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Disease Burden and Epidemiological Trends of Chronic Kidney Disease at the Global, Regional, National Levels from 1990 to 2019

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Keywords
Chronic kidney disease · Disease burden · Epidemiological trends · Etiology

Abstract
Background: Chronic kidney disease (CKD) is a serious public health issue worldwide, but the disease burden of CKD caused by different etiologies and changing trends has not been fully examined. ***Methods:*** We collected data from Global Burden of Disease Study 2019 (GBD 2019), including incident cases, age-standardized incidence rate (ASIR), disability-adjusted life years (DALYs), and age-standardized DALY rate between 1990 and 2019 by region, etiology, age, and sex, and calculated the estimated annual percentage change (EAPC) of the rate to evaluate the epidemiological trends. ***Results:*** Globally, incident cases of CKD increased from 7.80 million in 1990 to 18.99 million in 2019, and DALYs increased from 21.50 million to 41.54 million. ASIR increased with an EAPC of 0.69 (95% uncertainty interval [UI] 0.49–0.89) and reached 233.65 per 100,000 in 2019, while the age-standardized DALY rate increased with an EAPC of 0.30 (95% UI 0.17–0.43) and reached 514.86 per 100,000. North Africa and the Middle East, central Latin America, and North America had the highest ASIR in 2019. Central Latin America had the highest age-standardized DALY rate, meanwhile. Almost all countries experienced an increase in ASIR, and over 50% of countries had an increasing trend in age-standardized DALY rate from 1990 to 2019. CKD due to diabetes mellitus type 2 and hypertension accounted for the largest disease burden with 85% incident cases and 66% DALYs in 2019 of known causes, with the highest growth in age-standardized DALY rate and a similar geographic pattern to that of total CKD. Besides, the highest incidence rate of total and four specific CKDs were identified in people aged 70 plus years, who also had the highest DALY rate with a stable trend after 2010. Females had a higher ASIR, while males had a higher age-standardized DALY rate, the gap of which was most distinctive in CKD due to hypertension. ***Conclusion:*** The disease burden of CKD remains substantial and continues to grow globally. From 1990 to 2019, global incident cases of CKD have more than doubled and DALYs have almost doubled, and surpassed 40 million years. CKD due to diabetes mellitus type 2 and hypertension contributed nearly 2/3 of DALYs in 2019 of known causes, and had witnessed the highest growth in age-standardized DALY rate. Etiology-specific prevention strategies should be placed as a high priority on the goal of precise control of CKD.

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Introduction

Due to population growth and aging, chronic kidney disease (CKD) has become a serious public health problem, with its high prevalence of over 697.5 million cases worldwide in 2017 [1]. Simultaneously, CKD carries a high risk of accelerated cardiovascular disease and progression to end-stage renal disease, a serious complication with poor prognosis of costly renal replacement therapy by dialysis or transplantation, which compromises the quality of life individually and causes substantial disease burden globally [2]. According to the statistics from Global Burden of Disease Study (GBD), CKD resulted in 1.2 million deaths in 2017, ranking from 17 in 1990 to 12 in 2017 [1], and it is predicted to become the fifth leading cause of death by 2040 [3]. In response to the tremendous burden of CKD on global health, many countries have raised public awareness, developed prevention or intervention strategies, and provided integrated CKD care [4].

The main etiologies of CKD vary in different areas. For example, diabetes and hypertension were the leading causes of CKD in all developed countries and many developing countries. Glomerulonephritis and unknown causes were more common in countries in Asia and sub-Saharan Africa [5]. In addition, the burden of CKD was disproportionately distributed geographically and demographically. Generally, the number of years lost due to ill-health, disability, or early death caused by CKD is much more pronounced in low- and lower middle-income countries [6]. The prevalence of CKD was higher in females than in males and most common in older people [7]. Knowing the pattern of CKD, which is changing with time, would facilitate the implementation of targeted policies and promotion of precise prevention and treatment.

Most previous studies on the burden and trends of CKD were national and regional epidemiological investigations or data reports [8–10]. There have also been some global studies depicting the global distribution and analyzing age or sex disparities [6, 11, 12]; however, a thorough and detailed burden due to different etiologies has seldom been performed. A comprehensive study on the disease burden of CKD caused by different etiologies as well as changing trends using the most updated data will be of great value. Therefore, we analyzed the incidence and disability-adjusted life year (DALY) of CKD in the general population by region, etiology, age, and sex for the period 1990–2019 using the results from GBD 2019, aiming to provide a better understanding of the disease burden and trends in total and four specific CKDs at the global, regional, national, age, and sex levels and offer some constructive prevention strategies.

Materials and Methods

The GBD study provides a detailed epidemiologic assessment of 369 diseases and injuries by age and sex on a global scale and for 204 countries and territories from 1990 to 2019. Data were extracted from surveys, censuses, vital statistics, and other health-related data source. A Bayesian meta-regression modeling tool (DisMod-MR 2.1) and a systematized tool (CODEm) were used in the computation of GBD estimates of incidence and fatal outcomes, respectively [13].

We collected data from the Global Health Data Exchange query tool (http://ghdx.healthdata.org/gbd-results-tool), including annual incident cases, age-standardized incidence rate (ASIR), DALYs, age-standardized DALY rate of CKD, with 95% uncertainty intervals (UI), by region, etiology, age, and sex from 1990 to 2019. GBD 2019 had 21 regions and 7 superregions. Cause list code included total CKD (code B.8.2 “chronic kidney disease”) and five subtypes of CKD (B.8.2.1 “chronic kidney disease due to diabetes mellitus type 1,” B.8.2.2 “chronic kidney disease due to diabetes mellitus type 2,” B.8.2.3 “chronic kidney disease due to hypertension,” B.8.2.4 “chronic kidney disease due to glomerulonephritis,” B.8.2.5 “chronic kidney disease due to other and unspecified causes”). In our study, we selected the total and four specific CKDs with clear etiology (B.8.2.1–4). Based on the clinical prevalence, risk factors, and etiology of chronic kidney diseases across varied age ranges, study purpose, and the accessibility of data, we artificially categorized age into four groups [children (aged 0–14), young adult (aged 15–49), middle-aged adults (aged 50–70), elderly (aged 70 plus)].

