

Temporal trends and future projections of hip/knee osteoarthritis burden attributable to metabolic risk in women of reproductive age (1990–2021): A multidimensional analysis across 204 countries and territories

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Tables 1 and 2 are available in the Supplementary Files section

Temporal trends and future projections of hip/knee osteoarthritis burden attributable to metabolic risk in women of reproductive age (1990–2021): A multidimensional analysis across 204 countries and territories

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Abstract

Background: Osteoarthritis (OA) is a leading cause of disability worldwide, with women of reproductive age being particularly vulnerable to hip/knee OA (HOA/KOA) due to metabolic risks (e.g., obesity, high BMI). Leveraging Global Burden of Disease (GBD 2021) data, this study systematically analyzed the metabolic risk-attributable burden of HOA/KOA among women aged 15–49 years across 204 countries and territories from 1990--2021, with projections to 2050.

Methods: Data on disability-adjusted life years (DALYs), years lived with disability (YLDs), and age-standardized rates (ASRs) for HOA/KOA in women of reproductive age were extracted from the GBD 2021. The analyses were stratified by the sociodemographic index (SDI). Time series models (ARIMA, exponential smoothing) were employed to forecast disease burden trends (2022–2050), and decomposition analysis quantified contributions from population growth, aging, and epidemiological changes.

Results: Global trends: From 1990--2021, DALYs for HOA and KOA in women of reproductive age increased by 169% and 202%, respectively, with ASRs increasing by 24.5% and 41.2%, respectively. **Regional disparities:** Low-SDI countries exhibited the fastest case growth (HOA: +298%, KOA: +574%), whereas high-SDI regions had the highest absolute

burden (HOA cases accounted for 16.5% of all HOA cases globally). **Metabolic risk drivers:** Population growth (HOA: 48.9%, KOA: 46.6%) and increasing incidence rates (HOA: 47.7%, KOA: 48.5%) were the primary contributors. **Projections:** By 2050, ARIMA models predicted HOA/KOA cases to surge by 58.7% and 80.3%, respectively, whereas exponential smoothing indicated slower but significant growth.

Conclusions: Metabolic risk drives a substantial increase in the HOA/KOA burden among women of reproductive age, with the fastest growth occurring in low- and middle-SDI countries. High-SDI regions should prioritize chronic disease management, whereas low-SDI areas require enhanced community screening and health education. Early OA screening should be integrated into prepregnancy care systems, supported by multisectoral collaboration under the UN Sustainable Development Goals. Future research must elucidate the molecular mechanisms of metabolic risk and refine community-based interventions to mitigate disease progression.

Trial registration

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Keywords: Global burden of disease, Hip/knee osteoarthritis, Metabolic risk factors

Background

Osteoarthritis (OA) is a chronic joint disease characterized by the degeneration of articular cartilage, joint pain, stiffness, and functional impairment and represents a leading cause of disability worldwide [1]. Among the various joints affected, the knee is the most commonly

61 affected, with an estimated 365 million individuals suffering from knee osteoarthritis (KOA),
62 followed by the hip and hand [2]. KOA and hip osteoarthritis (HOA) account for more than 80%
63 of all OA cases [1,3]. Data from the World Health Organization (WHO) in 2019 indicate that the
64 global number of OA cases has increased by approximately 113% since 1990 [4]. By 2019, an
65 estimated 528 million people worldwide were living with OA, with individuals aged 55 years
66 and older accounting for 73% of the total population and women comprising up to 60% of those
67 affected [4]. Despite evidence suggesting that approximately 344 million individuals with
68 moderate to severe OA could benefit from rehabilitation, the global prevalence of OA is
69 projected to continue rising due to population aging and the increasing prevalence of metabolic
70 risk factors such as obesity and high body mass index (BMI) [5]. An increased BMI not only
71 exacerbates joint loading but also may accelerate the progression of OA through the induction of
72 inflammatory responses [6].

73 The Global Burden of Disease Study (GBD) indicated that the age-standardized
74 prevalence rate of KOA globally was 3.8% in 2019, with a significantly higher prevalence in
75 women (4.8%) than in men (2.8%) (1). Owing to hormonal changes, differences in muscle
76 strength, and a greater risk of obesity, postmenopausal women experience a yearly increase in
77 OA incidence, making them a high-risk group for this disease [3,7,8]. Therefore, women,
78 particularly those of reproductive age, constitute a unique population with a relatively high risk
79 of developing OA.

80 Although previous studies have provided valuable insights into the global trends in OA

incidence, they often focus on specific time periods, particular OA subtypes, specific sexes, or limited regions [9-12]. A comprehensive analysis stratified by age group, region, OA subtype, and sex is still lacking to summarize the global disease burden of OA. Currently, the GBD 2021 offers a comprehensive global health assessment covering four subtypes of arthritis, including the hip, knee, hand, and other joints, and employs disability-adjusted life years (DALYs) to quantify the gap between current and ideal health states [11,13-15]. This provides an unprecedented opportunity to gain an in-depth understanding of the epidemiological characteristics of OA among women of reproductive age.

Therefore, this study leverages the latest GBD 2021 data (1990--2021) to conduct a comprehensive analysis of the disease burden of HOA and KOA among women of reproductive age (15--49 years) across 204 countries and territories globally. This study explores the impact of metabolic risk factors on women across different age groups, identifies populations at high metabolic risk, and forecasts incidence trends from 2022--2050. These findings provide a scientific basis for the development of OA prevention and control strategies that specifically target women of reproductive age and contribute to a deeper understanding of the global disease burden of OA.

Methods

Data source

The data on HOA and KOA among women of reproductive age analyzed in this study were sourced from the GBD 2021. This dataset provides the latest epidemiological burden estimates for 371 diseases and injuries across 21 GBD regions and 204 countries and territories from 1990—2021 [14]. All the data are freely accessible through the Global Health Data Exchange (<https://ghdx.healthdata.org/gbd-2021/sources>). Information regarding the data, methods, and statistical models can be found in previously published literature [15]. All diseases were standardized according to the International Classification of Diseases (ICD) codes to ensure data accuracy and comparability.

This study utilized data from the GBD 2021 database, including DALYs, years lived with disability (YLDs), and their age-standardized rates (ASRs) for HOA and KOA among women of reproductive age from 1999--2021. Owing to the extremely low mortality rate and limited data availability for osteoarthritis patients, mortality data were excluded from the analysis.

Sociodemographic index

The sociodemographic index (SDI) is an indicator used to assess the development level of different regions and ranges from 0--1. It is a geometric mean of three indicators: the fertility rate, average years of education, and per capita income [11]. In the GBD 2021, the SDI for 204 countries and territories is categorized into five groups: high-SDI, high-middle-SDI, middle-SDI, low-middle-SDI, and low-SDI [13]. These classifications, developed by the Institute for Health Metrics and Evaluation (IHME), are used to compare health outcomes across different regions

[13].

Case definition

OA is the most common form of arthritis and is characterized by chronic inflammation, structural changes, and degradation of the entire joint. In this study, we analyzed HOA and KOA patients. The ICD-10 codes for HOA and KOA are M16 and M17, respectively, whereas the ICD-9 code is 715.

Estimated annual percentage change

The estimated annual percentage change (EAPC) is an effective and widely used indicator for describing the trend of an indicator over a specific period [16]. This study aims to estimate the dynamic trends in DALYs, YLDs and their ASRs for HOA and KOA among women of reproductive age from 1990--2021. The EAPC is calculated on the basis of a regression analysis of the natural logarithm of the rates (such as prevalence or incidence), with time as the independent variable. The natural logarithm of each observation is fitted to a straight line, and the calculation is based on the slope of this line [17]. The formula is as follows:

$$\ln(y_t) = \alpha + \beta t + \epsilon_t$$

$$EAPC = 100 \times (\alpha + \beta t - 1)$$

$$Percentage\ change = \frac{(2021\ cases - 1990\ cases)}{1990\ cases}$$

where t is the year, y is the natural logarithm of the rate (prevalence or incidence), α is the

intercept, β is the slope, and ϵ is the random error. The 95% confidence interval (CI) for the EAPC is also derived from this fitted model. The trend results are interpreted on the basis of the 95% CI: a lower limit of the 95% CI greater than 0 indicates an upward trend, an upper limit of the 95% CI less than 0 indicates a downward trend, and a 95% CI containing 0 indicates that the trend is not statistically significant [16].

Autoregressive integrated moving average model

The autoregressive integrated moving average (ARIMA) model is a widely used method for time series forecasting and statistical analysis. It combines three components: autoregression (AR), differencing (I), and moving average (MA) [18,19]. By adjusting the parameters (p, d, q), the ARIMA model can identify the characteristics of different types of time series. On the basis of the GBD 2021 data, this study forecasts the number of DALY and YLD cases of HOA and KOA among women of reproductive age from 2022--2050. The aim of this study was to predict the trend of disease burden and disability rates for HOA and KOA among women of reproductive age.

Exponential smoothing model

The exponential smoothing (ES) model is a commonly used method for time series forecasting that predicts future trends by weighting the average of historical data. When the ES model is applied, it is necessary to adjust the smoothing coefficient (smoothing parameter) to

balance the weights of the historical data and the latest data. The optimal smoothing coefficient is selected through cross-validation or grid search methods [19,20]. In this study, the ES model is used to forecast the number of DALY and YLD cases of HOA and KOA among women of reproductive age from 2022--2050. The aim of this study was to predict the trend of disease burden and disability rates for HOA and KOA among women of reproductive age.

By using the above two time series forecasting methods, we can determine whether the disease burden trends predicted by the two models are consistent.

Decomposition analysis

In this study, we conducted a decomposition analysis to elucidate the effects of epidemiological changes, age (15--49 years), and population growth on the DALYs and YLDs of HOA and KOA. Using the Das Gupta method [21], we analyzed the impacts of age structure, population dynamics, and sex changes on DALYs and YLDs from 1990--2021, with a focus on regions experiencing significant changes in the SDI.

All analyses and graphical presentations were performed via R software version 4.3.3, and data visualization was conducted via the ggplot2 package. A two-tailed p value of <0.05 was considered statistically significant.

Results

Hip osteoarthritis burden

Global level

In the past thirty years, from 1990--2021, according to data from the GBD 2021, the number of cases and ASRs for HOA among women of reproductive age in terms of the global burden of disease (DALYs/YLDs) have remained largely consistent. This may be because HOA is a nonfatal disease with a very low risk of death (YLLs), so the DALYs are almost entirely YLDs. The number of cases fluctuated significantly from 10426.34 (-837.35--29064.81) in 1990 to 28184.59 (-2550.1--77531.33) in 2021, showing a significant upward trend. The ASR per 100,000 people increased from 0.93 (-0.08--2.6) in 1990 to 1.37 (-0.12--3.77) in 2021, showing a significant upward trend. The average annual percentage change (EAPC) was 1.32 (1.29--1.35), indicating a long-term stable growth trend (Figure 1) (Table1) .

National level

From the distribution map, we can observe that in 2021, regions with high ASR values included the United States (ASR=3.57, -0.39--9.5), which ranked highest globally, followed by Saudi Arabia (ASR=1.92, -0.2--5.27) and Pakistan (ASR=1.91, -0.16--5.48). The low-ASR regions included Japan (ASR=0.96, -0.07--2.82) and Norway (ASR=2.38, -0.21--6.68), although the number of cases in these areas has gradually increased with population growth. In terms of absolute case burden, China (3,721.24, -299.69-10,576.52), India (4,307.28, -344.12-

12,011.32), and the United States (3,065.7, -331.76-8,161.53) had the highest numbers globally, with China leading worldwide and India being the core country in South Asia. Over time, Bangladesh (557.45, -44.38--1,624.84) showed a 713% increase compared with 1990, marking the fastest growth rate globally (Figure 2). Over the past three decades, the countries with the fastest estimated annual percentage change (EAPC) growth rates were Bangladesh (EAPC=4.35, 4.16--4.53), Vietnam (EAPC=3.11, 2.92--3.31), and Oman (EAPC=2.41, 2.35--2.48). In contrast, countries with the slowest growth or negative trends included Bulgaria (EAPC=0.57, 0.53--0.61) and Georgia (EAPC=0.51, 0.47--0.55). Notably, Bangladesh experienced the most significant case number increase, at 713% (Figure 3).

