 and older (EDU15+), and lag distributed income (LDI) per capita. As a composite, a location with an SDI of 0 would have a theoretical minimum level of development relevant to health, while a location with an SDI of 1 would have a theoretical maximum level. the sociodemographic index (SDI) is divided into five levels (Low SDI, Low-middle SDI, Middle SDI, High-middle SDI, and High SDI).

2.2. Descriptive analysis

To derive a comprehensive understanding in the burden of Gout, a descriptive analysis was performed at global, regional, and national levels. The global case number, and rate of incidence, prevalence, and DALYs for Gout in both sexes, males, and females from 1990 to 2021 were visually illustrated. Moreover, the case number and ASR of incidence, prevalence,and DALYs for Gout in both sexes in 1990 and 2021 were compared at global, regional (21 GBD geographical regions), and national (204 countries and territories, including subnational estimates for 21 countries and territories) levels, as well as five levels (Low SDI, Low-

middle SDI, Middle SDI, High-middle SDI, and High SDI).

2.3.Trend analysis

Exploring the temporal trends of diseases serves as an indispensable part of epidemiology and further facilitates the development of more precise preventive strategies. We aimed to explore the trends of Gout from the overall, local, and multi-dimension scopes.

Firstly, we used estimated annual percentage change (EAPC) to quantify the overall trend of Gout burden. It is necessary to implement standardization when comparing several groups with distinct age structures or one certain group with age profile changing over time. Therefore, the trend of ASR, which is measured by EAPC, appears to be a more robust index for monitoring the changes of disease pattern.

We used the estimated annual percentage change (EAPC) to quantify trends in Gout burden from 1990 to 2021. A linear regression model was established to describe the relationship between time and the natural logarithm (ln) of the age standardized rate: $y = \alpha + \beta x + e$, where y represents the ln (age-standardised rate), x is the calendar year, and e is the error term. The EAPC was calculated using $EAPC = 100 \times [\exp(\beta) — 1]$, with its 95% confidence interval (CI) derived from the regression model. An age standardized rate is deemed statistically increasing if both the EAPC estimate and its 95% CI are greater than 0, and statistically decreasing if both are less than 0. If the EAPC estimate and its 95% CI include 0, the trend in the age-standardised rate is considered stable, indicating no significant change over time [9].

Then, we used joinpoint regression analysis to detect the local trend of Gout burden. Joinpoint regression analysis (Joinpoint Trend Analysis Software, Version 5.3.0 November 12, 2024) could divide the overall trend into multiple subsegments according to the inflection points and further evaluate the magnitude of each epidemiological trend by calculating the annual percentage change (APC) and its 95 % CI of each subsegment. Moreover, the average APC (AAPC) between 1990 and 1999, between 2000 and 2009, and between 2010 and 2021 were also estimated by weighting the regression coefficient of each subsegment by the span width of segmented interval [10]. Monte Carlo permutation method [11] with 4499 randomly permuted data set was utilized to calculate the AAPC and its 95 % CI, and the overall asymptotic significance level was maintained through a Bonferroni correction. If the APC/AAPC estimation and its lower boundary of 95 % CI were both > 0, an increasing trend was deemed during one certain period. On the contrary, if the APC/AAPC estimation and its upper boundary of 95 % CI were both < 0, a decreasing trend was deemed during one certain period. Otherwise, the trend was deemed to be stable. In GBD 2021, high body-mass index (BMI), and impaired kidney function were identified as risk factors associated with the onset of gout, which remained leading contributors to risk-attributable DALYs, were stratified by Socio-demographic Index (SDI). High BMI was defined as the BMI of individuals aged ≥ 20 years ≥ 25 kg/m ^{2}.

3. Results

3.1. Descriptive analysis of Gout burden in aged 20-54 years at global, regional, and national levels using broad estimation method

Globally, the Rate of incidence, prevalence and DALYs of Gout for both sexes by aged 20-54 years elevated by an average of 1.11 (1.06, 1.16), 0.92 (0.88, 0.95) and 1.1 (1.05, 1.15) per year from 1990 to 2021, respectively. From a regional dimension, when it comes to the increases in the rates of incidence, prevalence and DALYs, the United States of America stands out as the region where the increases are the

most significant. Close behind are China and the East Asian region. In addition, from the scope of SDI quintiles, the largest increases in Rate of prevalence, and DALYs were detected in High SDI quintile, the largest increases in Rate of incidence was detected in High-middle SDI quintile. (**Table 1**, **Table 2**, **Table 3**). Nationally, the overall trends of disease burden varied considerably across all locations with the highest EAPC of incidence, prevalence and DALYs found in United States of America and the lowest EAPC of incidence, prevalence, and DALYs across countries and territories found in Niger.

Globally, the Number and Rate of incidence, prevalence and DALYs demonstrated dramatically increasing trends of these three metrics showed increasing trends from 1990 to 2021, with much higher values in males than in females (**Figure 1**). Nationally, the incidence, prevalence and DALYs of Gout varied remarkably across the world, with the highest number of incidence, prevalence, and DALYs cases found in China, and the highest Rate of incidence, prevalence, and DALYs found in the United States of America (**Figure 2**).

Table 1. The Number and Rate of incidence of Gout in 1990 and 2021 for both sexes by aged 20-54 years, with Rate EAPC from 1990 to 2021