We further calculated the annual percentage change (EAPC) of the age-standardized incidence or DALY rate to evaluate the epidemiological trend within a specific time interval. The natural logarithm of rate is assumed to fit a linear regression model, $Y = \alpha + \beta X + \varepsilon$, where Y is equal to ln (rate), β indicates the positive or negative changing trends, X refers to calendar year, and ε is error. Thus, $EAPC = 100 \times (e^{\beta-1})$ and its 95% confidence interval were obtained from the linear regression model. All statistical analyses and graphics were performed in R (version 3.5.3, R Foundation).

Results

The overall global number of incident cases of CKD was 7,796,328 (95% UI: 7,174,529–8,485,391) in 1990 and increased to 18,986,903 (95% UI: 17,556,535–20,518,156) in 2019. Globally, the incident cases of the four specific CKDs accounted for less than 30% of the total. As with 1990, the order from most to least was CKD due to diabetes mellitus type 2, hypertension, glomerulonephritis, and diabetes mellitus type 1 in 2019. CKD due to diabetes mellitus type 2 and hypertension accounted for the largest disease burden with 85% of incident cases in 2019 of known causes. ASIR increased from 192.45 per 100,000 (95% UI: 177.31–209.05) in 1990 to 233.65 per 100,000 (95% UI: 216.56–252.31) in 2019, with an EAPC of 0.69 (95% UI: 0.49–0.89). The highest EAPC was found in CKD due to diabetes mellitus

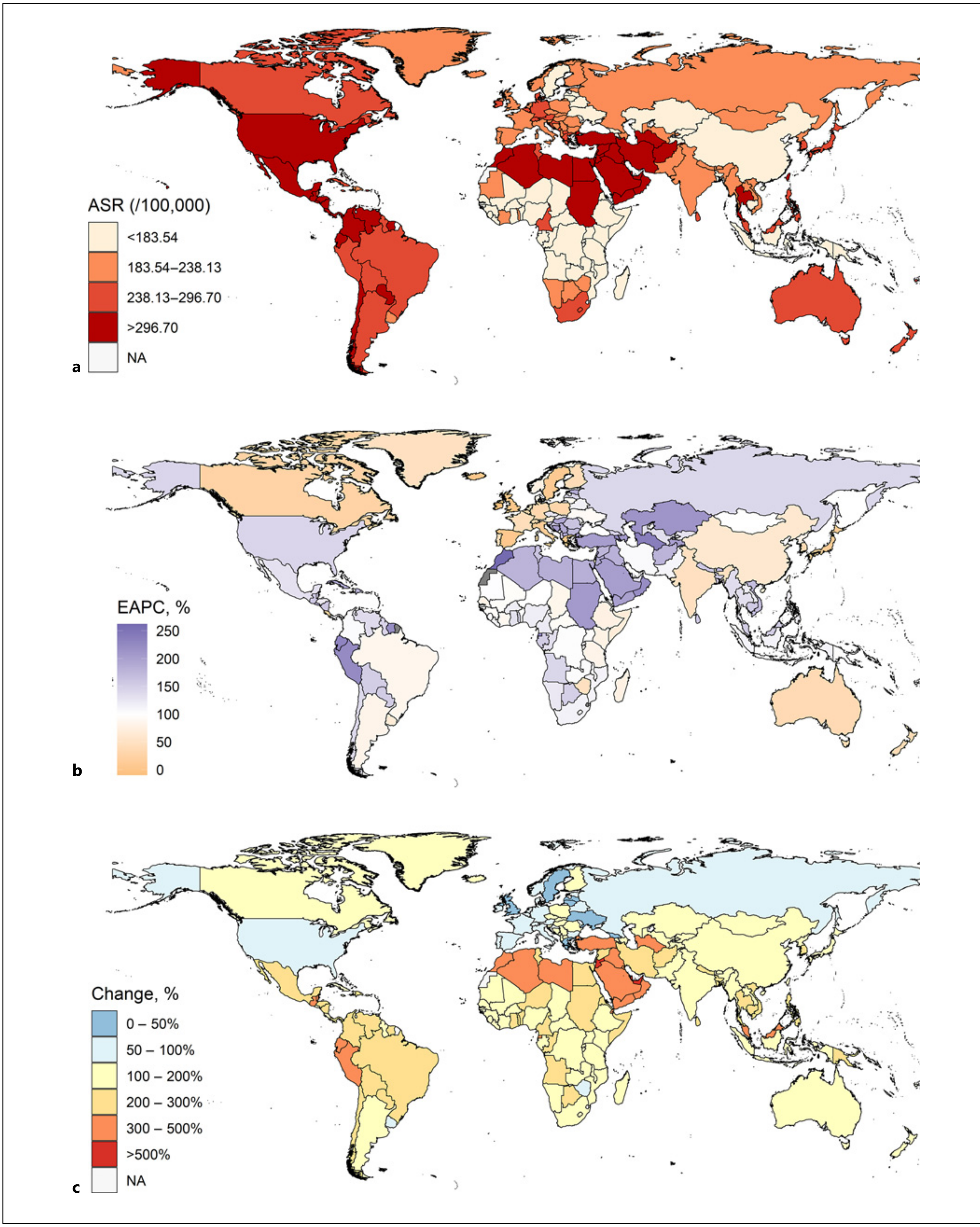
Table 1. The number and ASR of incidence and DALYs of CKD in 1990 and 2019, and EAPC of ASR from 1990 to 2019