GBD regional level

The DALYs and YLDs in 2021 revealed that the regions with the highest ASR were South Asia (e.g., India, Pakistan, and Bangladesh; ASR=0.788, 95% CI: 2.24–0.062) and Central Asia (ASR=0.821, 95% CI: 2.29–0.065). The regions with the highest case numbers were East Asia (e.g., China, Japan, South Korea; DALYs=3,820.82, 95% CI: 10,848.0–306.93; YLDs=3,820.82, 95% CI: 10,848.0–306.93) and South Asia (e.g., India, Thailand, Indonesia; DALYs=3,644.73, 95% CI: 10,361.3–288.59; YLDs=3,644.73, 95% CI: 10,361.3–288.59). Regions with relatively lower burdens included Oceania (e.g., Australia, New Zealand, Fiji; DALY ASR=0.345; 95% CI: 1.02–0.027; YLD ASR=0.345; 95% CI: 1.02–0.027) and Central Sub-Saharan Africa (DALY ASR=0.233; 95% CI: 0.71–0.015; YLD ASR=0.233; 95% CI:

0.71–0.015) (Table). Between 1990 and 2021, most GBD regions exhibited an increasing trend in HOA-related disease burden (Figure 4).

SDI level

In 2021, DALYs and YLDs across different SDI categories showed consistent and significant disparities. In high-SDI regions, the average DALYs were 1.52 (95% CI: 1.45–1.59), with similar YLDs. The middle-SDI regions reported DALYs of 2.10 (95% CI: 2.02–2.18), whereas the low-SDI regions reported the highest DALYs at 2.33 (95% CI: 2.24–2.42) (Table). In terms of case numbers, high-SDI regions accounted for approximately 16,500 (95% CI: 16,200–16,800), middle-SDI regions accounted for 25,000 (95% CI: 24,500–25,500), and low-SDI regions accounted for 43,300 (95% CI: 42,000–44,600) (Figure 5). From 1990–2021, the overall number of cases increased by 148%, increasing from approximately 11,500 (95% CI: 11,300–11,700) in 1990 to 28,500 (95% CI: 28,300–28,700) in 2021. The high-SDI regions experienced slower growth at 56%, the middle-SDI regions experienced a 95% increase, and the low-SDI regions experienced the fastest growth at 167% (Figure 6).

Age-stratified analysis

Analysis revealed a clear age-related pattern in DALYs and YLDs for female HOA. In 2021, under metabolic risk factors, DALYs and YLDs for female HOA were nearly identical: approximately 1,159 (95% CI: 1,138–1,180) for ages 30–34 and 2,853 (95% CI: 2,828–2,878)

for ages 45–49 (Figure 7). From 1990–2021, DALYs and YLDs for women aged 30–40 years increased from approximately 1,160 (95% CI: 1,138–1,182) in 1990 to 2,853 (95% CI: 2,828–2,878) in 2021, reflecting a 146.5% increase. For women aged 45–49 years, values increased from approximately 1,956 (95% CI: 1,922–1,990) in 1990 to 4,781 (95% CI: 4,738–4,824) in 2021, a 144.7% increase. The annualized percentage growth rates for DALYs and YLDs were consistent: 3.6% for ages 30–34 years and 3.5% for ages 45–49 years from 1990–2021 (Figures 8).

Sex description

In 2021, under metabolic risk factors, the DALY rate for female HOA was 0.934 (95% CI: 0.857–1.011), and the YLD rate was 0.934 (95% CI: 0.857–1.011). The disability burden caused by the disease closely aligns with DALYs, indicating its severity. In terms of case numbers, DALYs reached approximately 10,426 (95% CI: 837–29,064), with YLDs matching this figure, reflecting a substantially affected population (Figure 9). From 1990–2021, the DALY rate steadily increased from 0.933 (95% CI: 0.757–1.110) in 1990 to 1.347 (95% CI: 1.183–1.511) in 2021, a 44% increase (Figure 10). Concurrently, the number of cases increased from 10,426 in 1990 to 27,387 in 2021, representing a 163% increase (Figures 11 and 12).

Decomposition analysis

To further evaluate health losses systematically, we conducted a decomposition analysis

of changes in DALYs and YLDs by SDI quintile and sex, clarifying the contributions of age structure (a-effect), population growth (p-effect), and disease incidence rate changes (r-effect), aiming to provide evidence for precise prevention and control. Globally, from 1990--2021, the number of cases increased from 10,426 to 28,185, a rise of approximately 17,758 (+170%). Population growth (48.93%) and epidemiological changes (47.66%) were the dominant contributing factors, whereas aging had the smallest impact (3.41%).

By SDI classification:

- High-SDI regions: The number of cases increased from 3,908 to 6,872 (+75%), with epidemiological changes (62.92%) as the primary driver, whereas aging made a negative contribution (-3.23%).
- High-middle-SDI regions: The number of cases rose from 2,372 to 5,475 (+131%), driven mainly by epidemiological changes (71.44%) and population growth (40.04%), with aging exerting a negative influence (-11.49%).
- Low-SDI regions: Cases surged from 465 to 1,852 (+298%), primarily due to population growth (61.42%).
- Low-middle-SDI regions: The number of cases increased from 1,380 to 5,739 (+316%), driven jointly by epidemiological changes (55.05%) and population growth (44.66%), with minimal aging impact (0.29%) (Figure 13).

From a gender perspective, female cases increased from 10,426 in 1990 to 28,185 in 2021 (+170%, 17,758 additional cases), with population growth (48.93%) and epidemiological changes (47.66%) as key drivers, whereas aging played a minor role (3.41%) (Figure 14).

Forecasting analysis

ARIMA model

ASR and case number projections for DALYs and YLDs

Overall, the age-standardized rate (ASR) is projected to rise steadily from 1.386 in 2022 to 1.773 by 2050, with an average annual growth rate of approximately 0.013, reflecting a stable linear trend. The increase is expected to be gradual from 2022--2030, followed by a slightly accelerated pace from 2030--2050. The number of cases is predicted to surge by 49.4%, increasing from 28,692 in 2022 to 42,905 by 2050, with an average annual growth rate of 1.7%. 2022–2030: Rapid growth phase, increasing from 28,692 to 32,753 (average annual growth: 2.1%). 2030–2050: Slower growth phase, rising from 32,753 to 42,905 (average annual growth: 1.4%) (Figure 15).

ES model

Projections of ASR, case numbers, DALYs, and YLDs

The age-standardized rate (ASR) is projected to rise gradually from 1.384 in 2022 to 1.485 by 2050, with an average annual growth rate of approximately 0.00035, reflecting a slow upward trend. 2022–2030: Moderate growth phase (1.384 → 1.445), with an average annual increase of 0.0076. 2030–2050: Growth slows significantly (1.445 → 1.485), averaging 0.0020 annually. The 95% confidence intervals (CIs) gradually widened, although the growth rate remained more gradual than that of the ARIMA model. The number of cases is expected to increase from 28,641 in 2022 to 32,538 by 2050, a rise of 13.6% (average annual growth: 0.5%), which is significantly lower than the 49.4% growth projected by the ARIMA model. 2022–2030: Faster growth phase (28,641 → 30,983), averaging 1.1% annually. 2030–2050: Growth decelerates (30,983 → 32,538), averaging 0.3% annually. The 95% CIs also expand over time but remain narrower than those of the ARIMA model (Figure 16).

Cluster analysis

Significant Increase: Includes South Asia – WB, South Asia, Commonwealth Low Income, etc. Minor Increase: Includes Basic Health System, Southeast Asia, Eastern Mediterranean Region. Remained Stable or Minor Decrease: Includes North America, High-income North America, Africa Region. Significant decrease: Includes Andean Latin America, Tropical Latin America, Central Europe, and specific countries (Figure 17).

Knee osteoarthritis burden

Global level

In the past thirty years, from 1990--2021, according to data from the GBD 2021, the number of cases and ASRs for KOA among women of reproductive age in terms of the global burden of disease (DALYs/YLDs) have remained largely consistent. This may be because KOA is a nonfatal disease with a very low risk of death (YLLs), so the DALYs are almost entirely YLDs. The number of cases fluctuated significantly from 118483.85 (-10258.01--327305.17) in 1990 to 342005.11 (-32718.94--915646.95) in 2021, showing a significant upward trend. The ASR per 100,000 people increased from 10.95 (-0.95--30.22) in 1990 to 16.54 (-1.58--44.3) in 2021, showing a significant upward trend. The average annual percentage change (EAPC) was 1.57 (1.46--1.69), indicating a long-term stable growth trend (Figure 18) (Table2) .

National level

The ASR and case number distributions of DALYs and YLDs in 2021. According to the 2021 ASR distribution maps, the regions with high ASRs for DALYs include China: 22.54 (95% CI: -2.03--61.17); the United States: 24.32 (95% CI: -2.76--61.80); and Egypt: 21.67 (95% CI: -2.92--54.07). Vietnam showed the largest increase, with an EAPC of 3.34 (95% CI: 3.15--3.54), increasing from an ASR of 3.21 in 1990 to 7.76 in 2021 (Figure 19). For YLDs, regions with high ASR include Saudi Arabia: 22.30 (95% CI: -2.76--55.83); Oman: 21.67 (95%

CI: -2.86–55.01); and Singapore: 21.31 (95% CI: -1.99–60.48). Bangladesh had the highest EAPC (3.86, 95% CI: 3.67–4.04), with the ASR increasing from 5.19–14.07. Ethiopia showed the slowest growth (EAPC = 0.15, 95% CI: 0.11–0.19) (Figure 19).

In terms of YLD case numbers, high-burden regions align with DALY distributions: China, India, and the United States dominate globally. Brazil: 11,762 cases (95% CI: -1,216.5–30,833.34), EAPC = 0.90 (95% CI: 0.88–0.92) (Figure 18c, and d). Regional Trends: North Africa and the Middle East (e.g., Egypt, Saudi Arabia): Rising YLD rates and case numbers. Northern Europe (e.g., Sweden, Norway): Slower case growth (EAPC $\approx$ 0.8–1.0) (Figure 19). Historical trends (1990–2021): Vietnam: EAPC = 3.34 (95% CI: 3.15–3.54), and the ASR increased from 3.21 to 7.76. Laos: EAPC = 2.27 (95% CI: 2.14–2.39), the ASR rose from 6.09 to 11.25. Bangladesh: EAPC = 3.86 (95% CI: 3.67–4.04), the ASR increased from 5.19–14.07, reflecting significant DALY growth (Figure 19 and Table). Regional Highlights: Southeast Asia (e.g., Vietnam, Indonesia, EAPC > 2): Concurrent increase in YLD rates. In the Middle East, Saudi Arabia (EAPC = 1.30, 95% CI: 1.27–1.33), the YLD rate increased from 14.97 to 22.30 (Figure 20). Case number changes: Vietnam: DALY cases increased from 333.43 to 2,247.08 (+574%, 95% CI: -186.3–6,676.66). Nepal: Increased from 257.16 to 1,119.05 (+335%, EAPC = 2.43). United States: The number of cases rose from 13,435.8–21,169.71 (+58%, EAPC = 1.09). China: The number of cases tripled (28,553.68 $\rightarrow$ 98,767.67), with rapid growth (EAPC = 2.48). Eastern Mediterranean (e.g., Egypt): YLD cases increased from

1,644.84 to 4,938.88 (+200%, EAPC = 1.01). Eastern Europe (e.g., Ukraine, Bulgaria):

Declines observed (Figure 20).

GBD regional level

Regional trends in DALYs and ASR (1990–2021) From 1990–2021, Asia experienced substantial increases in DALY case numbers, increasing from 59,399.16 (95% CI: -4,805.12–167,295.06) to 210,656.63 (95% CI: -18,835.9–578,564.71), with the ASR increasing from 9.57 (95% CI: -0.77–26.91) to 16.62 (95% CI: -1.48–45.71). In contrast, high-income North America experienced smaller changes: DALY cases increased from 14,177.2 (95% CI: -1,334.61–38,110.11) to 22,459.38 (95% CI: -2,537.04–57,297.78), and the ASR increased from 18.66 (95% CI: -1.76–50.1) to 23.08 (95% CI: -2.6–58.96). In 2021, Asia had the highest disease burden globally, with DALY cases reaching 210,656.63 (95% CI: -18,835.9–578,564.71) and an ASR of 16.62 (95% CI: -1.48–45.71). The Eastern Mediterranean region ranked second, with DALY cases at 29,383.48 (95% CI: -3,249.99–75,285.68) and an ASR of 16.85 (95% CI: -1.87–43.1). In contrast, Central Sub-Saharan Africa reported a relatively lower burden, with DALY cases at 2,261.29 (95% CI: -171.31–6,373.6) and an ASR of 9.55 (95% CI: -0.72–26.88) (Figure 21).