location_name	Number_2021	Number_1990	Rate_2021	Rate_1990	EAPC_Rate
GLOBAL	3877062 (2758101, 5197993)	1930628 (1390664, 2574605)	102.85 (73.17, 137.9)	80.32 (57.86, 107.11)	0.92 (0.88, 0.95)
China	1218448 (855836, 1641884)	636826 (460132, 845644)	171.74 (120.63, 231.42)	108.32 (78.27, 143.84)	1.72 (1.62, 1.81)
United States of America	335593 (247513, 436702)	170545 (123751, 228528)	222.12 (163.83, 289.05)	133.67 (96.99, 179.12)	1.88 (1.73, 2.03)
Low-middle SDI	632473 (452251, 842685)	273555 (196296, 365253)	69.07 (49.39, 92.03)	58.25 (41.8, 77.78)	0.59 (0.55, 0.62)
High-middle SDI	868593 (605411, 1170160)	465026 (336823, 620201)	132.81 (92.57, 178.93)	89.28 (64.67, 119.08)	1.42 (1.37, 1.47)
Middle SDI	1331279 (944162, 1787476)	625721 (450156, 827739)	108.28 (76.79, 145.38)	79.73 (57.36, 105.47)	1.17 (1.11, 1.22)
Low SDI	261837 (187749, 351022)	100564 (72157, 135068)	58.04 (41.62, 77.81)	54.53 (39.13, 73.24)	0.24 (0.19, 0.29)
High SDI	780504 (565838, 1036657)	464434 (334472, 622171)	151.17 (109.59, 200.78)	105.14 (75.72, 140.84)	1.23 (1.16, 1.3)
Andean Latin America	17989 (12797, 24089)	5954 (4292, 7950)	55.26 (39.31, 74)	37.97 (27.37, 50.7)	1.3 (1.26, 1.33)
Australasia	25176 (18093, 34327)	12638 (9257, 16926)	172.61 (124.05, 235.35)	125.58 (91.98, 168.19)	0.93 (0.83, 1.03)
Caribbean	11364 (8068, 15399)	5624 (3992, 7579)	49.54 (35.17, 67.13)	35.41 (25.13, 47.72)	1.15 (1.1, 1.2)
Central Asia	34924 (24915, 46923)	16894 (12199, 22133)	74.89 (53.43, 100.62)	56.82 (41.03, 74.44)	1.03 (0.96, 1.09)
Central Europe	40118 (27843, 54608)	32952 (23461, 44548)	73.37 (50.92, 99.87)	55.56 (39.56, 75.12)	0.8 (0.76, 0.84)
Central Latin America	51498 (36444, 69415)	19928 (14478, 26802)	41.21 (29.17, 55.55)	29.22 (21.23, 39.29)	1.17 (1.15, 1.19)
Central Sub-Saharan Africa	32279 (22908, 43032)	10796 (7711, 14486)	59.4 (42.15, 79.18)	53.41 (38.15, 71.66)	0.36 (0.34, 0.39)
East Asia	1265287 (890899, 1704469)	663324 (479453, 880426)	171.98 (121.09, 231.68)	109.04 (78.81, 144.72)	1.69 (1.6, 1.78)

location_name	Number_2021	Number_1990	Rate_2021	Rate_1990	EAPC_Rate
Eastern Sub-Saharan Africa	98969 (70649, 132713)	35857 (25770, 48015)	57.72 (41.2, 77.39)	52.92 (38.03, 70.86)	0.32 (0.25, 0.38)
High-income Asia Pacific	111507 (77963, 150792)	93239 (66115, 126814)	132.5 (92.64, 179.19)	105.85 (75.06, 143.97)	0.72 (0.67, 0.76)
North Africa and Middle East	262354 (185918, 354169)	81012 (58308, 108187)	84.56 (59.92, 114.15)	60.39 (43.46, 80.64)	1.09 (1.04, 1.14)
Oceania	6889 (4934, 9214)	2588 (1884, 3442)	109.23 (78.23, 146.1)	95.77 (69.73, 127.38)	0.41 (0.4, 0.43)
South Asia	599907 (427678, 802171)	258747 (184479, 348227)	65.58 (46.75, 87.69)	56.74 (40.45, 76.36)	0.49 (0.46, 0.51)
Southeast Asia	423581 (303107, 565832)	169622 (122367, 225545)	119.49 (85.51, 159.62)	83.45 (60.2, 110.96)	1.29 (1.25, 1.33)
Southern Latin America	43704 (31696, 58606)	22721 (16408, 30346)	130.58 (94.7, 175.11)	102.18 (73.79, 136.46)	0.72 (0.67, 0.76)
Southern Sub-Saharan Africa	32868 (23577, 44342)	14405 (10409, 19126)	83.63 (59.99, 112.82)	66.9 (48.34, 88.82)	0.67 (0.61, 0.72)
Tropical Latin America	60850 (43032, 83365)	24168 (17171, 32713)	52.17 (36.89, 71.47)	35.46 (25.2, 48)	1.28 (1.25, 1.31)
Western Europe	189782 (135048, 255727)	149375 (105223, 201130)	96.56 (68.71, 130.11)	79.05 (55.69, 106.44)	0.71 (0.65, 0.76)
Western Sub-Saharan Africa	113252 (81233, 151777)	41206 (29544, 54922)	59.89 (42.96, 80.26)	57.85 (41.48, 77.11)	0.11 (0.09, 0.13)

Table 2. The Number and Rate of Prevalence of Gout in 1990 and 2021 for both sexes by aged 20-54 years, with Rate EAPC from 1990 to 2021

location_name	Number_2021	Number_1990	Rate_2021	Rate_1990	EAPC_Rate
GLOBAL	19221517 (13705460, 25371091)	9120289 (6521824, 12216297)	509.92 (363.59, 673.06)	379.44 (271.33, 508.25)	1.11 (1.06, 1.16)
China	5931952 (4177272, 7868531)	2899204 (2075500, 3853742)	836.09 (588.77, 1109.05)	493.15 (353.04, 655.51)	1.98 (1.88, 2.09)
United States of America	2336377 (1752051, 3000584)	996181 (719723, 1351202)	1546.42 (1159.66, 1986.05)	780.79 (564.1, 1059.04)	2.56 (2.37, 2.76)
Low-middle SDI	2810521 (1993372, 3793537)	1197835 (854074, 1622846)	306.95 (217.7, 414.3)	255.08 (181.88, 345.59)	0.65 (0.61, 0.68)
High-middle SDI	4251812 (2993876, 5647044)	2155699 (1541292, 2857558)	650.13 (457.79, 863.47)	413.89 (295.92, 548.64)	1.62 (1.56, 1.69)
Middle SDI	6277279 (4455095, 8357876)	2811512 (2012811, 3773148)	510.56 (362.35, 679.78)	358.25 (256.48, 480.78)	1.37 (1.3, 1.43)
Low SDI	1127468 (805385, 1531040)	433701 (310316, 590883)	249.93 (178.53, 339.39)	235.18 (168.27, 320.41)	0.24 (0.19, 0.29)
High SDI	4743293 (3468645, 6280731)	2515487 (1802383, 3421372)	918.69 (671.81, 1216.46)	569.44 (408.01, 774.5)	1.68 (1.57, 1.8)
Andean Latin America	84734 (60334, 114495)	27172 (19113, 37542)	260.29 (185.34, 351.72)	173.28 (121.89, 239.41)	1.41 (1.37, 1.46)
Australasia	142642 (100415, 195415)	66830 (48247, 88365)	977.98 (688.46, 1339.8)	664.08 (479.42, 878.06)	1.2 (1.07, 1.33)
Caribbean	54255 (38523, 73762)	25960 (18187, 35661)	236.53 (167.95, 321.57)	163.44 (114.5, 224.51)	1.28 (1.22, 1.35)