	1990				2019				1990–2019	
	incidence		DALY		incidence		DALY		EAPC	
	n	ASR	*n*	ASR	*n*	ASR	*n*	ASR	incidence	DALY
Global	7,796,328 (7,174,529, 8,485,391)	192.45 (177.31, 209.05)	21,504,571 (20,039,116, 23,065,777)	484.46 (452.28, 518.67)	18,986,903 (17,556,535, 20,518,156)	233.65 (216.56, 252.31)	41,538,592 (38,291,809, 45,037,865)	514.86 (474.91, 558.86)	0.69 (0.49, 0.89)	0.3 (0.17, 0.43)
Gender										
Male	3,356,431 (3,091,622, 3,652,853)	179.21 (164.8, 194.74)	11,200,513 (10,402,023, 12,151,424)	537.61 (499.52, 580.01)	8,513,914 (7,844,266, 9,232,226)	223.02 (206.07, 241.18)	21,980,114 (20,140,022, 23,965,104)	574.23 (527.52, 625.27)	0.76 (0.46, 1.05)	0.34 (0.17, 0.52)
Female	4,439,897 (4,083,045, 4,836,083)	203.64 (187.5, 221.38)	10,304,057 (9,457,909, 11,216,130)	443.69 (409.36, 481.56)	10,472,989 (9,698,600, 11,315,584)	243.63 (225.94, 262.66)	19,558,479 (17,699,940, 21,467,977)	463.61 (419.34, 509.95)	0.65 (0.38, 0.93)	0.21 (0.02, 0.40)
Age group										
0–14 years	590,749.68 (503,766.99, 687,500.67)	33.68 (28.72, 39.2)	2,618,720.72 (1,868,782.35, 3,121,233.56)	149.3 (106.55, 177.95)	746,879.73 (634,921.82, 869,766.54)	38.11 (32.4, 44.38)	1,822,320.39 (1,529,259.14, 2,150,532.34)	92.99 (78.03, 109.74)	0.75 (−0.06, 1.57)	−1.28 (−1.68, −0.87)
15–49 years	1,197,736 (992,070, 1,420,036)	44.16 (37.58, 52.36)	7,671,714 (6,981,046,8,464,868)	283 (257, 312)	2,475,000 (2,053,391,2,942,793)	62.90 (52.18, 74.78)	12,040,931 (10,773,750,13,425,222)	305.99 (273.79, 341.16)	0.85 (0.06, 1.65)	−0.13 (−0.39, 0.14)
50–70 years	3,205,465.16 (2,683,772.72, 3,820,326.45)	469.91 (393.44, 560.05)	6,909,115.33 (6,411,747.09, 7,490,063.96)	1,012.86 (939.95, 1,098.03)	8,066,250.81 (6,869,934.52, 9,522,478.63)	584.96 (498.2, 690.56)	15,594,180.74 (14,221,778.29,17,068,749.73)	1,130.87 (1,031.35, 1,237.81)	0.83 (0.56, 1.10)	0.34 (0.18, 0.51)
70 plus years	2,802,377.58 (2,354,579.08, 3,288,631.2)	1,390.44 (1,168.26, 1,631.7)	4,305,020.86 (3,979,117.83, 4,692,623.64)	2,135.99 (1,974.29, 2,328.31)	7,698,772.75 (6,569,756.91, 8,871,552.6)	1,660.38 (1,416.89, 1,913.31)	12,081,160.08 (10,964,833.8, 13,090,216.08)	2,605.52 (2,364.77, 2,823.15)	0.60 (0.49, 0.72)	0.74 (0.65, 0.83)
Type of CKD										
T1DM	70,172 (62,365, 78,392)	1.27 (1.14, 1.41)	1,866,951 (1,353,965, 2,463,898)	39.48 (28.4, 52.75)	122,866 (110,253, 136,582)	1.63 (1.46, 1.82)	3,222,948 (2,280,070, 4,373,189)	38.83 (27.73, 52.35)	1.21 (−2.2, 4.8)	−0.08 (−0.73, 0.57)
T2DM	975,171 (881,612, 1,077,106)	24.88 (22.6, 27.39)	4,083,275 (3,296,982, 4,859,145)	101.71 (82.95, 120.08)	2,501,248 (2,279,950, 2,740,780)	30.29 (27.65, 33.05)	9,870,472 (8,114,784, 11,736,440)	120.2 (99.16,142.85)	0.65 (−0.14, 1.44)	0.73 (0.35, 1.12)
HTN	602,690 (548,661, 659,099)	15.97 (14.6, 17.4)	4,424,386 (3,817,916, 5,211,065)	111.27 (96.36, 129.18)	1,578,842 (1,447,111, 1,715,250)	19.45 (17.85, 21.09)	9,962,410 (8,582,331, 11,544,122)	123.41 (106.86,142.66)	0.69 (−0.30, 1.68)	0.48 (0.10, 0.86)
GN	342,840 (315,081, 372,702)	6.42 (5.92, 6.96)	4,152,955 (3,463,945, 80)	84.82 (71.11, 99.23)	606,349 (560,091, 658,077)	7.89 (7.27, 8.54)	6,900,802 (5,777,229, 8,125,653)	86.17 (72.32, 101.17)	0.80 (−0.76, 2.38)	0.038 (−0.41, 0.48)
Southeast Asia, East Asia, and Oceania										
Southeast Asia	454,912 (419,707, 491,190)	152.65 (140.55, 165.93)	2,704,033 (2,493,288, 2,945,170)	806.56 (741.95, 875.79)	1,427,209 (1,313,238, 1,547,890)	227.98 (210.24, 246.38)	5,113,222 (4,614,551, 5,673,542)	796.69 (720.03, 881.21)	1.4 (1.19, 1.62)	−0.02 (−0.12, 0.09)
Oceania	4,850 (4,473, 5,252)	122.53 (112.38, 133.56)	28,009 (24,253, 32,151)	664.24 (581.19, 758.07)	13,790 (12,644, 14,892)	158.68 (145.3, 172.89)	70,091 (58,471, 83,482)	747.22 (629.25, 880.16)	0.79 (0.54, 1.05)	0.25 (0.15, 0.36)
East Asia	1,328,136 (1,206,034, 1,465,639)	148.49 (135.05, 163.27)	4,195,661 (3,729,511, 4,664,949)	416.47 (371.77, 461.55)	3,273,864 (2,975,852, 3,599,052)	164.52 (150.62, 179.18)	6,208,087 (5,358,646, 7,049,939)	320.44 (277.88, 362.19)	0.61 (0.37, 0.85)	−0.58 (−0.73, −0.42)
Sub-Saharan Africa										
Western	158,290 (147,743, 168,988)	137.2 (126.96, 148.29)	1,029,807 (874,845, 1,218,236)	813.99 (702.78, 957.03)	440,870 (410,365, 470,758)	181.8 (167.29, 197.54)	2,005,253 (1,666,776, 2,371,299)	738.79 (627.78,857.08)	1.13 (0.89, 1.36)	−0.27 (−0.37, −0.16)
Southern	53,033 (48,673, 57,562)	168.63 (154.1, 184.7)	221,353 (200,858, 249,550)	636.93 (576.23, 723.35)	137,466 (126,480, 149,598)	231.14 (212.43, 251.73)	497,546 (452,002, 545,964)	803.81 (733.62, 878.51)	1.08 (0.87, 1.3)	0.88 (0.78, 0.99)
Central	28,101 (26,049, 30,156)	93.07 (86.17, 100.24)	260,257 (219,958, 303,286)	769.07 (656.59, 891.05)	82,675 (76,387, 89,016)	125.99 (115.7, 136.67)	463,973 (369,323, 563,409)	635.98 (510.34, 766.78)	1.12 (0.83, 1.42)	−0.73 (−0.84, −0.62)
Eastern	93,337 (86,677, 99,994)	94.39 (87.18, 102.21)	842,860 (711,405, 949,634)	752.43 (668.49, 837.88)	240,520 (223,053, 258,062)	119.54 (109.76, 130.11)	1,395,756 (1,214,795, 1,581,032)	626.45 (557.9, 698.14)	0.87 (0.57, 1.16)	−0.73 (−0.85, −0.62)
South Asia										
South Asia	1,012,694 (927,257, 1,104,529)	148.9 (136.4, 162.57)	4,690,790 (4,050,846, 5,324,903)	647.1 (557.75, 731.83)	2,669,411 (2,429,984, 2,918,850)	181.87 (165.91, 198.75)	9,886,435 (8,796,773, 11,052,833)	640.65 (568.76, 715.48)	0.61 (0.38, 0.83)	−0.06 (−0.18, 0.05)