SDI level analysis

Trends in DALYs and ASR by SDI categories (1990–2021) Low-middle SDI: DALY ASR increased significantly from 8.07 (95% CI: -0.7–22.43) to 13.55 (95% CI: -1.29–37.18) (Figures 21 and 22). The high SDI: DALY ASR moderately increased from 13.85 (95% CI: -1.23–38.15) to 18.74 (95% CI: -1.9–49.42) (Figures 22 and 23). Case Number Changes: Middle SDI: DALY cases increased from 37,034.95 (95% CI: -3,164.64–102,364.94) to 127,536.77 (95% CI: -12,200.35–344,389.03). Low-middle SDI: DALY cases increased substantially from 16,450.19 (95% CI: -1,416–45,761.99) to 61,732.84 (95% CI: -5,845.93–169,528.03) (Figure 22). High SDI: DALY cases increased from 32,718.44 (95% CI: -2,910.5–90,162.49) to 57,645.88 (95% CI: -5,852.68–151,777.77). Low SDI: DALY cases rose gradually from 5,135.15 (95% CI: -404.38–14,403.54) to 19,478.68 (95% CI: -1,649.38–54,852.69) (Figures 22 and 23).

Age-stratified description

All the age groups presented significant increases in the age-standardized rates (ASRs). The largest change occurred in the 30–34 age group, where the ASR rose by 58%, from 0.81 (95% CI: -0.07–2.33) in 1990 to 1.28 (95% CI: -0.11–3.70) in 2021. In contrast, the 45–49 age group saw a smaller increase of 50% (Figures 24). Notably, the 45–49 age group experienced the most substantial increase in case numbers, increasing by 211% from 65,445.73 (95% CI: -5,824.14–177,333.26) in 1990 to 203,528.15 (95% CI: -19,992.81–533,920.69) in 2021, whereas the 30–34 age group had the smallest relative change in case numbers (Figures 25).

Sex-stratified description

The ASR for females gradually increased, increasing from 0.93 (95% CI: -0.08–2.6) in 1990 to 1.37 (95% CI: -0.12–3.77) in 2021 (Figure 26). The number of cases rose significantly from 10,426.34 (95% CI: -837.35–29,064.81) in 1990 to 28,184.59 (95% CI: -2,550.1–77,531.33) in 2021, with the peak in case numbers occurring between 2010 and 2021 (Figure 27, 28 and 29).

Decomposition analysis

To further evaluate health losses systematically, we conducted a decomposition analysis of the changes in DALYs and YLDs by SDI and sex, clarifying the contributions of age structure (a-effect), population growth (p-effect), and disease change rate (r-effect), aiming to provide evidence for precise prevention and control. From 1990--2021, the total increase in DALYs was 223,521.25, driven primarily by population growth (46.62%), with a contribution value = 339,265.45. Epidemiological changes (48.49%): Contribution value = 352,859.64. Aging effects (4.88%) included minimal impact, SDI-specific drivers, and high-SDI regions. DALY growth was driven mainly by epidemiological changes (61.84%). High-middle-SDI regions: Epidemiological changes dominated (81.32%). Low-SDI regions: Population growth was the core driver (62.87%). Middle-SDI regions: Combined influence of epidemiological changes (52.91%) and population growth (41.06%) (Figure 30). Sex-Specific Trends:

Similar patterns were observed in sex-stratified analyses, with epidemiological changes and population growth as key drivers across all categories (Figure 31).

Forecasting analysis

ARIMA model

DALYs: This number is projected to increase from 346,873 in 2022 to 537,673 by 2050, with an average annual growth rate of approximately 1.8%. YLDs: YLDs are expected to increase from 16.62 in 2022 to 20.85 by 2050, with an average annual growth of 0.8%. By 2050, female DALYs are predicted to increase by 55% (compared with 2022), and YLDs are predicted to increase by 25%. Post-2030, confidence intervals for projections exceed 100,000 for DALYs and 5 for YLDs (Figure 32).

ES model

DALYs: This model is forecast to increase from 346,007 in 2022 to 380,138 by 2050, with a slower annual growth rate of 0.7% compared with the ARIMA model (1.8%). YLDs: YLDs are projected to increase from 16.63 in 2022 to 17.43 by 2050, with an annual growth rate of 0.3%, which is also lower than that of the ARIMA model (0.8%). By 2050, DALYs are expected to increase by 9.8% (vs. 2022), which is significantly lower than ARIMA's 55%, whereas YLDs increase by 4.8%, which is far lower than ARIMA's 25% (Figure 33).

Cluster analysis

Minor Increase: Includes southern sub-Saharan Africa, Central Asia, and Oceania. Remained Stable or Minor Decrease: Includes Sub-Saharan Africa – WB, Middle East & North Africa – WB, African Region. Significant Decrease: Includes Southeast Asia Region, East Asia & Pacific – WB, Asia. Significant Increase: Includes East Asia, Commonwealth Low Income. The specific clusters are detailed in Figure 34.

Discussion

This study, which is based on GBD 2021 data, is the first to systematically analyze the global disease burden of HOA and KOA among women of reproductive age driven by metabolic risk from 1990--2021. The analysis revealed that the DALYs of HOA and KOA among women of reproductive age globally increased by 169% and 202%, respectively, due to metabolic risk. The ASR increased significantly, by 24.5% and 41.2%, respectively. Analysis by SDI level revealed that high-SDI countries had the highest absolute burden, but middle–low-SDI countries experienced the fastest growth rates. This finding, to some extent, reflects the complex interaction between the global spread of metabolic risk and the unequal distribution of healthcare resources [22,23].

Previous studies have emphasized the associations between various metabolic risks and the progression of OA, such as increased mechanical load on joints due to obesity, local pressure

on joints, adipokines and inflammatory cytokines promoting cartilage degradation, and high blood sugar and insulin resistance damage chondrocytes through the accumulation of advanced glycation end products (AGEs) and oxidative stress [24].

Compared with other populations, women of reproductive age have certain physiological characteristics, such as changes in hormone levels, fluctuations in metabolic stress during the childbearing period, and unique regulation of the immune system [25,26]. Therefore, unlike previous studies on OA in the general population, this study focused on analyzing the disease burden and related incidence trends of HOA and KOA among women of reproductive age. The study revealed that the growth rate of KOA among women of reproductive age was significantly greater than that among men, which may be related to weight gain during pregnancy and fluctuations in estrogen levels accelerating cartilage degeneration [27-29]. Furthermore, the decomposition analysis in this study also revealed heterogeneity across different regions, with high-SDI countries being driven primarily by the aggravation of aging and the accumulation of chronic diseases (residual effect >60%), whereas low-SDI countries were driven mainly by population growth contribution >60%). This finding provides strong evidence for the development of stratified intervention strategies for different regions.

The results of the ARIMA and ES prediction models showed some differences: ARIMA predicted a continuous increase in ASR (HOA +17.7% by 2050; KOA +20.7% by 2050), whereas the ES model suggested that standardized rates might slightly decrease due to the implementation of interventions. However, both models warned that the global number of cases

would soar with global population growth (HOA +58.7% by 2050; KOA +80.3% by 2050). The differences between the two models also reflect the complexity of metabolic risks, which require continuous dynamic monitoring and evaluation.

On the basis of the above findings, this study proposes the following stratified intervention strategies. Global level: The WHO is recommended to incorporate metabolic risk prevention and control into the noncommunicable disease (NCD) management framework and develop a "Guideline for Metabolic Risk Prevention and Control of Osteoarthritis," emphasizing monitoring indicators such as BMI, waist-to-hip ratio, fasting blood glucose, and the promotion of anti-inflammatory diets (e.g., the Mediterranean diet) [24,30,31]. A "Metabolic Arthropathy Special Project" is also suggested to fund the purchase of low-cost medical equipment for grassroots HOA and KOA screening in low-SDI countries [32,33]. An "OA Policy Effectiveness Index" (including ASR changes, screening coverage, intervention costs, etc.) should be established and released globally every two years [23]. Prospective Cohort Studies on Metabolic Risk Factors-HOA/KOA" should be piloted in 10 high/low-SDI countries to track the effects of 5-year interventions and provide evidence for policy adjustments [34,35].

High-SDI countries: Optimize chronic disease management systems, promote community-based weight reduction programs, implement precise remote medical and rehabilitation interventions to reduce ASR effectively and reduce related medical expenditures [36-38]. Low-SDI countries: Strengthen grassroots prevention and control through low-cost community screening and a tiered medical system, promote health education, advocate for

healthy diets and cultural interventions, curb the rapid rise of metabolic risk, and effectively reduce the growth rate of the disease (EAPC) [37,39,40].

Population level: Integrating HOA and KOA screening into the prepregnancy healthcare system for women of reproductive age; promoting awareness of joint function management throughout the prepregnancy, pregnancy, and postpartum periods; reducing the risk of HOA and KOA among women of reproductive age; and increasing the rate of early intervention [41-43].

This study has certain limitations. First, the GBD database relies on model estimates, which may underestimate the real disease burden in remote areas. For example, in rural Africa, there is a lack of relevant imaging-based diagnostic data, and the diagnosis rates of HOA and KOA are low [44]. Second, there are limitations in the population range. This study focused on women of reproductive age (15–49 years) but did not subdivide the impact of reproductive history (e.g., nulliparous, multiparous) on HOA and KOA. Finally, this study analyzed only the metabolic risks defined in the GBD database and did not include other potential metabolic indicators (such as insulin resistance and dyslipidemia). To address these limitations, future research can make the following improvements. First, joint regional health surveys can be promoted to supplement clinical data and improve data coverage. Second, high-quality cohort studies should be conducted, incorporating variables such as the number of pregnancies and duration of breastfeeding in the study design, and a fertility-related HOA and KOA risk score should be developed. Finally, multiple clinical databases (such as NHANES and the UK Biobank) were integrated to obtain more comprehensive metabolic indicators, a multifactorial

risk model was constructed, and Mendelian randomization analysis was used to validate the causal relationships between metabolic biomarkers and HOA and KOA, providing more reliable evidence for this research.

Conclusions

In summary, metabolic risk factors have led to a significant increase in the global incidence of HOA and KOA, with the fastest growth observed in countries with middle and low sociodemographic indices (SDIs). It is projected that global cases will continue to surge by 2050. High-SDI regions are affected primarily by aging populations and chronic diseases, whereas low-SDI regions are experiencing rapid growth due to population expansion and the spread of metabolic risk. Although standardized interventions may slow the rising trend of incidence, population growth and aging will still increase the absolute burden of the disease. Therefore, the incorporation of early screening for HOA and KOA into prepregnancy care for women of childbearing age and the establishment of a multisectoral collaborative prevention and control mechanism under the framework of the United Nations Sustainable Development Goals are urgently needed. Future efforts should focus on further elucidating the molecular mechanisms of metabolic risk and optimizing community-based intervention strategies.

List of abbreviations

HOA **Hip osteoarthritis**

537 **KOA** **Knee osteoarthritis**

538 **SDI** **Socio-demographic index**

539 **ASR** **Age-standardized rates**

540 **DALYs** **Disability-adjusted life years**

541 **EAPC** **The estimated annual percentage changes**

542 **ARIMA** **Autoregressive integrated moving average**

543 **ES** **Exponential smoothing**

544 **GHDx** **Global Health Data Exchange**

545 **Declarations**

546

547 *Ethics approval and consent to participate*

548 Not applicable

549 *Consent for publication*

550 Not applicable

551 *Availability of data and materials*

552 Data can be obtained from the following website: <http://ghdx.healthdata.org/gbd-results-tool>.

553 *Competing interests*

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Authors' contributions

Conception and design: XFM. Acquisition of data: XFM and XFM. Analysis and
interpretation of data: XFM, WWR, SLQ, KSW, ZGZ and TDX. ZGZ and TDX finally checked
the contents of the manuscript. All authors were involved drafting the article or revising it
critically for important intellectual content, and all authors approved the final version to be
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Figure legends

Figure 1 The numbers and age-standardized rates of DALYs (a) and YLDs (b) of hip osteoarthritis attributable to metabolic risks in women of reproductive age from 1990 to 2021. Bars and broken lines indicate numbers and age-standardized rates, respectively. DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 2 Age-standardized rates and cases distribution of hip osteoarthritis attributable to metabolic risks in women of reproductive age worldwide in 2021. (a) Age-standardized DALYs rate. (b) Age-standardized YLDs rate. (c) Number of DALYs cases. (d) Number of YLDs cases. DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 3 Cases change and EAPC distribution of hip osteoarthritis attributable to metabolic risks in women of reproductive age from 1990 to 2021. (a) EAPC of age-standardized DALYs rate. (b) EAPC of age-standardized YLDs rate. (c) Change of number of DALYs. (d) Change of number of YLDs. EAPC, estimated annual percentage change; DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 4 Age-standardized rates and cases distribution of hip osteoarthritis attributable to metabolic risks in women of reproductive age in 204 countries in 2021, by GBD regions. (a) Age-standardized rate of DALYs and YLDs. (b) Number of DALYs and YLDs cases. DALYs,

disability-adjusted life years; YLDs, years lived with disability.