location_name	Number_2021	Number_1990	Rate_2021	Rate_1990	EAPC_Rate
Central Asia	158772 (112501, 214399)	74731 (53495, 100948)	340.46 (241.24, 459.74)	251.33 (179.91, 339.5)	1.16 (1.08, 1.24)
Central Europe	183066 (128511, 250062)	147147 (104738, 199023)	334.8 (235.03, 457.33)	248.13 (176.61, 335.6)	0.85 (0.81, 0.9)
Central Latin America	246939 (174539, 339994)	92546 (65769, 127118)	197.63 (139.69, 272.1)	135.68 (96.43, 186.37)	1.25 (1.24, 1.27)
Central Sub-Saharan Africa	139320 (99086, 186301)	46350 (32803, 63743)	256.37 (182.33, 342.82)	229.3 (162.27, 315.34)	0.4 (0.36, 0.43)
East Asia	6176028 (4351221, 8185390)	3027376 (2168016, 4022545)	839.47 (591.44, 1112.6)	497.64 (356.38, 661.23)	1.95 (1.84, 2.06)
Eastern Sub-Saharan Africa	423799 (303935, 580844)	153125 (109887, 208976)	247.15 (177.25, 338.73)	225.98 (162.17, 308.4)	0.32 (0.25, 0.39)
High-income Asia Pacific	603685 (418251, 824249)	477759 (334198, 652590)	717.36 (497.01, 979.45)	542.38 (379.4, 740.86)	0.9 (0.86, 0.95)
North Africa and Middle East	1187839 (844972, 1606479)	354534 (254400, 478614)	382.83 (272.33, 517.76)	264.27 (189.63, 356.76)	1.19 (1.13, 1.26)
Oceania	31480 (22639, 42355)	11583 (8478, 15327)	499.12 (358.94, 671.55)	428.6 (313.73, 567.13)	0.48 (0.47, 0.49)
South Asia	2623251 (1867585, 3558220)	1120630 (795351, 1524285)	286.76 (204.16, 388.97)	245.73 (174.4, 334.24)	0.53 (0.5, 0.55)
Southeast Asia	1966364 (1401354, 2630795)	752270 (536916, 1013725)	554.72 (395.33, 742.16)	370.09 (264.15, 498.72)	1.47 (1.42, 1.51)
Southern Latin America	246592 (176827, 332270)	122223 (86337, 166342)	736.78 (528.34, 992.78)	549.62 (388.25, 748.02)	0.89 (0.82, 0.95)
Southern Sub-Saharan Africa	144400 (103359, 191902)	62105 (43963, 83950)	367.39 (262.97, 488.25)	288.42 (204.17, 389.87)	0.71 (0.65, 0.77)
Tropical Latin America	288193 (204140, 397448)	110497 (77778, 152336)	247.08 (175.02, 340.75)	162.14 (114.13, 223.53)	1.39 (1.36, 1.42)
Western Europe	1079110 (744800, 1478030)	796679 (548775, 1093081)	549.04 (378.95, 752.01)	421.62 (290.43, 578.49)	0.94 (0.88, 1.01)
Western Sub-Saharan Africa	491910 (351958, 666116)	178840 (127544, 241994)	260.12 (186.11, 352.24)	251.08 (179.06, 339.74)	0.12 (0.09, 0.14)

Table 3. The Number and Rate of DALYs of Gout in 1990 and 2021 for both sexes by aged 20-54 years, with Rate EAPC from 1990 to 2021

location_name	Number_2021	Number_1990	Rate_2021	Rate_1990	EAPC_Rate
GLOBAL	629303 (386588, 959547)	300043 (186574, 451667)	16.69 (10.26, 25.46)	12.48 (7.76, 18.79)	1.1 (1.05, 1.15)
China	195318 (118227, 300653)	96058 (59672, 146121)	27.53 (16.66, 42.38)	16.34 (10.15, 24.85)	1.96 (1.86, 2.07)
United States of America	74808 (47127, 111523)	32337 (19865, 49071)	49.51 (31.19, 73.82)	25.35 (15.57, 38.46)	2.53 (2.33, 2.73)
Low-middle SDI	92207 (56944, 142624)	39371 (24561, 60194)	10.07 (6.22, 15.58)	8.38 (5.23, 12.82)	0.65 (0.62, 0.69)
High-middle SDI	139671 (83936, 216686)	71074 (44169, 108249)	21.36 (12.83, 33.13)	13.65 (8.48, 20.78)	1.62 (1.55, 1.68)
Middle SDI	206310 (126463, 314454)	92961 (57225, 140854)	16.78 (10.29, 25.58)	11.85 (7.29, 17.95)	1.35 (1.29, 1.41)