Table 1 (continued)

	1990				2019				1990–2019	
	incidence		DALY		incidence		DALY		EAPC	
	n	ASR	*n*	ASR	*n*	ASR	*n*	ASR	incidence	DALY
Latin America and Caribbean										
Tropical	193,090 (178,256, 210,137)	191.28 (176.52, 209.33)	612,636 (575,548, 650,993)	559.23 (528.14, 592.5)	602,990 (556,740, 655,918)	250.85 (233.24, 272.18)	1,236,331 (1,146,826, 1,332,949)	513.36 (476.05, 553.4)	0.88 (0.68, 1.07)	−0.37 (−0.5, −0.25)
Caribbean	44,825 (41,286, 48,735)	161.46 (148.31, 176.22)	171,757 (158,191, 189,986)	587 (541.65, 647.03)	130,902 (121,121, 141,711)	256.39 (237.73, 277)	392,005 (337,600, 454,011)	774.89 (668, 896.08)	1.55 (1.35, 1.76)	1.32 (1.2, 1.43)
Andean	35,689 (33,186, 38,299)	154.8 (142.57, 167.62)	180,050 (166,472, 196,150)	680.42 (626.59, 742.08)	163,193 (150,106, 175,886)	288.34 (264.91, 311.21)	480,076 (403,713, 564,868)	836.34 (704.25, 981.59)	2.15 (1.95, 2.35)	0.81 (0.7, 0.91)
Central	267,723 (245,923, 292,010)	276.65 (252.64, 304.54)	778,416 (720,465, 840,288)	739.23 (689.04, 794.6)	991,397 (926,149, 1,060,802)	409.61 (383.06, 437.91)	3,275,591 (2,921,023, 3,697,817)	1,348.14 (1,203.58, 1,521.61)	1.27 (1.11, 1.43)	2.17 (2.08, 2.26)
North Africa and the Middle East										
North Africa and the Middle East	505,955 (466,448, 550,245)	261.9 (240.97, 285.91)	1,767,039 (1,616,931, 1,930,042)	834.93 (762.27, 947.15)	2,034,879 (1,875,830, 2,202,724)	447.48 (415.13, 482.83)	3,381,323 (2,920,288, 3,897,905)	744.36 (646.14, 851.75)	1.93 (1.78, 2.09)	−0.37 (−0.48, −0.27)
Central Europe, Eastern Europe, and Central Asia										
Central Asia	68,794 (62,921, 75,254)	123.99 (113.45, 135.88)	232,464 (215,305, 256,326)	397.89 (367.64, 442.65)	162,301 (146,761, 178,526)	193.3 (176.73, 211.27)	431,001 (386,369, 481,733)	506.72 (456.51, 562.2)	1.75 (1.5, 1.99)	0.44 (0.31, 0.57)
Central Europe	207,448 (186,938, 229,950)	144.36 (131.43, 158.87)	409,647 (383,838, 437,532)	297.3 (278.39, 317.88)	436,707 (395,418, 481,166)	216.5 (197.99, 236.75)	460,311 (401,375, 523,544)	243.84 (212.01, 278.04)	1.2 (0.98, 1.41)	−0.63 (−0.8, −0.45)
Eastern Europe	335,665 (304,515, 370,224)	130.48 (119.44, 142.71)	492,854 (445,924, 547,255)	197 (177.48, 218.85)	542,325 (492,092, 599,177)	181.85 (166.07, 199.03)	563,547 (491,455, 638,341)	196.77 (170.51, 224.02)	1.36 (1.11, 1.61)	−0.52 (−0.72, −0.32)
High income										
Western Europe	1,281,443 (1,164,676, 1,410,446)	216.75 (198.62, 236.36)	1,081,597 (991,487, 1,188,026)	197.18 (179.66, 216.97)	2,159,534 (1,986,853, 2,344,505)	235.6 (216.93, 254.91)	1,747,147 (1,560,646, 1,921,102)	186.58 (166.88, 208.38)	0.25 (0.06, 0.44)	−0.04 (−0.25, 0.18)
Southern Latin America	97,357 (88,192, 106,639)	211.66 (193.13, 230.93)	231,493 (218,354, 245,131)	501.82 (472.93, 530.86)	234,216 (215,393, 253,702)	282.02 (260.12, 304.6)	439,964 (407,699, 472,115)	540.08 (500.88, 579.63)	1 (0.82, 1.19)	0.24 (0.11, 0.36)
North America	1,036,204 (942,599, 1,140,523)	295.47 (270.34, 323.33)	934,395 (846,929, 1,032,342)	273.54 (247.51, 303.34)	1,888,592 (1,726,464, 2,062,595)	310.44 (284.74, 336.3)	2,424,222 (2,224,488, 2,641,088)	413.63 (379.73, 450.68)	0.04 (−0.13, 0.2)	1.64 (1.48, 1.79)
Asia Pacific	527,587 (485,498, 577,290)	265.13 (244.47, 287.79)	594,878 (547,519, 642,565)	310.61 (285.7, 334.9)	1,212,312 (1,112,733, 1,315,461)	277.51 (255.67, 300.82)	962,281 (840,036, 1,067,607)	218.58 (192.71, 243.9)	0.09 (−0.09, 0.26)	−1.15 (−1.33, −0.97)
Australasia	61,196 (57,502, 65,231)	254.5 (240.37, 269.78)	44,574 (40,819, 48,980)	196.75 (180.03, 215.38)	141,748 (130,757, 153,729)	286.14 (264.78, 308.93)	104,430 (92,941, 115,709)	214.3 (191.2, 238.39)	0.37 (0.19, 0.55)	0.45 (0.25, 0.66)