Figure 5 Burden of hip osteoarthritis attributable to metabolic risks in 204 countries in 2021, by SDI. (a) Age-standardized rates of DALYs and YLDs. (b) Numbers of DALYs and YLDs cases. DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 6 Burden of hip osteoarthritis attributable to metabolic risks in 204 countries from 1990 to 2021, by SDI. (a) Age-standardized rates of DALYs and YLDs. (b) Numbers of DALYs and YLDs cases. DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 7 Burden of hip osteoarthritis attributable to metabolic risks in 204 countries in 2021, by age. (a) Age-standardized rates of DALYs and YLDs. (b) Numbers of DALYs and YLDs cases. DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 8 Burden of hip osteoarthritis attributable to metabolic risks in 204 countries from 1990 to 2021, by age. (a) Age-standardized rates of DALYs and YLDs. (b) Numbers of DALYs and YLDs cases. DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 9 Burden of hip osteoarthritis attributable to metabolic risks in 204 countries in 2021 for female. (a) Age-standardized rates of DALYs and YLDs. (b) Numbers of DALYs and YLDs cases. DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 10 Burden of hip osteoarthritis attributable to metabolic risks in 204 countries from 1990 to 2021 for female. (a) Age-standardized rates of DALYs and YLDs. (b) Numbers of DALYs

and YLDs cases. DALYs, disability-adjusted life years; YLDs, years lived with disability

Figure 11 Burden of hip osteoarthritis attributable to metabolic risks in 204 countries in 2021, by sex and age. (a) DALYs. (b) YLDs. DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 12 Burden of hip osteoarthritis attributable to metabolic risks in 204 countries from 1990 to 2021 for female. (a) DALYs. (b) YLDs. DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 13 Changes in the DALYs, YLDs of hip osteoarthritis (HOA) according to population-level determinants of population growth, aging, and epidemiological change from 1990 to 2021 at the global level and by Sociodemographic Index (SDI) quintile.

Figure 14 Changes in the DALYs, YLDs of hip osteoarthritis (HOA) according to population-level determinants of population growth, aging, and epidemiological change from 1990 to 2021 at the global level and by sex quintile.

Figure 15 Forecasts of numbers and age-standardized rates for DALYs and YLDs of hip osteoarthritis attributable to metabolic risks in 204 countries, stratified by sex, from 2022 to 2050 using the ARIMA model. DALYs, disability-adjusted life years; YLDs, years lived with disability; ARIMA, autoregressive integrated moving average.

Figure 16 Forecasts of numbers and age-standardized rates for DALYs and YLDs of hip osteoarthritis attributable to metabolic risks in 204 countries, stratified by sex, from 2022 to 2050 using the ES model. DALYs, disability-adjusted life years; YLDs, years lived with disability;

777 ES, Exponential Smoothing.

778 **Figure 17** Global Hip osteoarthritis Burden Cluster Analysis by Region (1990–2021). This
779 dendrogram illustrates the hierarchical clustering of regions based on their burden trends Hip
780 osteoarthritis over three decades

781 **Figure 18** The numbers and age-standardized rates of DALYs (a) and YLDs (b) of knee
782 osteoarthritis attributable to metabolic risks in women of reproductive age from 1990 to 2021.
783 Bars and broken lines indicate numbers and age-standardized rates, respectively. DALYs,
784 disability-adjusted life years; YLDs, years lived with disability.

785 **Figure 19** Age-standardized rates and cases distribution of knee osteoarthritis attributable to
786 metabolic risks in women of reproductive age worldwide in 2021. (a) Age-standardized DALYs
787 rate. (b) Age-standardized YLDs rate. (c) Number of DALYs cases. (d) Number of YLDs cases.
788 DALYs, disability-adjusted life years; YLDs, years lived with disability.

789 **Figure 20** Cases change and EAPC distribution of knee osteoarthritis attributable to metabolic
790 risks in women of reproductive age from 1990 to 2021. (a) EAPC of age-standardized DALYs
791 rate. (b) EAPC of age-standardized YLDs rate. (c) Change of number of DALYs. (d) Change of
792 number of YLDs. EAPC, estimated annual percentage change; DALYs, disability-adjusted life
793 years; YLDs, years lived with disability.

794 **Figure 21** Age-standardized rates and cases distribution of knee osteoarthritis attributable to
795 metabolic risks in women of reproductive age in 204 countries in 2021, by GBD regions. (a)
796 Age-standardized rate of DALYs and YLDs. (b) Number of DALYs and YLDs cases. DALYs,

disability-adjusted life years; YLDs, years lived with disability.

Figure 22 Burden of knee osteoarthritis attributable to metabolic risks in 204 countries from 1990 to 2021, by SDI. (a) Age-standardized rates of DALYs and YLDs. (b) Numbers of DALYs and YLDs cases. DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 23 Burden of knee osteoarthritis attributable to metabolic risks in 204 countries in 2021, by SDI. (a) Age-standardized rates of DALYs and YLDs. (b) Numbers of DALYs and YLDs cases. DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 24 Burden of knee osteoarthritis attributable to metabolic risks in 204 countries from 1990 to 2021, by age. (a) Age-standardized rates of DALYs and YLDs. (b) Numbers of DALYs and YLDs cases. DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 25 Burden of knee osteoarthritis attributable to metabolic risks in 204 countries in 2021, by age. (a) Age-standardized rates of DALYs and YLDs. (b) Numbers of DALYs and YLDs cases. DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 26 Burden of knee osteoarthritis attributable to metabolic risks in 204 countries from 1990 to 2021 for female. (a) Age-standardized rates of DALYs and YLDs. (b) Numbers of DALYs and YLDs cases. DALYs, disability-adjusted life years; YLDs, years lived with disability.

Figure 27 Burden of knee osteoarthritis attributable to metabolic risks in 204 countries in 2021 for female. (a) Age-standardized rates of DALYs and YLDs. (b) Numbers of DALYs and YLDs cases. DALYs, disability-adjusted life years; YLDs, years lived with disability.

817 **Figure 28** Burden of knee osteoarthritis attributable to metabolic risks in 204 countries in 2021,
818 by sex and age. (a) DALYs. (b) YLDs. DALYs, disability-adjusted life years; YLDs, years lived
819 with disability.

820 **Figure 29** Burden of knee osteoarthritis attributable to metabolic risks in 204 countries from
821 1990 to 2021 for female. (a) DALYs. (b) YLDs. DALYs, disability-adjusted life years; YLDs,
822 years lived with disability.

823 **Figure 30** Changes in the DALYs, YLDs of Knee osteoarthritis (KOA) according to population-
824 level determinants of population growth, aging, and epidemiological change from 1990 to 2021
825 at the global level and by Sociodemographic Index (SDI) quintile.

826 **Figure 31** Changes in the DALYs, YLDs of Knee osteoarthritis (KOA) according to population-
827 level determinants of population growth, aging, and epidemiological change from 1990 to 2021
828 at the global level and by sex quintile.

829 **Figure 32** Forecasts of numbers and age-standardized rates for DALYs and YLDs of knee
830 osteoarthritis attributable to metabolic risks in 204 countries, stratified by sex, from 2022 to 2050
831 using the ARIMA model. DALYs, disability-adjusted life years; YLDs, years lived with
832 disability; ARIMA, autoregressive integrated moving average.

833 **Figure 33** Forecasts of numbers and age-standardized rates for DALYs and YLDs of knee
834 osteoarthritis attributable to metabolic risks in 204 countries, stratified by sex, from 2022 to 2050
835 using the ES model. DALYs, disability-adjusted life years; YLDs, years lived with disability;
836 ES, Exponential Smoothing.

837 **Figure 34** Global Knee osteoarthritis Burden Cluster Analysis by Region (1990–2021). This
838 dendrogram illustrates the hierarchical clustering of regions based on their burden trends Knee
839 osteoarthritis over three decades

840 **Table1**

841 **Table2**

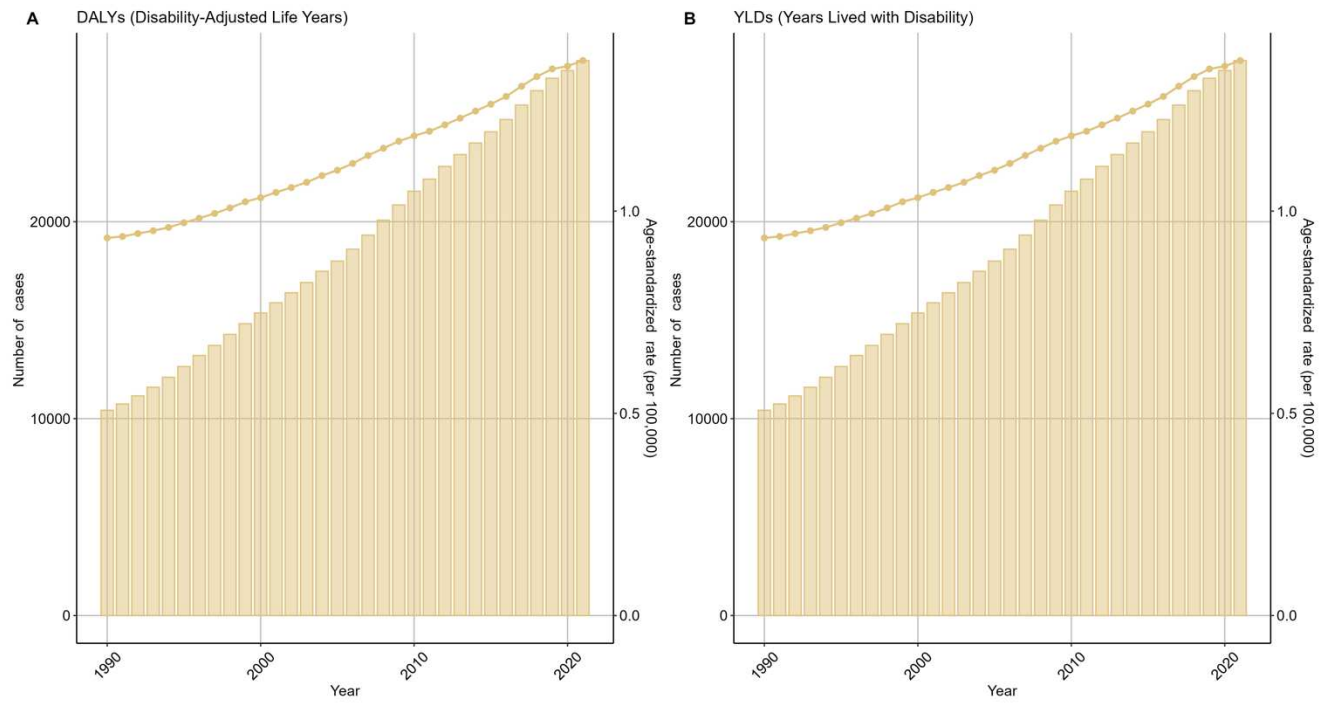
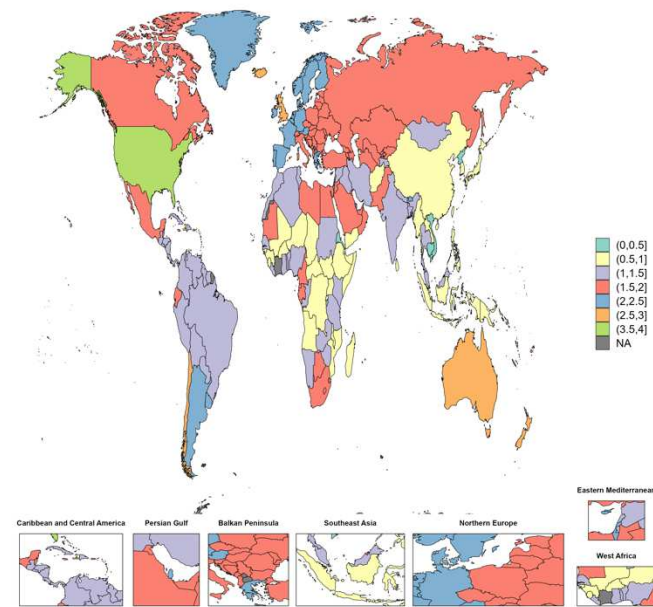
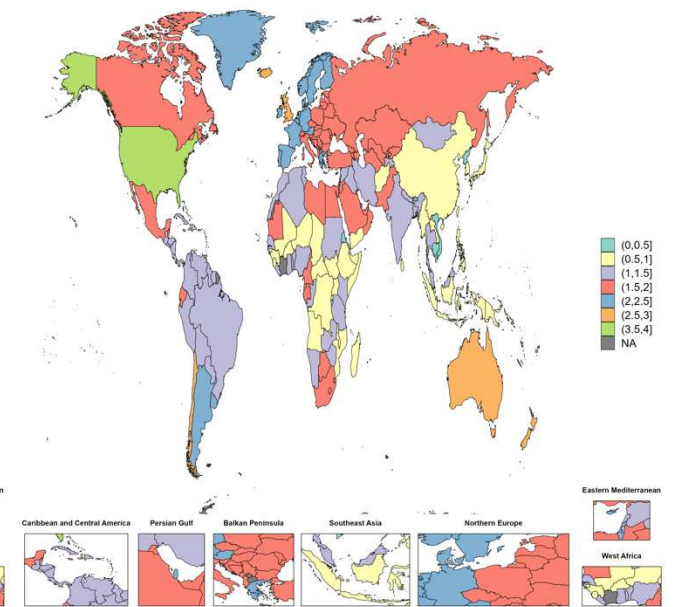