location_name	Number_2021	Number_1990	Rate_2021	Rate_1990	EAPC_Rate
Low SDI	37046 (23083, 57143)	14175 (8711, 21798)	8.21 (5.12, 12.67)	7.69 (4.72, 11.82)	0.26 (0.21, 0.32)
High SDI	153703 (96509, 233985)	82263 (51159, 124724)	29.77 (18.69, 45.32)	18.62 (11.58, 28.23)	1.66 (1.54, 1.77)
Andean Latin America	2816 (1674, 4440)	908 (554, 1408)	8.65 (5.14, 13.64)	5.79 (3.53, 8.98)	1.38 (1.33, 1.42)
Australasia	4629 (2723, 7305)	2174 (1338, 3271)	31.74 (18.67, 50.08)	21.61 (13.3, 32.51)	1.19 (1.06, 1.32)
Caribbean	1799 (1093, 2785)	865 (514, 1351)	7.84 (4.76, 12.14)	5.44 (3.24, 8.5)	1.26 (1.2, 1.33)
Central Asia	5234 (3266, 8103)	2463 (1498, 3734)	11.22 (7, 17.37)	8.28 (5.04, 12.56)	1.14 (1.07, 1.22)
Central Europe	5999 (3551, 9298)	4831 (2959, 7498)	10.97 (6.49, 17)	8.15 (4.99, 12.64)	0.86 (0.82, 0.9)
Central Latin America	8185 (5048, 12771)	3086 (1849, 4719)	6.55 (4.04, 10.22)	4.52 (2.71, 6.92)	1.23 (1.21, 1.24)
Central Sub-Saharan Africa	4552 (2763, 7244)	1507 (909, 2342)	8.38 (5.08, 13.33)	7.45 (4.49, 11.59)	0.43 (0.4, 0.46)
East Asia	203374 (123245, 313345)	100326 (62415, 152245)	27.64 (16.75, 42.59)	16.49 (10.26, 25.03)	1.93 (1.82, 2.04)
Eastern Sub-Saharan Africa	13949 (8578, 21811)	5020 (3091, 7863)	8.13 (5, 12.72)	7.41 (4.56, 11.6)	0.34 (0.27, 0.41)
High-income Asia Pacific	19865 (12085, 30838)	15739 (9493, 24238)	23.61 (14.36, 36.65)	17.87 (10.78, 27.52)	0.9 (0.85, 0.95)
North Africa and Middle East	38830 (23688, 59399)	11700 (7222, 18470)	12.51 (7.63, 19.14)	8.72 (5.38, 13.77)	1.18 (1.11, 1.24)
Oceania	1031 (613, 1558)	380 (232, 582)	16.35 (9.72, 24.71)	14.05 (8.6, 21.52)	0.48 (0.46, 0.49)
South Asia	85827 (52712, 133820)	36683 (22519, 56898)	9.38 (5.76, 14.63)	8.04 (4.94, 12.48)	0.53 (0.51, 0.55)
Southeast Asia	64801 (39390, 97405)	24879 (15348, 37954)	18.28 (11.11, 27.48)	12.24 (7.55, 18.67)	1.46 (1.42, 1.51)
Southern Latin America	8010 (4878, 11986)	3995 (2457, 5970)	23.93 (14.57, 35.81)	17.96 (11.05, 26.84)	0.88 (0.82, 0.94)
Southern Sub-Saharan Africa	4640 (2835, 7104)	2022 (1247, 3091)	11.81 (7.21, 18.07)	9.39 (5.79, 14.35)	0.66 (0.6, 0.72)
Tropical Latin America	9474 (5739, 14366)	3664 (2224, 5633)	8.12 (4.92, 12.32)	5.38 (3.26, 8.27)	1.38 (1.34, 1.41)
Western Europe	35280 (21003, 54590)	26079 (15516, 40144)	17.95 (10.69, 27.78)	13.8 (8.21, 21.25)	0.94 (0.87, 1.01)
Western Sub-Saharan Africa	16244 (10005, 25023)	5870 (3582, 9035)	8.59 (5.29, 13.23)	8.24 (5.03, 12.68)	0.14 (0.12, 0.17)

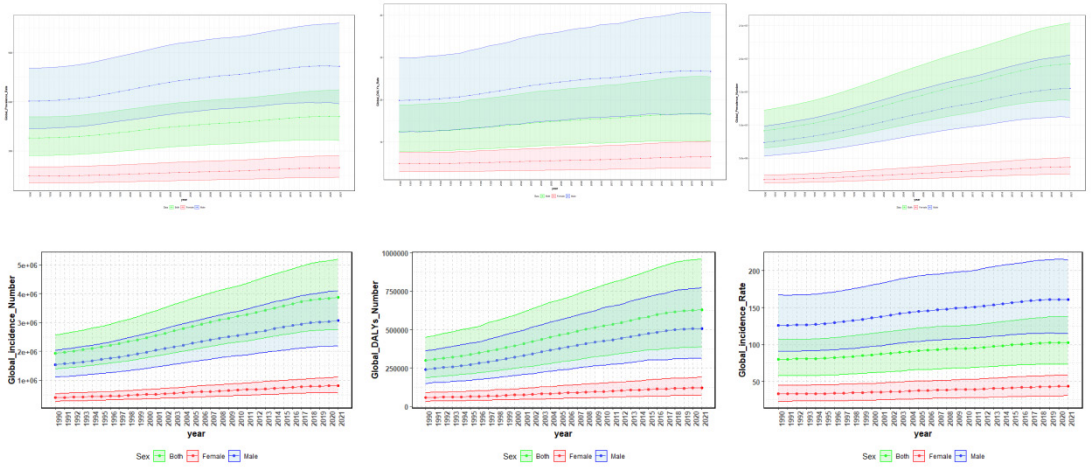

Figure 1. Global number and rate of incidence, prevalence, and DALYs of gout from 1990 to 2021, by sex

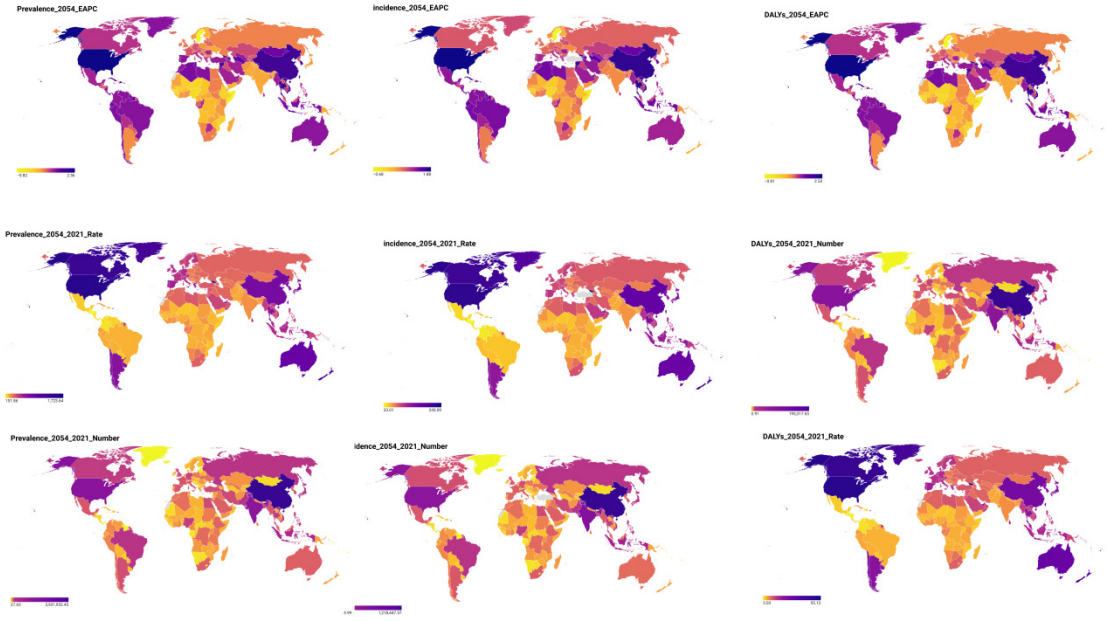

Figure 2. Nationallevel burden of gout: number and rate of incidence, prevalence, and DALYs across the world

3.2. Global trends in Gout burden using joinpoint regression analysis

The results of joinpoint regression analysis on the burden of Gout were demonstrated in **Figure 3** and **Table 4**.