Point estimates with 95% UIs. ASR, age-standardized rate (per 100,000 person-years); DALYs, disability-adjusted life years; CKD, chronic kidney disease; EAPC, estimated annual percent of change.



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type 1 (1.21). DALYs increased from 21,504,571 (95% UI: 20,039,116–23,065,777) in 1990 to 41,538,592 (95% UI: 38,291,809–45,037,865) in 2019. The DALYs of four specific CKDs accounted for more than 60% of total CKD globally, with CKD due to hypertension contributing the largest part, followed by diabetes mellitus type 2, glomerulonephritis, and diabetes mellitus type 1 in 2019. CKD due to diabetes mellitus type 2 and hypertension accounted for the largest disease burden with 66% DALYs in 2019 of known causes. The age-standardized DALY rate increased from 484.46 per 100,000 (95% UI: 452.28–518.67) to 514.86 per 100,000 (95% UI: 474.91–558.86), with an EAPC of 0.30 (95% UI: 0.17–0.43). The highest EAPC was CKD due to diabetes mellitus type 2 and hypertension, namely, 0.73, 0.48 (Table 1).

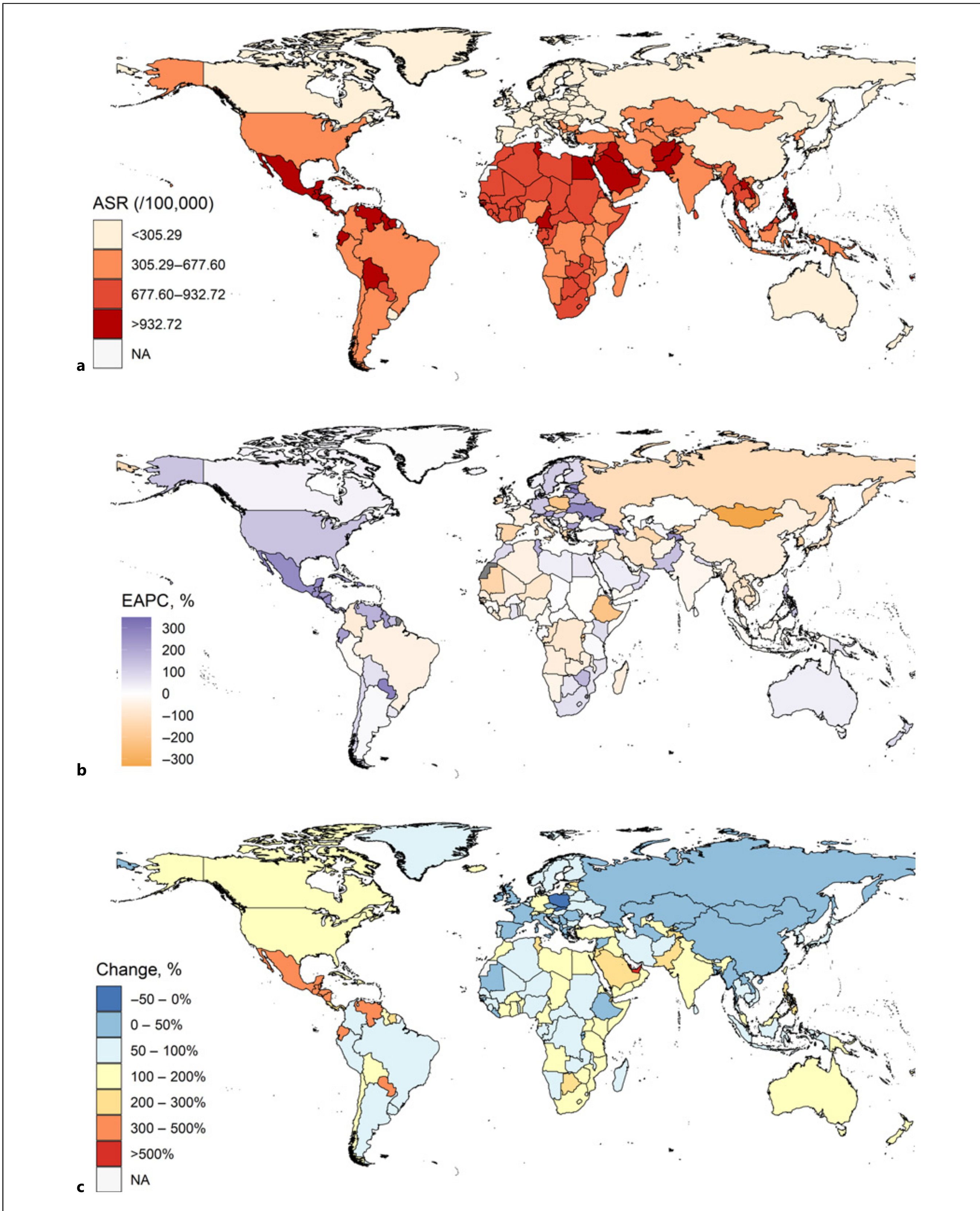
The highest ASIR in 2019 was observed in the regions of North Africa and the Middle East, central Latin America, and North America, while the lowest ASIR was seen in sub-Saharan Africa, Oceania, Eastern Europe and Asia, except Southeast Asia (Fig. 1a). CKD due to diabetes mellitus type 2 and hypertension shared a similar geographic pattern of ASIR with total CKD. For CKD due to glomerulonephritis and diabetes mellitus type 1, the highest ASIR was also identified in Eastern Europe, and Central Asia, while the lowest were no longer found in Eastern Europe and western sub-Saharan Africa compared to total CKD (online suppl. Material pp. 2–5; for all online suppl. material, see https://doi.org/10.1159/000534071). The age-standardized DALY rate varied considerably across the world, with the highest found in central Latin America and the lowest found in Europe and Australasia (Fig. 2a). Looking at the four specific CKDs, the age-standardized DALY rate was also notably high in Southeast Asia and Oceania for CKD due to diabetes mellitus type 1 (online suppl. Material pp. 6–9).

The ASIR from 1990 to 2019 increased in 204 countries except Ireland (online suppl. Material pp. 11–45). The most increased regions were Andean Latin America, North Africa and the Middle East, Central Asia, while the least increased regions were high-income North America, high-income Asia Pacific, Western Europe, and Australasia (Fig. 1b). Among the four specific etiologies, CKD due to glomerulonephritis and diabetes mellitus type 1 differed from total CKD. CKD due to diabetes mellitus type 1 had the highest EAPC in Eastern Europe, and the