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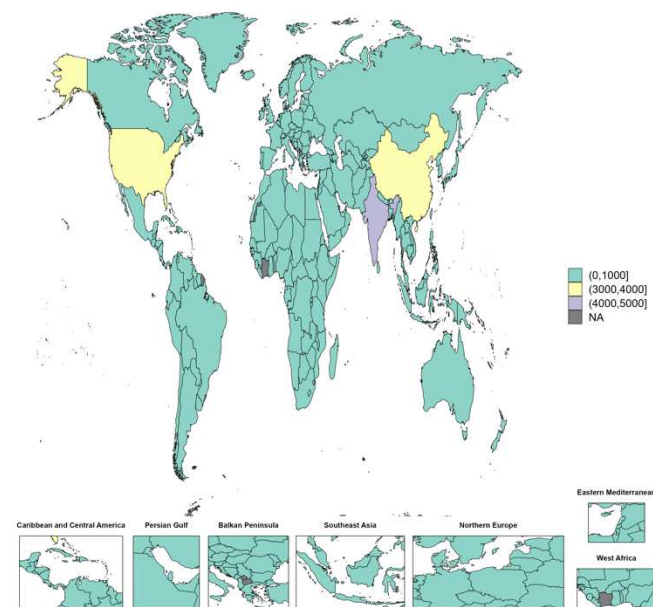
A Age-standardized DALYs rate



B Age-standardized YLDs rate



C Number of DALYs cases



D Number of YLDs cases

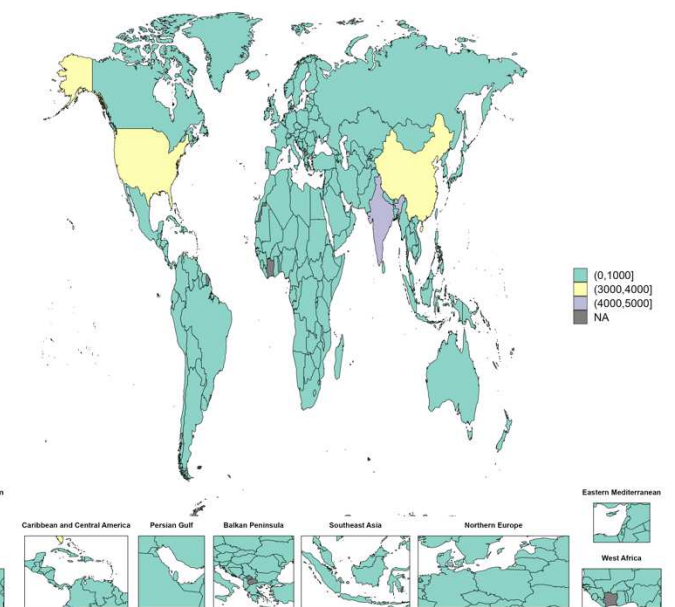
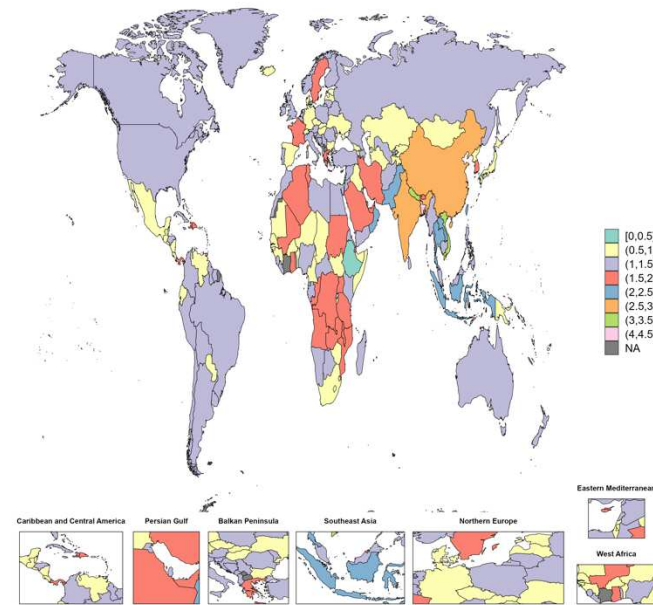
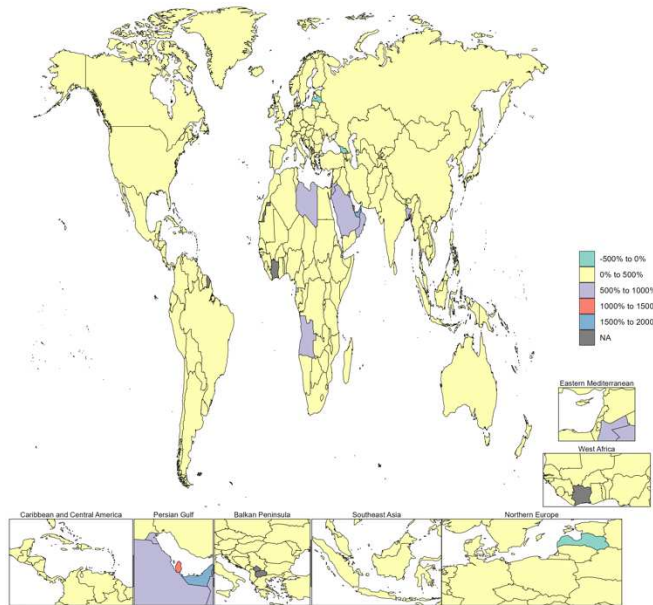


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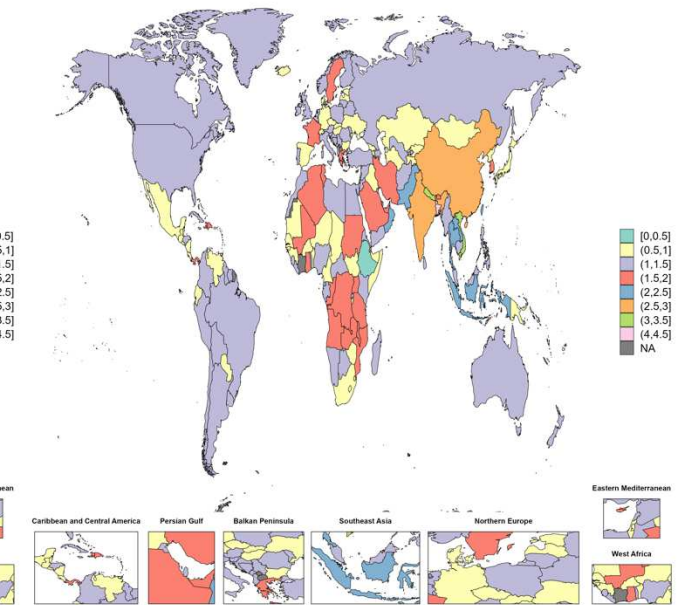
A Age-standardized DALYs Rate



C Change in the number of DALYs cases



B Age-standardized YLDs Rate



D Change in the number of YLDs cases

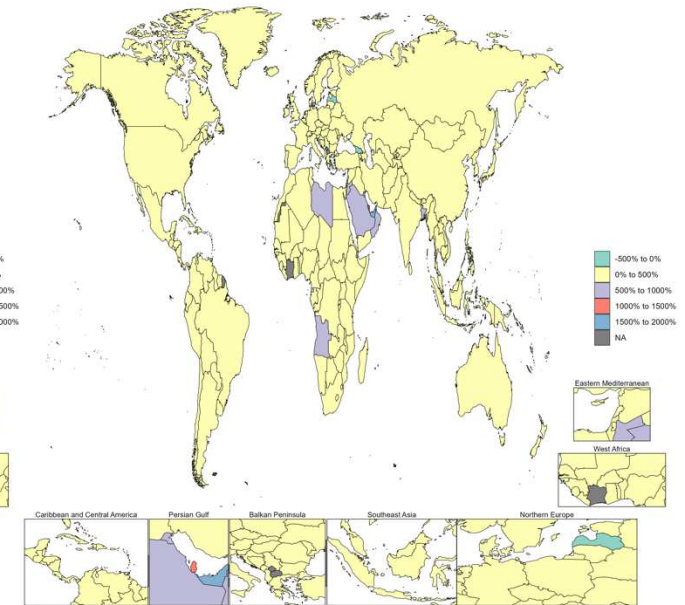


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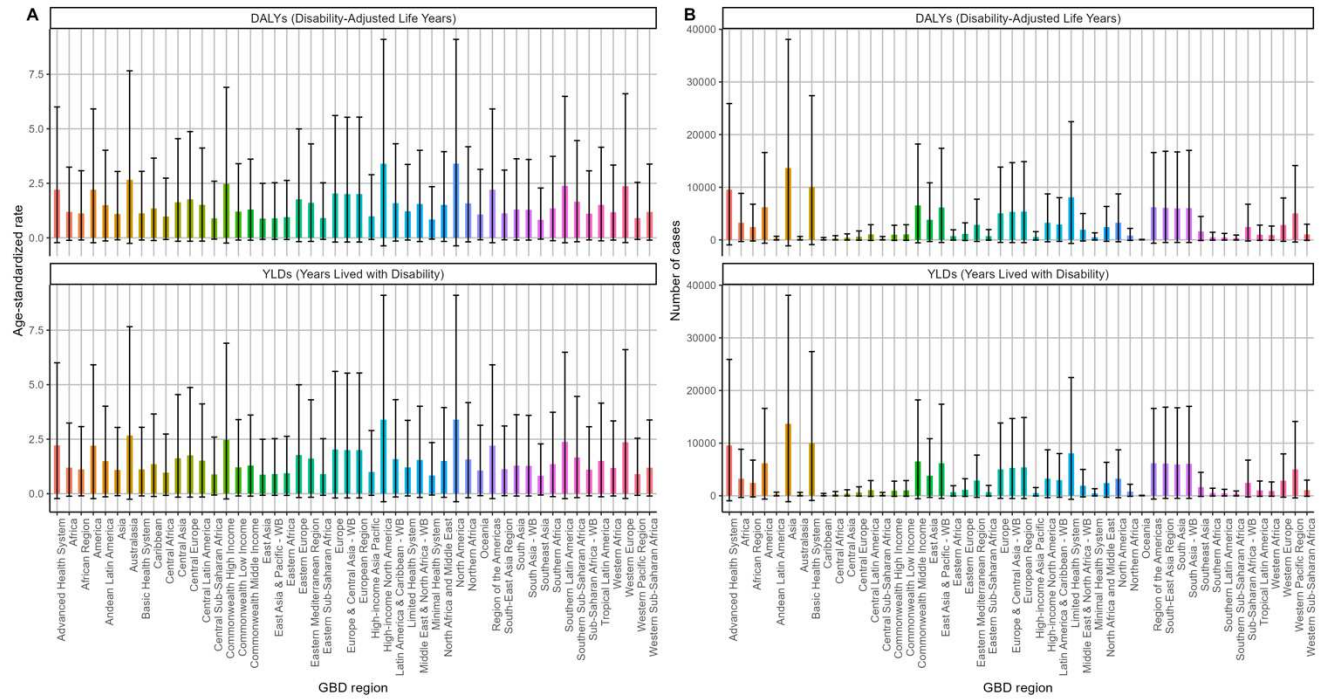