Between 1990 and 2021, continuously dramatically increasing trends for aged 20-54 years (Number and Rate) of incidence, prevalence and DALYs of Gout occurred. Globally, the gout incidence Rate in individuals aged 20–54 years increased between 1990 and 2021 ,AAPC 0.80 [95% CI 0.75 to 0.88] ,with the most rapidly increasing period at 1996–2005 after undergoing six joinpoints; As for the gout incidence Number also increased between 1990 and 2021, AAPC 2.28 [95% CI 2.24 to 2.32] ,with the most rapidly increasing period at 1996–2004 after undergoing six joinpoints. Accordingly, the gout prevalence also increased between 1990 and 2021. Specifically, the trend for the Rate of Prevalence experienced six joinpoints of no changes in 2018–2021, with the most rapidly increasing period at 1996–2004 , AAPC 0.96 [95% CI 0.93 to 1.00]. Meanwhile, the trend for the Number of prevalence demonstrated six joinpoints of increases in all periods, with the most rapidly increasing period at 1996–2003 , AAPC 2.44 [95% CI 2.38 to 2.50]. Regarding the trend for the Rate

of DALYs, it underwent six joinpoints of no changes in 2018–2021, with the most rapidly increasing period at 1996–2004 , AAPC 0.95 [95% CI 0.91 to 0.99]; the Rate of DALYs, it underwent six joinpoints of increase in all periods, with the most rapidly increasing period at 1996–2003 , AAPC 2.42 [95% CI 2.36 to 2.48]. The Joinpoint regression analysis of globally in aged 20-54 years incidence, prevalence and DALYs for gout Rate and Number in each period between 1990 and 2021 can be found in online supplemental data.

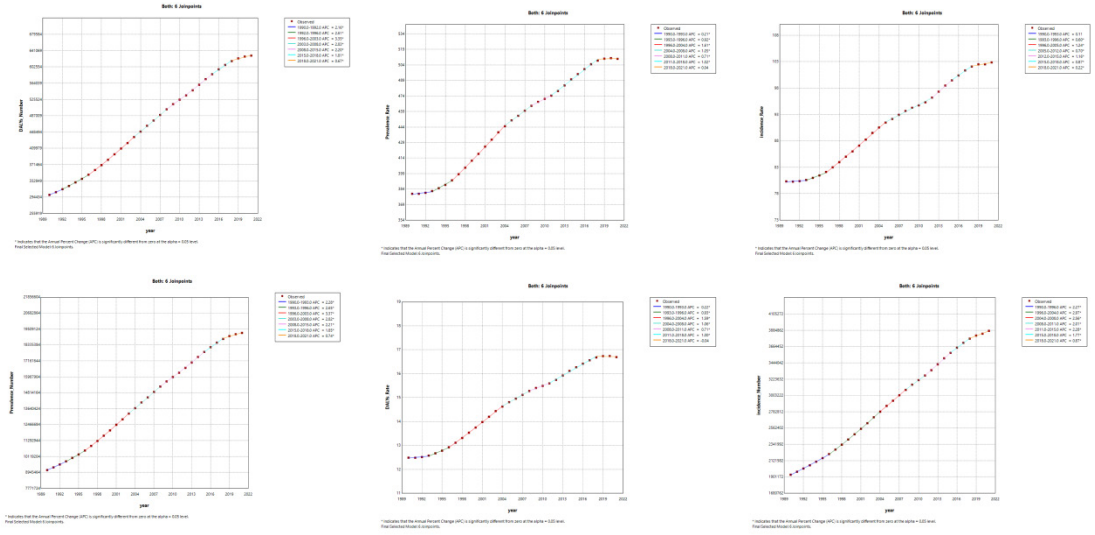

Figure 3. The joinpoint regression analysis on the number and rate of incidence, prevalence, and DALYs for gout globally in individuals aged 20–54 years from 1990 to 2021.

Table 4. The APC and AAPC in 20-54 years of Gouts incidence, prevalence and DALYs for both sexes from 1990 to 2021

Incidence_Rate_APC

Cohort	Segment	Lower Endpoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob > |t|
Both	1	1990	1993	0.1098	-0.0551	0.2750	1.4504	0.172575
Both	2	1993	1996	0.5964*	0.2666	0.9273	3.9455	0.001944
Both	3	1996	2005	1.2388*	1.2021	1.2754	74.0910	< 0.000001
Both	4	2005	2012	0.6982*	0.6421	0.7543	27.2192	< 0.000001
Both	5	2012	2015	1.1602*	0.8271	1.4945	7.6196	0.000006
Both	6	2015	2018	0.8655*	0.5321	1.1999	5.6714	0.000104
Both	7	2018	2021	0.2223*	0.0535	0.3913	2.8710	0.014063

Incidence_Rate_AAPC

Cohort	Range	Lower Endpoint	Upper Endpoint	AAPC	Lower CI	Upper CI	Test Statistic	P-Value
Both	Full Range	1990	2021	0.8024*	0.7462	0.8587	28.0852	< 0.000001

Incidence_Number_APC

Cohort	Segment	Lower Endpoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob > |t|
Both	1	1990	1996	2.2669*	2.2284	2.3055	129.5219	< 0.000001

Cohort	Segment	Lower Endpoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob > |t|
Both	2	1996	2004	2.9710*	2.9401	3.0020	212.3716	< 0.000001
Both	3	2004	2008	2.5621*	2.4470	2.6773	49.0858	< 0.000001
Both	4	2008	2011	2.0141*	1.7883	2.2405	19.6018	< 0.000001
Both	5	2011	2015	2.2840*	2.1698	2.3984	44.0223	< 0.000001
Both	6	2015	2018	1.7689*	1.5409	1.9974	17.0343	< 0.000001
Both	7	2018	2021	0.8707*	0.7556	0.9859	16.5476	< 0.000001

Incidence_Numer_AAPC

Cohort	Range	Lower Endpoint	Upper Endpoint	AAPC	Lower CI	Upper CI	Test Statistic	P-Value
Both	Full Range	1990	2021	2.2794*	2.2428	2.3160	123.3639	< 0.000001

Prevalence_Rate_APC

Cohort	Segment	Lower Endpoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob > |t|
Both	1	1990	1993	0.2122*	0.0856	0.3389	3.6539	0.003303
Both	2	1993	1996	0.9245*	0.6730	1.1766	8.0367	0.000004
Both	3	1996	2004	1.6092*	1.5758	1.6425	105.9631	< 0.000001
Both	4	2004	2008	1.0537*	0.9328	1.1748	19.0682	< 0.000001
Both	5	2008	2011	0.7142*	0.4758	0.9531	6.5434	0.000028
Both	6	2011	2018	1.0217*	0.9816	1.0618	55.7997	< 0.000001
Both	7	2018	2021	0.0427	-0.0788	0.1644	0.7657	0.458663