lowest EAPC was not seen in Western Europe and Australasia. High-income North America and Asia Pacific had the lowest EAPC among the four specific causes; strikingly, these two regions even showed decreasing trends of ASIR in CKD due to glomerulonephritis. The age-standardized DALY rate from 1990 to 2019 decreased in nearly half of the countries (online suppl. Material pp. 11–45). The most pronounced increase was detected in central Latin America, high-income North America, and the Caribbean, while the most significant decrease was detected in high-income Asia Pacific, followed by eastern and central sub-Saharan Africa, East Asia, central and Eastern Europe (Fig. 2b). The four specific causes had roughly similar highest and lowest regions with total CKD.

From 1990 to 2019, Andean Latin America, North Africa, and the Middle East experienced the largest increase, while Eastern and Western Europe and North America saw the lowest increase in incident cases (Fig. 1c). CKD due to diabetes mellitus type 2 and hypertension shared a geographic pattern similar to that of total CKD. For CKD due to glomerulonephritis and diabetes mellitus type 1, the highest increases were found in North Africa and the Middle East and western sub-Saharan Africa, while the lowest increases were also identified in East Asia, Asia Pacific, southern Latin America, and central Europe. The largest increase in DALYs was found in central Latin America, while the lowest increase was found in central and Eastern Europe and East Asia (Fig. 2c). For the specific etiologies of CKD, the age-standardized DALY rate was notably decreased in East Asia for CKD due to diabetes mellitus type 1, in Eastern Europe for CKD due to glomerulonephritis, and in central Europe, Asia Pacific for both causes.

Figure 3 presents the age-specific CKD incidence and DALY rate. Among the four age groups, the elderly had the highest incidence rate, followed by middle-aged adults, young adults, and children in total, and four specific CKDs except for CKD due to diabetes mellitus type 1, in which the incidence rate was found to be extraordinarily high in children. Similarly, the elderly had the highest DALY rate except for CKD due to diabetes mellitus type 1, where middle-aged adults possessed the highest DALY rate. With regard to the trends, the increase in incidence was most pronounced with the year,

Fig. 1. The ASIR in 2019, EAPC of ASIR, and change of incident cases between 1990 and 2019 due to total CKD. ASIR in 2019 (**a**), EAPC of ASIR between 1990 and 2019 (**b**), changes of incident cases between 1990 and 2019 (**c**). ASIR, age-standardized incidence rate; EAPC, estimated annual percentage change; CKD, chronic kidney disease.