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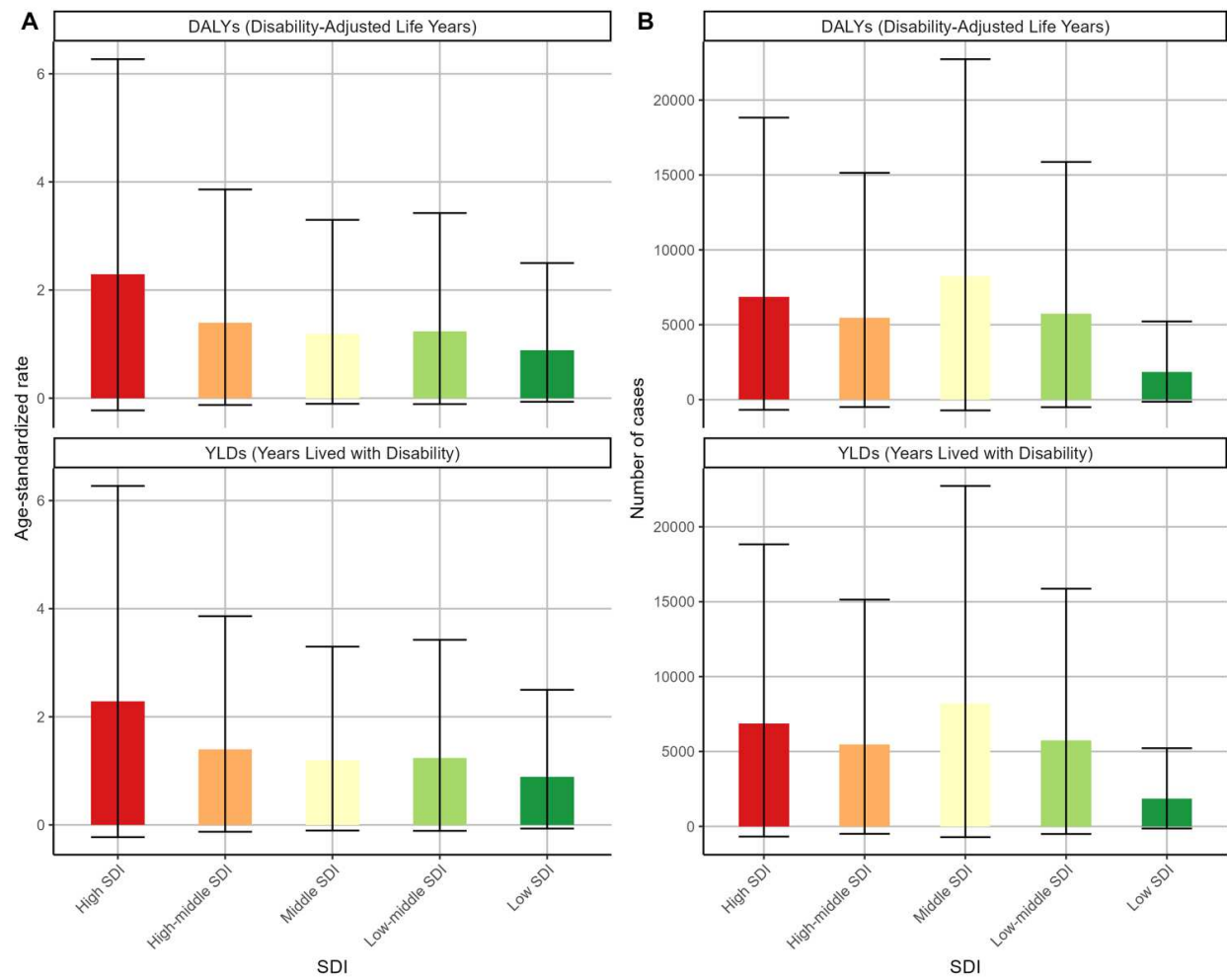


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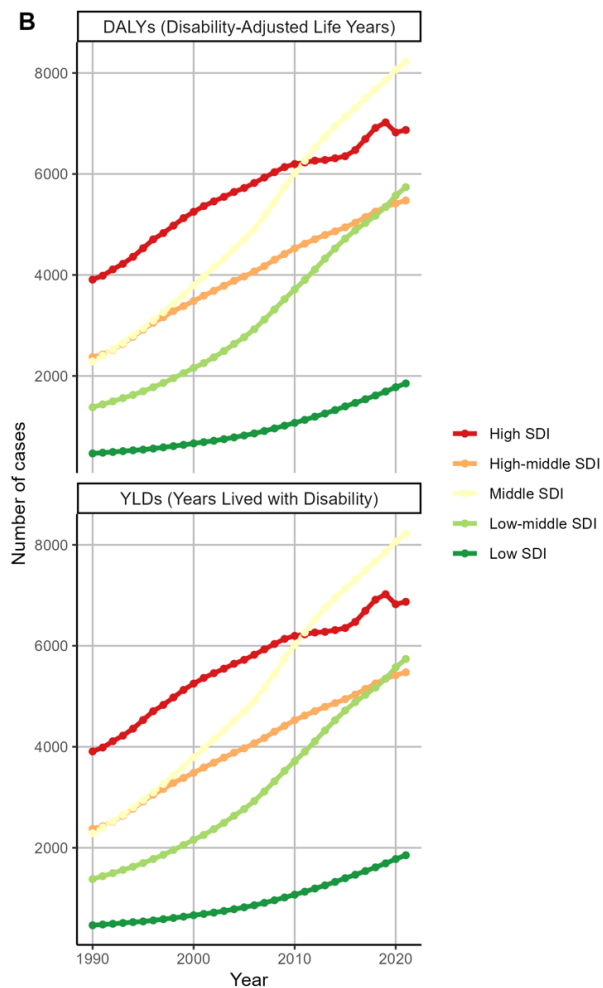
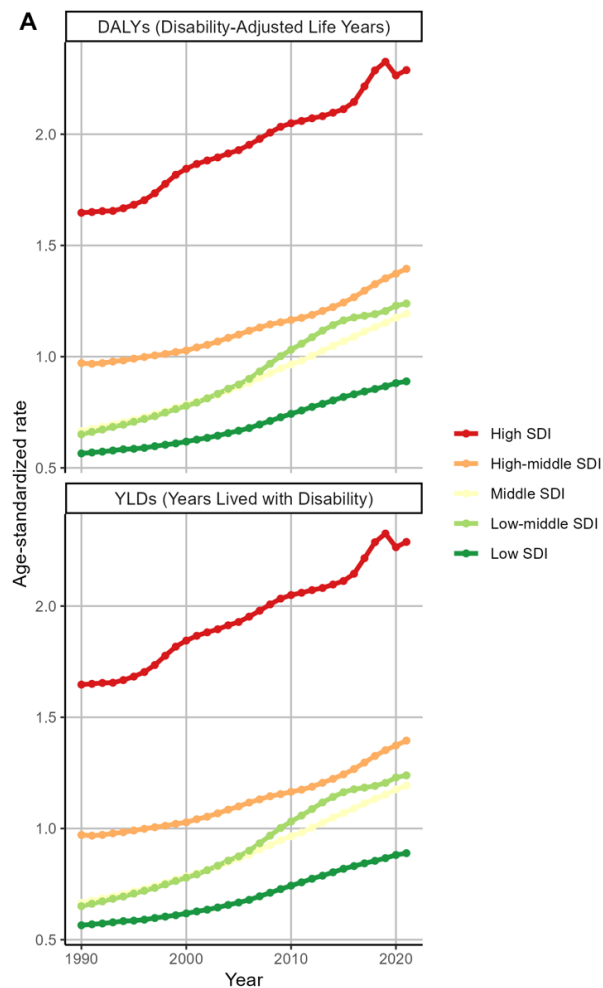


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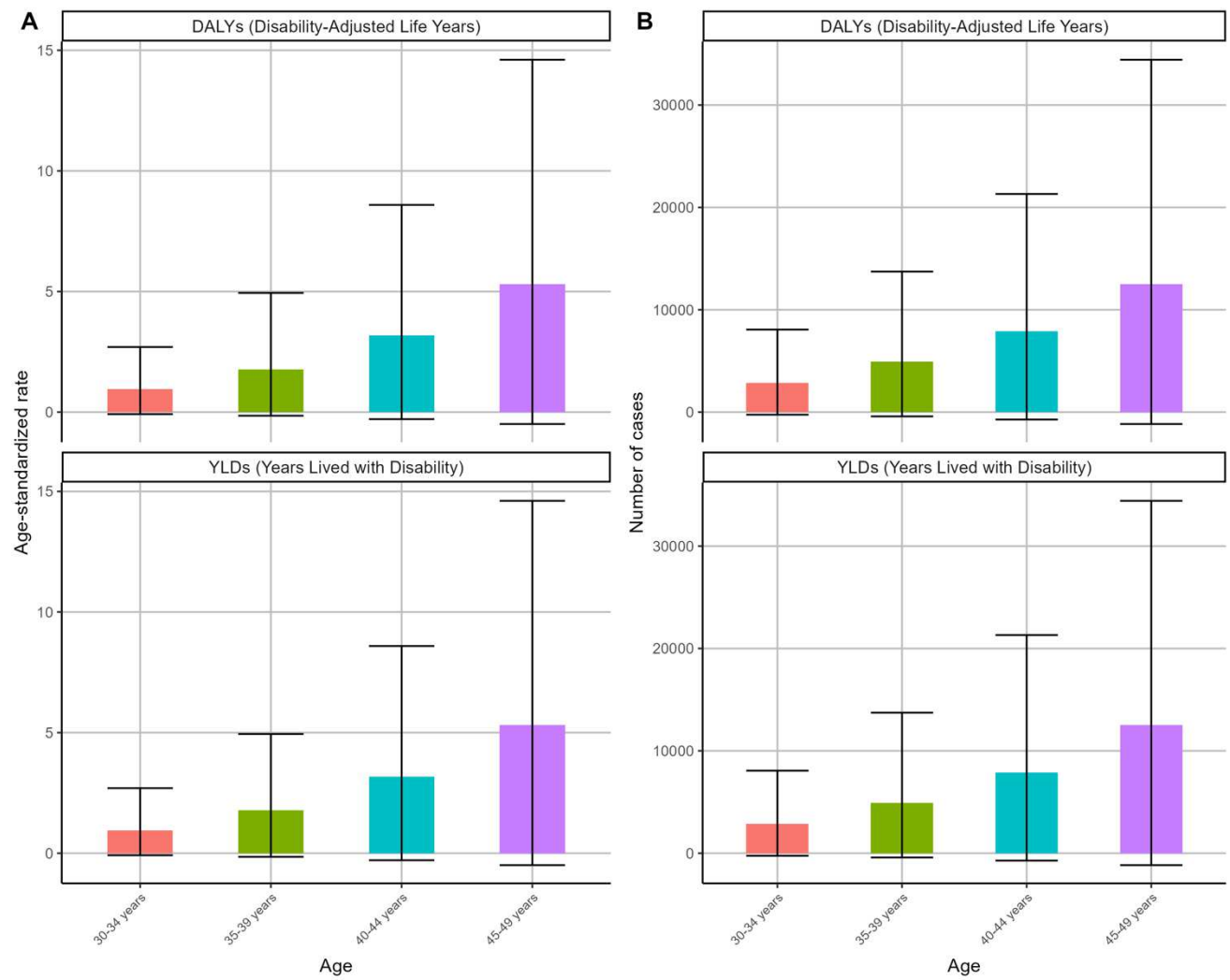