Prevalence_Rate _AAPC

Cohort	Range	Lower Endpoint	Upper Endpoint	AAPC	Lower CI	Upper CI	Test Statistic	P-Value
Both	Full Range	1990	2021	0.9639*	0.9255	1.0023	49.4356	< 0.000001

Prevalence _Number_APC

Cohort	Segment	Lower Endpoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob > |t|
Both	1	1990	1993	2.2757*	2.0756	2.4762	25.0361	< 0.000001
Both	2	1993	1996	2.6542*	2.2582	3.0518	14.7664	< 0.000001
Both	3	1996	2003	3.3676*	3.3010	3.4342	112.0176	< 0.000001
Both	4	2003	2008	2.8230*	2.7021	2.9441	51.5376	< 0.000001
Both	5	2008	2015	2.2126*	2.1497	2.2755	77.4956	< 0.000001
Both	6	2015	2018	1.8465*	1.4770	2.2174	10.9672	< 0.000001
Both	7	2018	2021	0.7408*	0.5513	0.9307	8.5391	0.000002

Prevalence _Numer_AAPC

Cohort	Range	Lower Endpoint	Upper Endpoint	AAPC	Lower CI	Upper CI	Test Statistic	P-Value
Both	Full Range	1990	2021	2.4401*	2.3812	2.4991	82.1059	< 0.000001

DALYs_Rate_APC

Cohort	Segment	Lower Endpoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob > |t|
Both	1	1990	1993	0.2241*	0.0813	0.3672	3.4202	0.005077
Both	2	1993	1996	0.9326*	0.6450	1.2211	7.0868	0.000013
Both	3	1996	2004	1.5924*	1.5536	1.6312	90.1849	< 0.000001
Both	4	2004	2008	1.0611*	0.9189	1.2036	16.3309	< 0.000001
Both	5	2008	2011	0.7133*	0.4310	0.9965	5.5161	0.000133
Both	6	2011	2018	0.9984*	0.9497	1.0471	44.9236	< 0.000001
Both	7	2018	2021	-0.0368	-0.1831	0.1096	-0.5483	0.593510

DALYs_Rate _AAPC

Cohort	Range	Lower Endpoint	Upper Endpoint	AAPC	Lower CI	Upper CI	Test Statistic	P-Value
Both	Full Range	1990	2021	0.9494*	0.9046	0.9943	41.6973	< 0.000001

DALYs_Number_APC

Cohort	Segment	Lower Endpoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob > |t|
Both	1	1990	1992	2.1614*	1.7782	2.5460	12.3994	< 0.000001
Both	2	1992	1996	2.6087*	2.4143	2.8034	29.5906	< 0.000001
Both	3	1996	2003	3.3535*	3.2874	3.4197	112.2600	< 0.000001
Both	4	2003	2008	2.8272*	2.7052	2.9495	51.1354	< 0.000001
Both	5	2008	2015	2.2024*	2.1380	2.2668	75.3416	< 0.000001
Both	6	2015	2018	1.8057*	1.4181	2.1948	10.2215	< 0.000001
Both	7	2018	2021	0.6694*	0.4743	0.8650	7.4920	0.000007

DALYs_Numer_AAPC

Cohort	Range	Lower Endpoint	Upper Endpoint	AAPC	Lower CI	Upper CI	Test Statistic	P-Value
Both	Full Range	1990	2021	2.4233*	2.3674	2.4792	85.9967	< 0.000001

3.3. Proportional attributable fraction of Risk factors by sex, age subgroup, and regions

Globally, in 2021, aged in 20-54 years, High body-mass index (High BMI) and Impaired kidney function accounted for 34.95% (28.43% to 42.46%,95% UI) of DALYs and 2.58% (2.00% to 3.26%,95% UI) of DALYS, respectively. DALYS attributable to high BMI was silght lower in males (34.73%, 95% UI 28.25% to 42.25%) than in females (35.89%, 95% UI 28.73% to 43.55%), also in Impaired kidney function (**Figure 4**).

The DALYS attributable to high BMI increased with age and reached its highest level in the 50–54 years age groups among young and middle adults (36.33%, 95% UI 29.39% to 44.26%), lowest level in the 20–24 years age groups (24.04%, 95% UI 19.60% to 29.16%). The regional attributable risk fraction of high BMI ranged from 11.36% to 58.52% and Impaired kidney function ranged from 1.13% to 6.83% in all locations, ranged from 22.59% to 49.79% in GBD regions with the highest observed in North America (49.79%, 95% UI 40.66% to 58.75%), the lowest observed in South Asia (22.59%, 95% UI 17.96% to 27.88%) (**Table 5**) ; also Impaired kidney function ranged from 1.53% to 5.74% in GBD regions with the highest observed in

Central Asia (5.74%, 95% UI 4.43% to 7.26%), the lowest observed in Australasia (1.53%, 95% UI 1.16% to 2.00%) (**Table 6**)

The countries and teriritories attributable risk fraction of high BMI ranged from 14.93% to 58.52%, with the highest observed in the American Samoa (58.52%, 95% UI 48.92% to 67.43%) with the lowest observed in Eritrea (14.93%, 95% UI 11.30% to 19.23%).

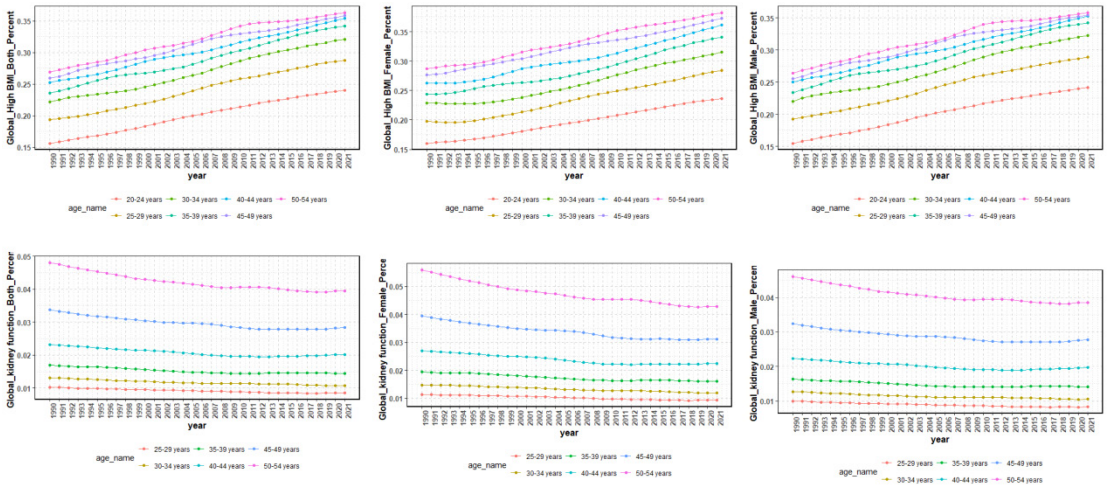

Figure 4. Percentage of DAYLs due to gout attributable to risk factors (High BMI and Kidney function) in the Global Burden of Disease study in 2021, according to sex and age_name.