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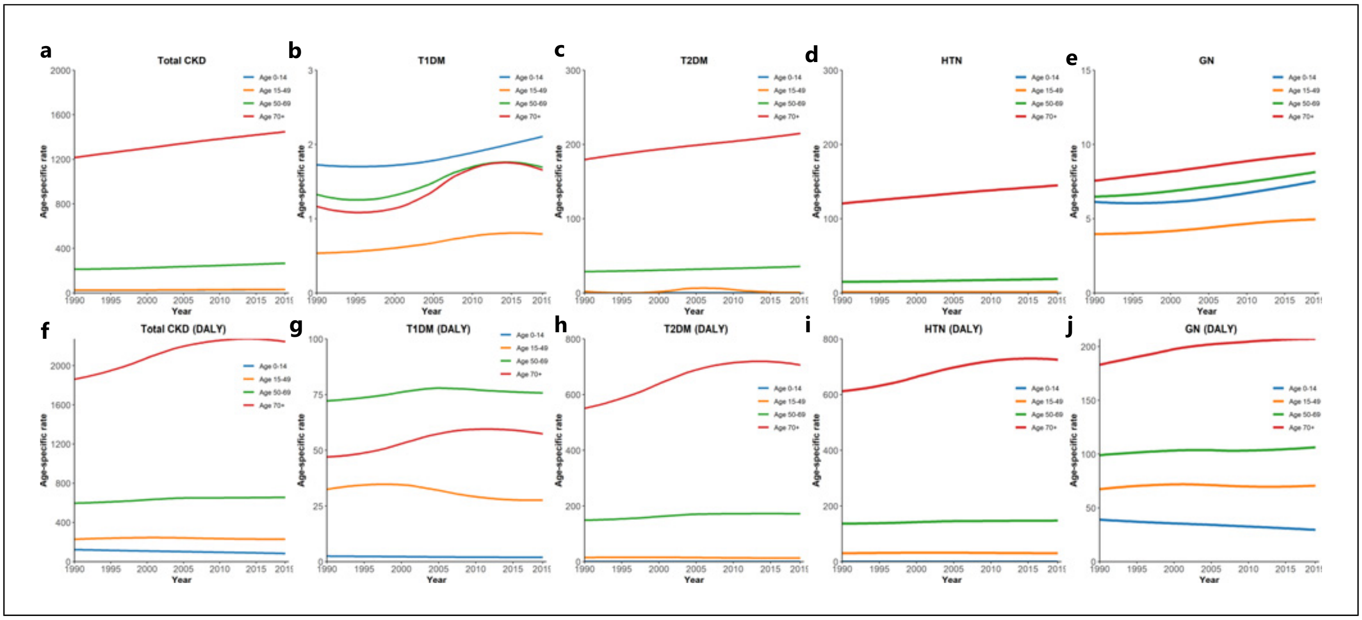

Fig. 3. The incidence rate and DALY rate of total and four specific CKDs among different age groups between 1990 and 2019. **a–e** Age-specific incidence rate among between 1990 and 2019. **f–j** Age-specific DALY rate between 1990 and 2019. Blue lines indicate 0–14 years of age, orange lines indicate 15–49 years of age, green lines indicate 50–69 years of age, red lines indicate 70+ years of age. CKD, chronic kidney disease; DALY, disability-adjusted life year; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; HTN, hypertension; GN, glomerulonephritis.

especially in the elderly. The DALY rate changed from an upward trend to a stable trend in approximately 2010.

The ASIR was higher in females for total CKD (online suppl. Material p. 10). Among the four etiologies, of special note, the ASIR in males surprisingly exceeded that in females. In contrast, the age-standardized DALY rate was higher in males for total CKD and all specific CKDs. For trends, generally, total CKD had a steady increase in ASIR and a relatively stable age-standardized DALY rate after 2010. Notably, the age-standardized DALY rate of CKD due to hypertension varied dramatically by sex, with males showing significantly higher rates than females, even though the ASIR was slightly higher in males.

Discussion

Our study highlights that CKD is still a serious global public health issue, considering the upward trend in the incidence rate and a substantial DALY rate of total CKD. Geographically, North Africa and the Middle East were the "hotspot" regions with the highest ASIR, and central Latin America had the highest age-standardized DALY rate of total CKD in 2019. Almost all countries experienced an increase in ASIR, and over 50% of countries had an increase in age-standardized DALY rates from 1990 to 2019. Demographically, the elderly had the highest DALY rate, which peaked in 2010 and remained at a high level thereafter. Males had higher age-standardized DALY rate than females, and the gap in the DALY rate was most distinctive in CKD due to hypertension.

We found the highest ASIR of total CKD in North Africa and the Middle East in 2019, which might be potentially shortage in the noncommunicable disease prevention strategy in this region [14, 15], where the prevalence of diabetes and hypertension – common etiologies of CKD – were increased significantly over the past three decades [16–18]. Meanwhile, despite larger budgets for health services, some higher income

Fig. 2. The age-standardized DALY rate in 2019, EAPC of age-standardized DALY rate, and change of DALYs between 1990 and 2019 due to total CKD. Age-standardized DALY rate in 2019 (**a**), EAPC of age-standardized DALY rate between 1990 and 2019 (**b**), changes in DALYs between 1990 and 2019 (**c**). DALY, disability-adjusted life year; EAPC, estimated annual percentage change; CKD, chronic kidney disease.

countries might be subject to limited resources for the prevention of CKD and its risk factors, diabetes, hypertension, and obesity [19]. Additionally, a lack of awareness of knowledge about risk factors of CKD was also observed in some high-income countries [20]. Thus, it is a pressing issue for the government to call for cost-effective management in CKD, such as enhancing primary care to improve people's awareness of CKD prevention and implementing early detection and preventive measures for the potential etiologies and risk factors for CKD. Unexpectedly, sub-Saharan Africa with extremely poor life expectancies and little government health expenditure had the lowest ASIR from 1990 to 2019. The less advanced laboratory testing and unavailable data in many African countries might be responsible for the low "detected and reported" incident cases [21, 22]. Therefore, it is important to raise the testing capacity and develop sustainable approaches to data measurement in these countries to discover the probably "masked" cases and develop more suitable prevention strategies in accordance with the real situation.