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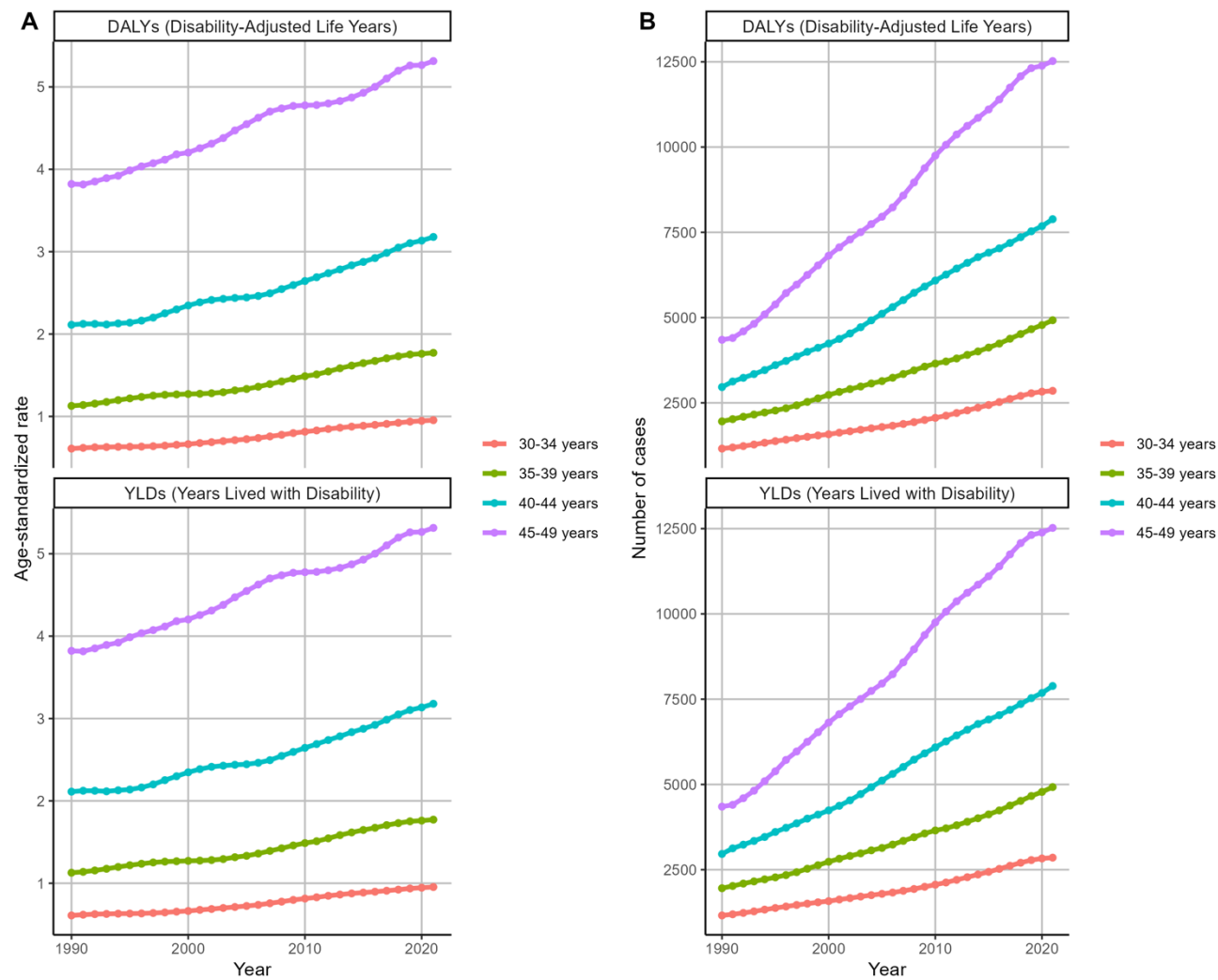


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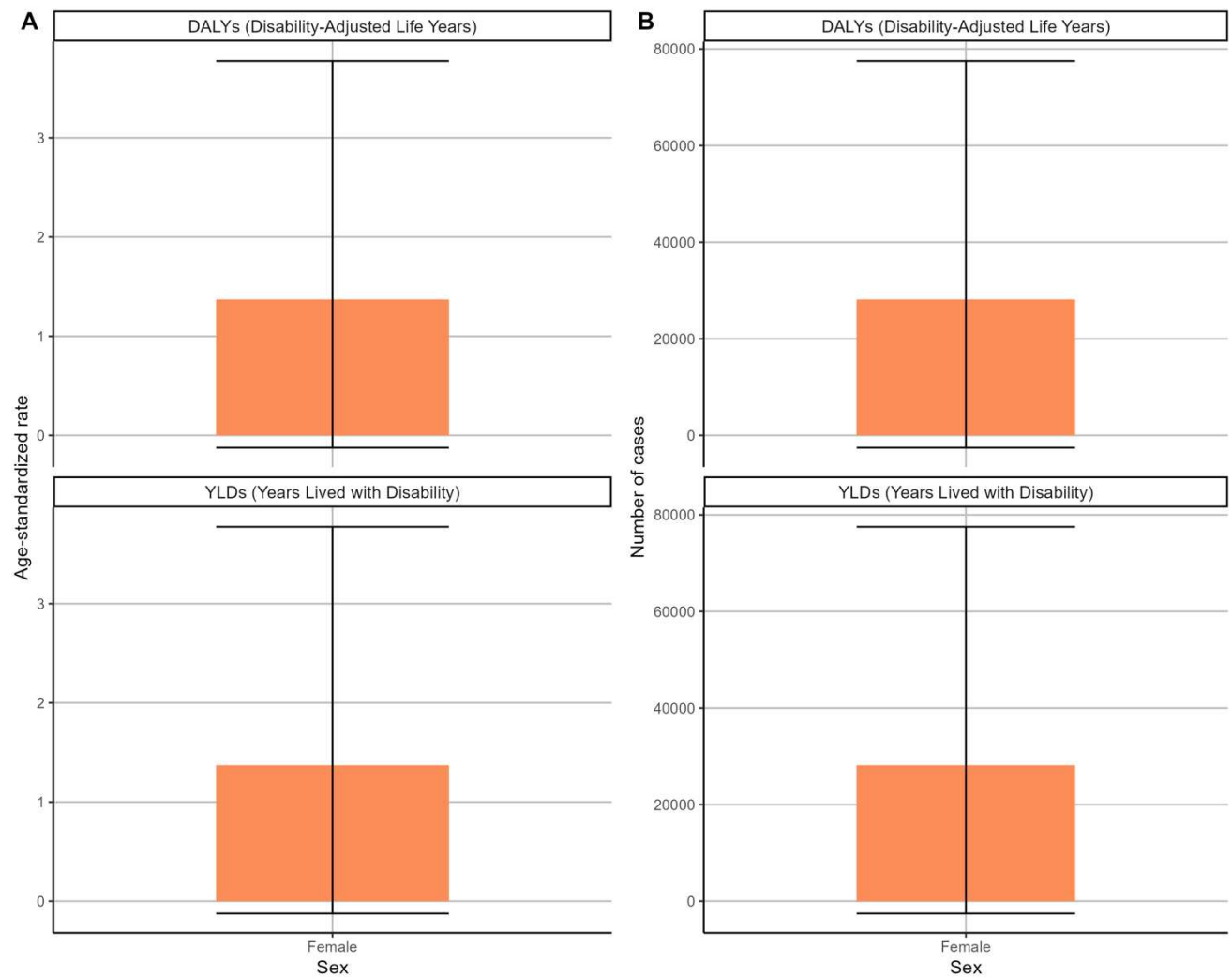


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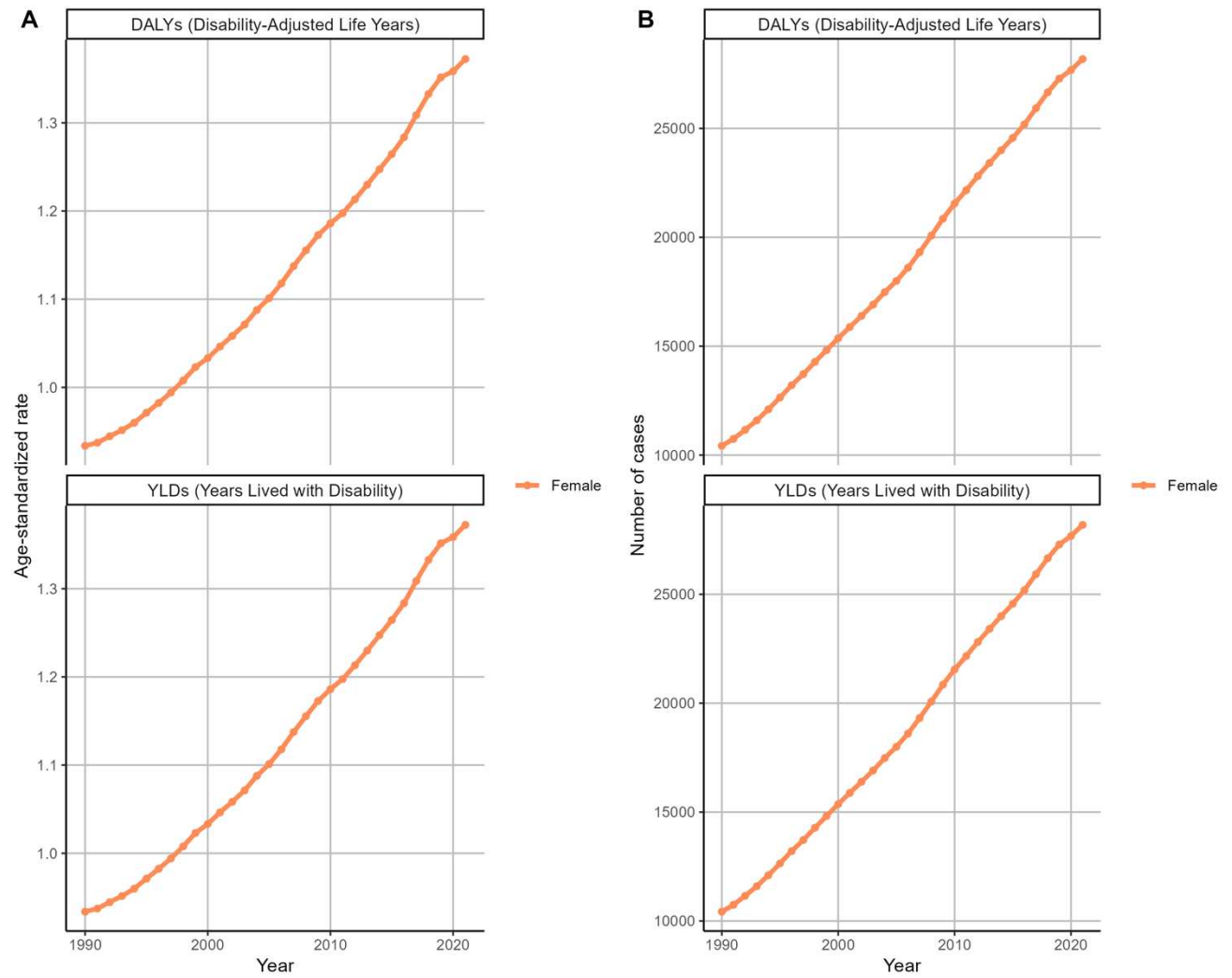


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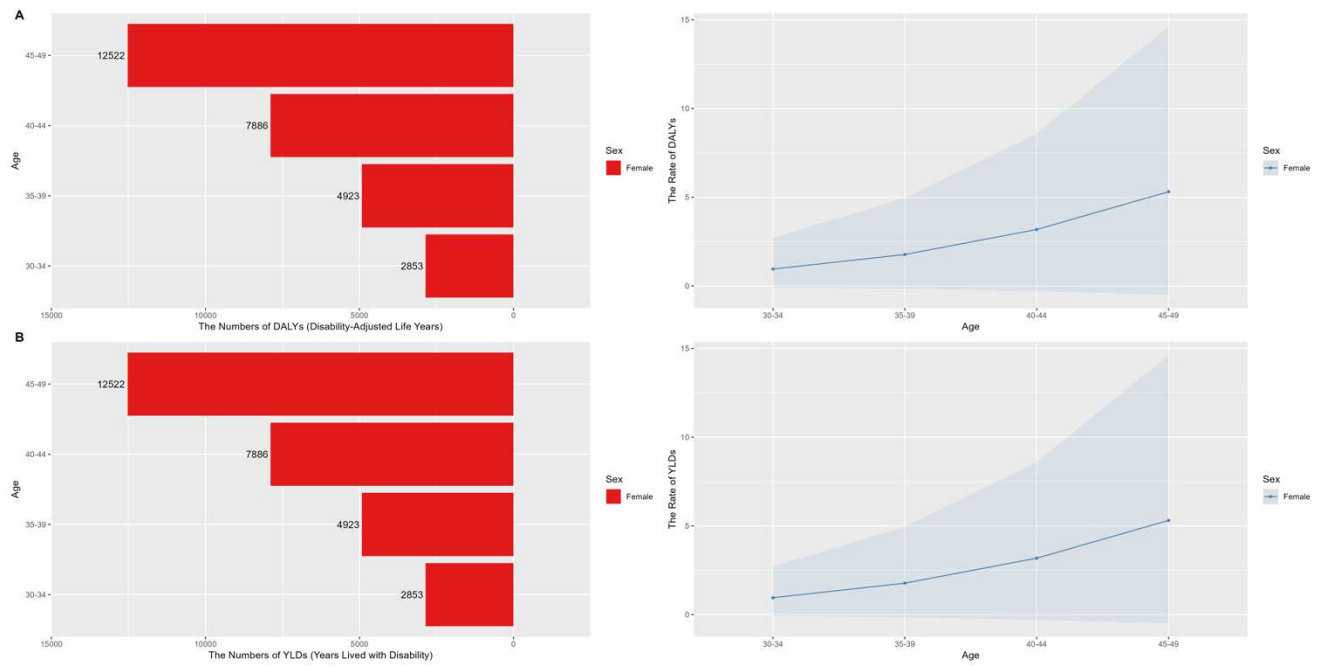