Tabble 5. Proportional attributable fraction of high-BMI by GBD regions.

location_name	Percent	upper	lower
NORTH AMERICA	49.79%	58.75%	40.66%
High-income North America	49.79%	58.75%	40.65%
America	48.44%	57.57%	39.37%
Region of the Americas	48.44%	57.57%	39.37%
Middle East & North Africa - WB	47.96%	57.22%	39.00%
North Africa and Middle East	47.81%	57.07%	38.85%
Northern Africa	46.91%	56.24%	37.85%
Australasia	46.91%	56.58%	38.09%
Central Latin America	46.51%	55.81%	37.50%
Southern Latin America	46.26%	55.53%	36.90%
World Bank High Income	45.80%	54.85%	37.37%
Commonwealth High Income	45.12%	54.72%	36.24%
Advanced Health System	44.83%	53.77%	36.54%
Latin America & Caribbean - WB	44.77%	54.08%	35.99%
High SDI	44.67%	53.49%	36.50%
Andean Latin America	44.14%	53.27%	35.28%
Eastern Mediterranean Region	43.77%	52.48%	35.53%
Tropical Latin America	42.97%	52.48%	34.21%
Central Europe	42.53%	51.37%	34.04%
Eastern Europe	42.34%	51.47%	33.55%
Europe	42.27%	51.24%	33.70%

location_name	Percent	upper	lower
Europe & Central Asia - WB	42.14%	51.05%	33.61%
European Region	42.11%	51.01%	33.58%
Western Europe	41.18%	50.14%	32.73%
Caribbean	40.49%	49.21%	32.55%
Central Asia	40.32%	49.32%	31.96%
Southern Sub-Saharan Africa	39.56%	47.94%	31.50%
Oceania	38.01%	46.72%	30.53%
High-middle SDI	36.78%	44.92%	29.39%
Global	34.95%	42.46%	28.43%
Southern Africa	34.65%	41.94%	27.74%
World Bank Upper Middle Income	34.06%	41.78%	27.17%
Basic Health System	33.85%	41.57%	27.14%
Africa	33.85%	40.95%	27.40%
East Asia	32.67%	40.34%	25.93%
Middle SDI	32.05%	39.19%	26.00%
Western Pacific Region	32.03%	39.32%	25.58%
Western Sub-Saharan Africa	31.61%	38.92%	25.62%
East Asia & Pacific - WB	31.13%	38.25%	24.97%
Western Africa	31.00%	38.16%	25.10%
African Region	30.41%	37.08%	24.56%
Asia	30.23%	37.14%	24.51%
Sub-Saharan Africa - WB	30.04%	36.57%	24.24%
High-income Asia Pacific	29.35%	35.99%	23.63%
Central Africa	29.25%	35.90%	23.49%
World Bank Lower Middle Income	27.90%	34.22%	22.60%
Central Sub-Saharan Africa	27.40%	33.87%	22.00%
Low-middle SDI	26.98%	32.95%	21.98%
Eastern Africa	26.50%	32.30%	21.33%
Minimal Health System	25.60%	31.50%	20.52%
Southeast Asia	25.49%	30.98%	20.64%
Commonwealth Middle Income	25.23%	31.08%	20.22%
Commonwealth Low Income	24.55%	30.44%	19.58%
World Bank Low Income	24.49%	29.77%	19.78%
Limited Health System	24.46%	30.18%	19.60%
Eastern Sub-Saharan Africa	24.06%	29.37%	19.31%
Low SDI	23.60%	28.81%	19.00%
South-East Asia Region	23.14%	28.42%	18.49%
South Asia - WB	22.89%	28.22%	18.20%
South Asia	22.59%	27.88%	17.96%

Table 6. Proportional attributable fraction of Impaired kidney function by GBD regions.

location_name	percent	upper	lower
SOUTHEAST ASIA	2.96%	3.76%	2.28%

location_name	percent	upper	lower
East Asia	1.87%	2.38%	1.42%
Global	2.58%	3.26%	2.00%
Oceania	2.86%	3.65%	2.20%
Central Asia	5.74%	7.26%	4.43%
Central Europe	3.04%	3.86%	2.33%
Eastern Europe	3.07%	3.93%	2.34%
High-income Asia Pacific	2.36%	3.02%	1.83%
Australasia	1.53%	2.00%	1.16%
Western Europe	1.74%	2.23%	1.33%
Southern Latin America	1.53%	1.96%	1.18%
High-income North America	2.57%	3.23%	1.98%
Caribbean	2.86%	3.66%	2.20%
Andean Latin America	2.15%	2.84%	1.65%
Central Latin America	3.79%	4.86%	2.88%
Tropical Latin America	3.99%	5.14%	3.02%
North Africa and Middle East	3.23%	4.15%	2.50%
South Asia	3.19%	4.02%	2.44%
Central Sub-Saharan Africa	5.73%	7.31%	4.29%
Eastern Sub-Saharan Africa	1.71%	2.20%	1.30%
Southern Sub-Saharan Africa	4.80%	6.09%	3.60%
Western Sub-Saharan Africa	4.55%	5.85%	3.45%
East Asia & Pacific - WB	2.14%	2.71%	1.64%
Latin America & Caribbean - WB	3.05%	3.92%	2.34%
Sub-Saharan Africa - WB	3.68%	4.71%	2.79%
South Asia - WB	3.18%	4.01%	2.44%
Eastern Africa	1.87%	2.42%	1.43%
Middle East & North Africa - WB	3.28%	4.22%	2.53%
Northern Africa	3.01%	3.85%	2.30%
Southern Africa	4.03%	5.16%	3.04%
Western Africa	4.42%	5.67%	3.34%
Europe & Central Asia - WB	2.53%	3.19%	1.96%
Commonwealth High Income	1.82%	2.31%	1.40%
Africa	3.53%	4.50%	2.69%
Commonwealth Middle Income	3.39%	4.28%	2.60%
America	2.70%	3.41%	2.09%
South-East Asia Region	3.06%	3.87%	2.36%
Europe	2.31%	2.94%	1.80%
Western Pacific Region	1.97%	2.49%	1.50%
European Region	2.53%	3.19%	1.96%
Commonwealth Low Income	2.36%	3.03%	1.81%
World Bank High Income	2.41%	3.03%	1.86%
High SDI	2.35%	2.95%	1.81%
African Region	3.69%	4.73%	2.80%
Region of the Americas	2.70%	3.41%	2.09%