We identified that central Latin America had the highest age-standardized DALY rate of total CKD in 2019, while Europe and Australasia had the lowest. The reasons for the high disease burden in central Latin America are likely attributed to poor public health funding, shortage of health care workers [23]. Among these, the most important was supposed to be unaffordable costs and underutilization of cost-effective dialysis therapies such as peritoneal dialysis, which are widely accessible for most countries in Europe [24, 25]. Of note, an epidemic of rapidly progressive kidney disease (mesoamerican nephropathy or CKD of unknown etiology) with a high mortality rate has affected some central Latin American countries, which possibly causes a large number of deaths in young male workers in El Salvador and Salvadoran [26, 27]. Although the latest study identified heavy physical labor in heat as a key risk factor [28], we still have little knowledge about this rare etiology of CKD, and more comparative studies and evidence are needed. In contrast, well-equipped dialysis/transplant centers, an adequate number of nephrologists, and abundant public funding ensured a low age-standardized DALY rate in Europe [24, 25]. Of the four specific etiologies, with hypertension and diabetes being the major causes for most regions, CKD due to glomerulonephritis was the main contributor to the age-standardized DALY rate in Eastern Europe and Australasia. Geographic disparities in causes should be fully considered by policy-makers when assessing the impact of prevention and control programs and allocating health resources in their countries.

We revealed a higher incidence rate and DALY rate in the elderly than in other age groups for total CKD. Elderly individuals are more likely to develop CKD since a physiological aging process and intrinsic renal disease [29]. Due to increasing life expectancy, the growing geriatric population has led to an increased number of CKDs and other chronic diseases [30]. In addition, improved testing and early screening recommended by government and professional organizations promote the detection of CKD [31]. The National Kidney Foundation Kidney Early Evaluation Program (KEEP), for instance, is a free community screening program aimed at the early detection of kidney disease in people at high risk, such as hypertension or diabetes patients and elderly people [32]. Among the four specific etiologies, the elderly had the highest incidence rate except for CKD due to diabetes mellitus type 1, in which the children's group had the highest incidence rate. However, considering the small proportion of CKD due to diabetes mellitus type 1 attributed to DALY of total CKD, the elderly population is still the focus. In our trend analysis, the incidence rate of the elderly rapidly increased from 1990 to 2019, with CKD due to hypertension and diabetes mellitus type 2 as the main contributors. Elderly individuals are prone to a variety of complications, even CKD-related death, before the development of end-stage renal disease [33, 34]. In contrast, the DALY rate of the elderly peaked in 2010 and remained stable thereafter, which may strongly correlate with the control of etiology evidenced by the global implementation of prevention and control action plans in approximately 2010 [35].

Our study found that females generally had a higher ASIR but a lower age-standardized DALY rate than males for total CKD, which aligned with previous findings [12, 36, 37]. However, the ASIR of males surprisingly exceeded that of females in the four specific etiologies, implying that females have a higher ASIR in CKD due to other and unspecified causes, which warrant better screening in females. Males had higher age-standardized DALY rate, possibly due to the androgen effects, NO metabolism, and excessive oxidative stress [38]. In addition, previous studies have shown that females are more likely to adopt healthier lifestyles and have better control overcomorbidities [39, 40]. Therefore, it is necessary to develop sex-specific management strategies for more precise control of CKD.

Several limitations of our study should be acknowledged. First, primary data were not available for all countries, and mathematical models were used to estimate incidence and DALYs for countries where information was missing, while available data might not have been obtained by the preferred CKD definition or measurement method, which restricted the precision of estimates. Second, in the GBD, total CKD was categorized into five CKDs. The subtype of CKD due to other and unspecified causes contains diverse and complex etiologies, with no further detailed, specific data description. Our study analyzes four specific etiologies of CKD and may miss some causes with high incidence or DALYs. Third, the 95% UIs are frequently wide, reflecting the low precision of the estimates and potentially limiting the ability to detect smaller differences among countries.

The disease burden of CKD remains substantial and continues to grow globally. From 1990 to 2019, global incident cases of CKD have more than doubled and DALYs have almost doubled, and surpassed 40 million years. CKD due to diabetes mellitus type 2 and hypertension accounted for the largest disease burden with 85% incident cases and 66% DALYs in 2019 of known causes, and had witnessed the highest growth in age-standardized DALY rate. Elderly individuals tended to have a higher incidence and DALY burden in CKD due to diabetes mellitus type 2, hypertension, and glomerulonephritis, along with an increasing trend before 2010. Males have a higher DALY burden than females, especially in CKD due to hypertension. Therefore, cost-effective management is still needed to curb these increasing trends, and etiology-specific prevention strategies should be given high priority.

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Statement of Ethics

An ethics statement is not applicable in this manuscript because this study is based exclusively on published data/literature [Ethics Committee name and affiliation: Ethics Review Board of the First Affiliated Hospital, School of Medicine, Zhejiang University]. No human participants were involved in this study. This study is not a case report, nor a clinical trial, nor a research involving human embryonic stem cells.

Conflict of Interest Statement

All the authors declared no competing interests.

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Author Contributions

Meike Ying: designed the study, analyzed the data and interpreted the results, drew the figures, and wrote the manuscript. Xue Shao: analyzed the data, interpreted the results, drew the figures, and revised the manuscript from preliminary draft to submission. Hongli Qin and Pei Yin: analyzed the data, interpreted the results, and revised the manuscript from preliminary draft to submission. Yushi Lin: analyzed the data, interpreted the results, and drew the figures. Jie Wu: revised the manuscript from preliminary draft to submission. Jingjing Ren: revised the manuscript from preliminary draft to submission, approved the final version, and made decision for submission. Yang Zheng: designed the study, analyzed the data and interpreted the results, drew the figures, wrote the manuscript, approved the final version, and made decision for submission.

Data Availability Statement

All the data used to support the findings of this study are included in the article and online supplementary materials.

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