location_name	percent	upper	lower
World Bank Lower Middle Income	3.35%	4.23%	2.57%
Asia	2.47%	3.11%	1.90%
World Bank Low Income	2.74%	3.51%	2.10%
Advanced Health System	2.43%	3.06%	1.87%
High-middle SDI	2.01%	2.56%	1.54%
World Bank Upper Middle Income	2.15%	2.72%	1.65%
Basic Health System	2.38%	3.01%	1.83%
North America	2.57%	3.23%	1.98%
Low SDI	3.22%	4.11%	2.47%
Limited Health System	3.20%	4.04%	2.45%
Middle SDI	2.73%	3.43%	2.10%
Eastern Mediterranean Region	3.49%	4.45%	2.68%
Low-middle SDI	3.27%	4.12%	2.50%
Central Africa	5.54%	7.05%	4.18%
Minimal Health System	3.90%	4.97%	2.96%

4. Discussion

To the best of our knowledge, this is the first study to describe the gout burden and its changing trends between 1990 and 2021 among people aged 20-54 years by age, gender and Sustainable Development Index (SDI) at global, regional and country levels. The results showed that the prevalence, incidence, and YLD of gout in people aged 20-54 years increased significantly worldwide, with significant differences across age, gender, SDI level, region, and country. These findings highlight the need for increased awareness, early detection, and effective management strategies to mitigate the impact of gout on young and middle-aged populations worldwide.

The total number of patients with gout has doubled between 1990 and 2021, and the age-standardized prevalence has increased by 22.5% from 1990, with increases in most Global Burden of Disease (GBD) regions [8,12]. Consistent with the previous literature, the average annual percentage changes of prevalence, incidence and disability-adjusted life years rate among young and middle-aged people were 1.11 (1.06, 1.16), 0.92 (0.88, 0.95) and 1.1 (1.05, 1.15), respectively, indicating a steady upward trend. The simultaneous increases in prevalence, incidence, and disability-adjusted life-years suggest that prevention and treatment of gout in young and middle-aged patients are often ineffective [13].

In 2021, there were 190, 200 million cases and 6.29 million disability-adjusted life years (DALYs) of gout in people aged 20-54 years worldwide. Globally, the number of cases, incidence and prevalence, and disability-adjusted life years (DALYs) of gout have all shown significant increases between 1990 and 2021. The value of males is much higher than that of females, which may be due to the fact that males in this age group are more likely to consume foods related to gout attack and gout attack aggravation and to have hyperuricemia [14]. From a regional perspective, the United States of America was the region with the most significant increases in incidence, prevalence and disability-adjusted life-year rates. It is followed by China and East Asia. The country with the largest number of cases, number of cases, and disability-adjusted life years (DALYs) is China, probably due to its large population, while the country with the highest

incidence, prevalence, and DALYs is the United States of America, as a typical highly developed country, Dietary habits, obesity and renal dysfunction, and greater access to healthcare services in the United States of America, thereby facilitating better diagnosis and reporting [14,15], may account for the highest incidence of gout in the country, as reflected by the EAPC.

From 1990 to 2021, the incidence, prevalence and disability-adjusted life years (DALYs) of gout among people aged 20-54 years continued to increase substantially. The fastest increasing period of gout incidence was from 1996 to 2004, with an average annual percent change (AAPC) of 0.80, and the fastest increasing period of prevalence was from 1996 to 2004, with an AAPC of 0.96. The disability-adjusted life years increased most rapidly from 1996 to 2003, with an AAPC of 2.42. It shows that the global burden of gout is increasing over time. Changes in the prevalence of major factors leading to the occurrence and progression of the disease, as well as the ways in which governments and individuals respond to these factors, may jointly change the time trend of the disease burden, resulting in direct and indirect economic costs (including drug treatment, surgery, premature death, etc.) [16-18]. It also causes intangible personal costs (pain, activity limitation, etc.) [19], so it is particularly important to develop prevention strategies, improve management, and more evidence-based treatment of gout.

The results of this study showed that the regional attributable risk proportion of high BMI among young and middle-aged adults ranged from 11.36% to 58.52%, with the highest value in North America (49.79%) among GBD regions. The lowest value was found in South Asia (22.59%). The disability-adjusted life years (DALYS) attributable to high BMI increased with age. BMI is associated with hyperuricemia, and being overweight or obese may affect liver enzyme levels and lead to elevated uric acid levels. Controlling body weight and liver enzyme levels may help prevent and treat hyperuricemia [20]. For obese gout patients, lifestyle interventions, including a balanced diet, behavioral therapy, and exercise, are recommended, especially since high body mass index (BMI) accounts for nearly 50% of gout disability-adjusted life-years in North America [21]. However, the highest values of renal impairment were found in Central Asia (5.74%) and the lowest values were found in Australasia (1.53%).

5. Conclusion

In conclusion, as a major public health issue, this study describes for the first time the burden of gout, its trends and risk factors in people aged 20-54 years at global, regional and country levels. Although the incidence, prevalence and disability-adjusted life years (DALYs) of gout among young and middle-aged people vary widely across countries, the burden is generally on the rise from 1990 to 2021. We call for more research on gout in young and middle-aged people and more representative data for each country. Young and middle-aged people are the backbone of society. Further research is needed to understand the long-term impact of gout treatment on young and middle-aged people, especially its relationship with high BMI and impaired renal function. Continuous research to address key risk factors and improve diagnosis and treatment methods is essential to reduce the global burden of gout.

6. Limitations

The study relies entirely on the data from the 2021 Global Burden of Disease (GBD) study. Although GBD employs comprehensive and standardized methods, potential errors or biases in the original data collection

processes across different regions and countries could impact the accuracy of the results. For instance, variations in the diagnostic criteria and reporting practices for gout might exist, leading to inconsistent data quality. While BMI and renal dysfunction were analyzed as risk factors, other potential contributors to gout burden in the 20 - 54-year-old population were not explored. The findings, although presented at global, regional, and national levels, might have limitations in generalizability within specific subgroups or regions. For example, within large and diverse countries, there could be significant heterogeneity in gout prevalence and risk factor profiles among different ethnic, socioeconomic, or geographical subgroups that were not fully captured by the current analysis.

Disclosure statement

The authors declare no conflict of interest.

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