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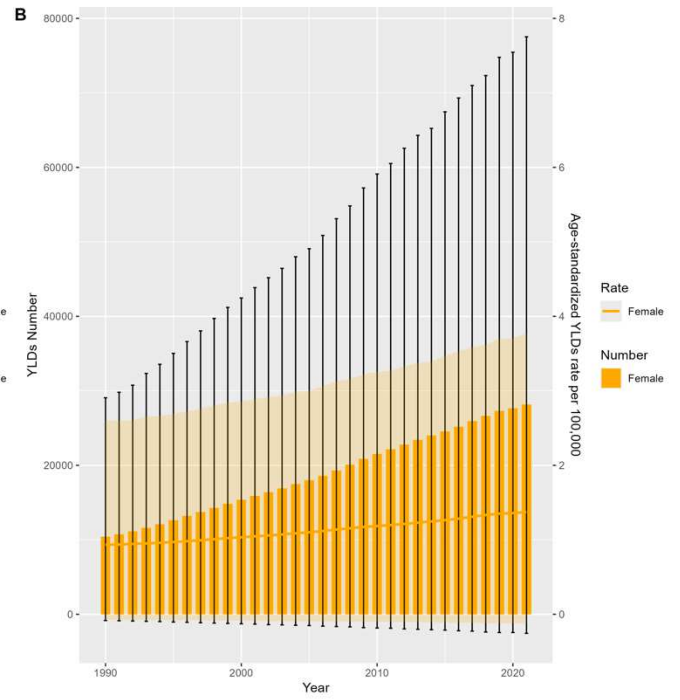
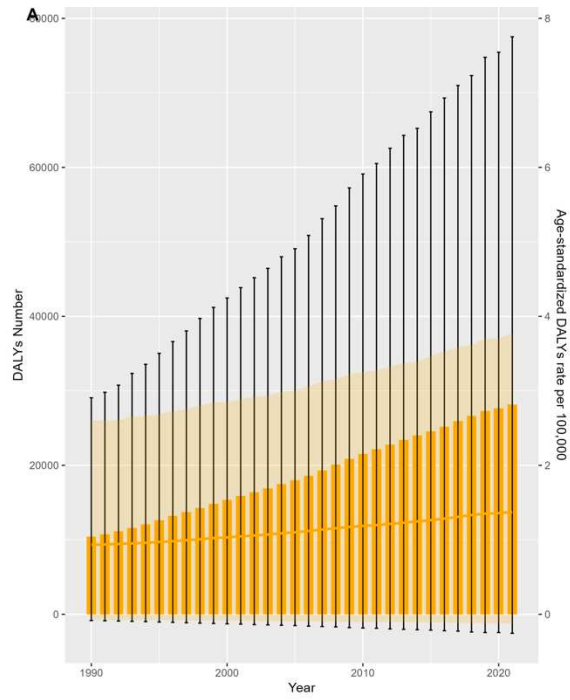


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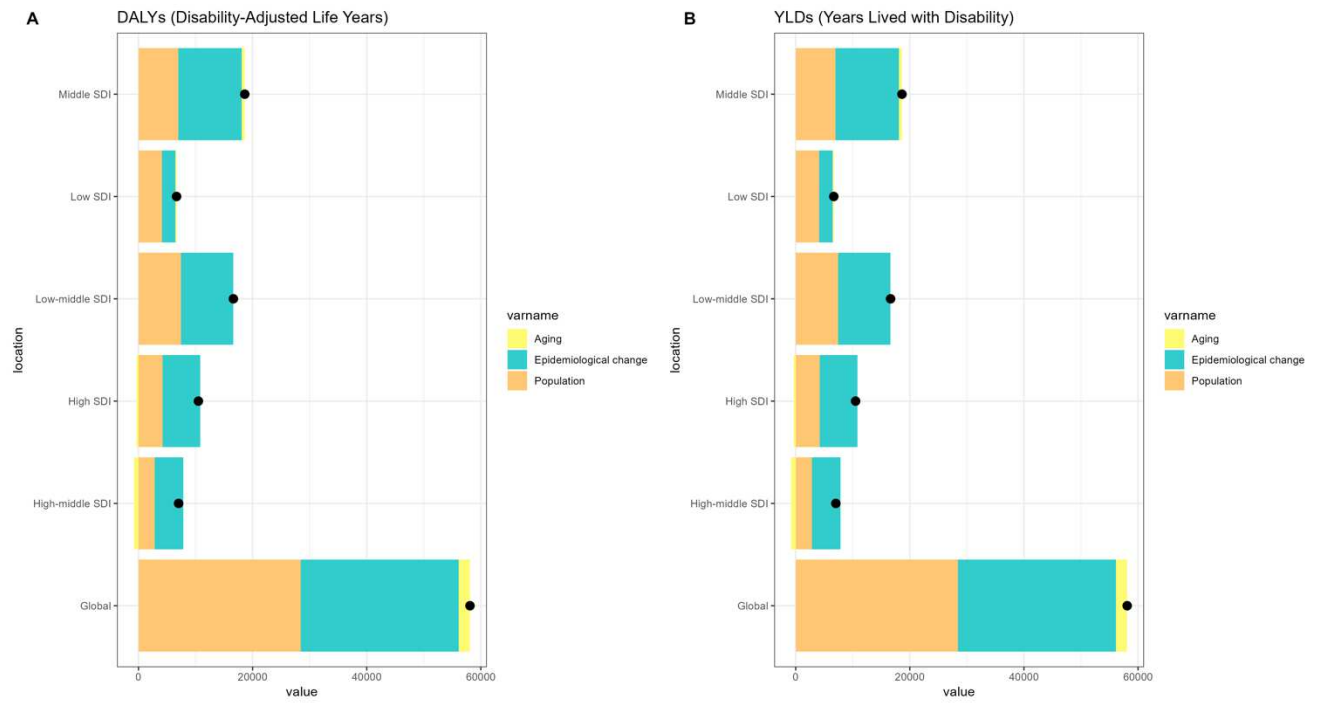


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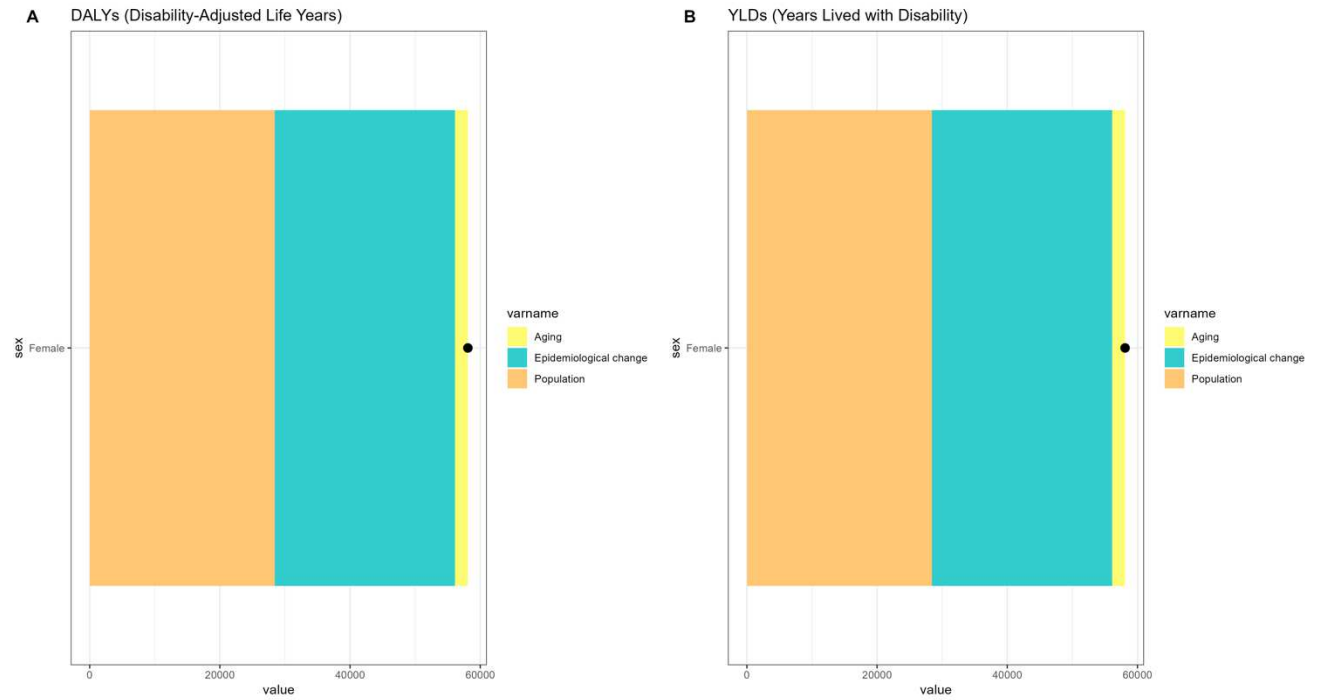
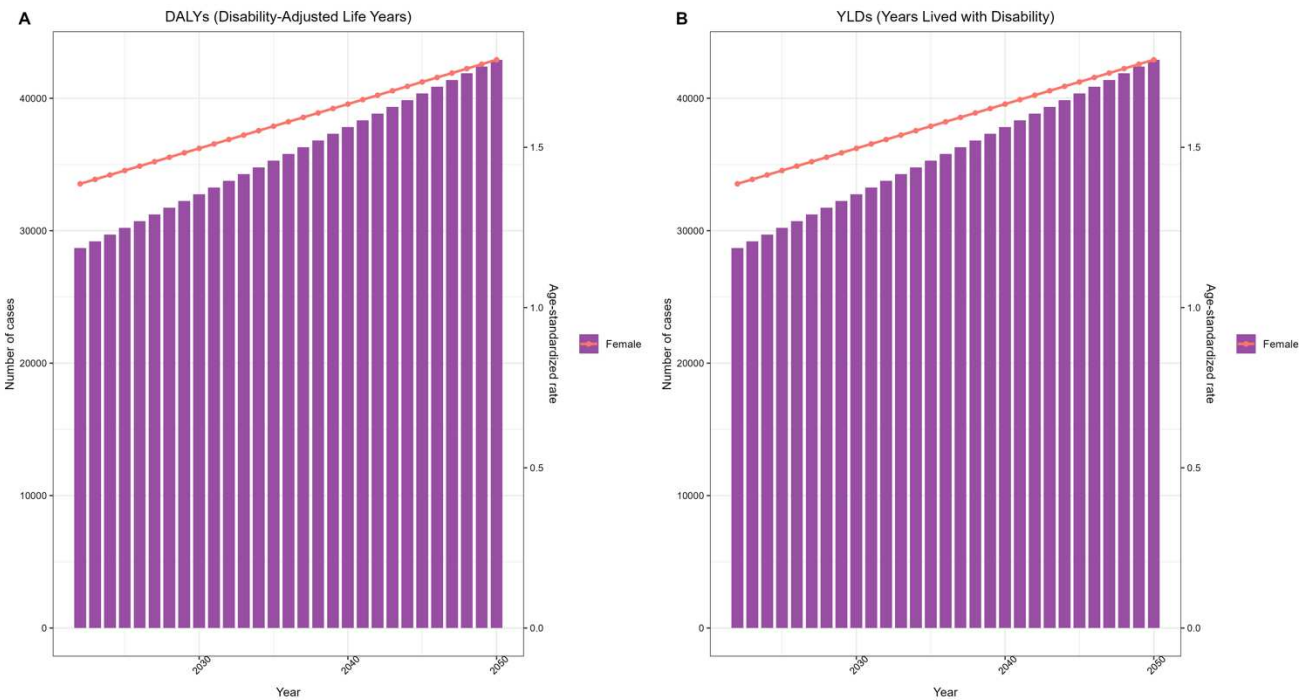


Figure 14

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46 **Figure 15**

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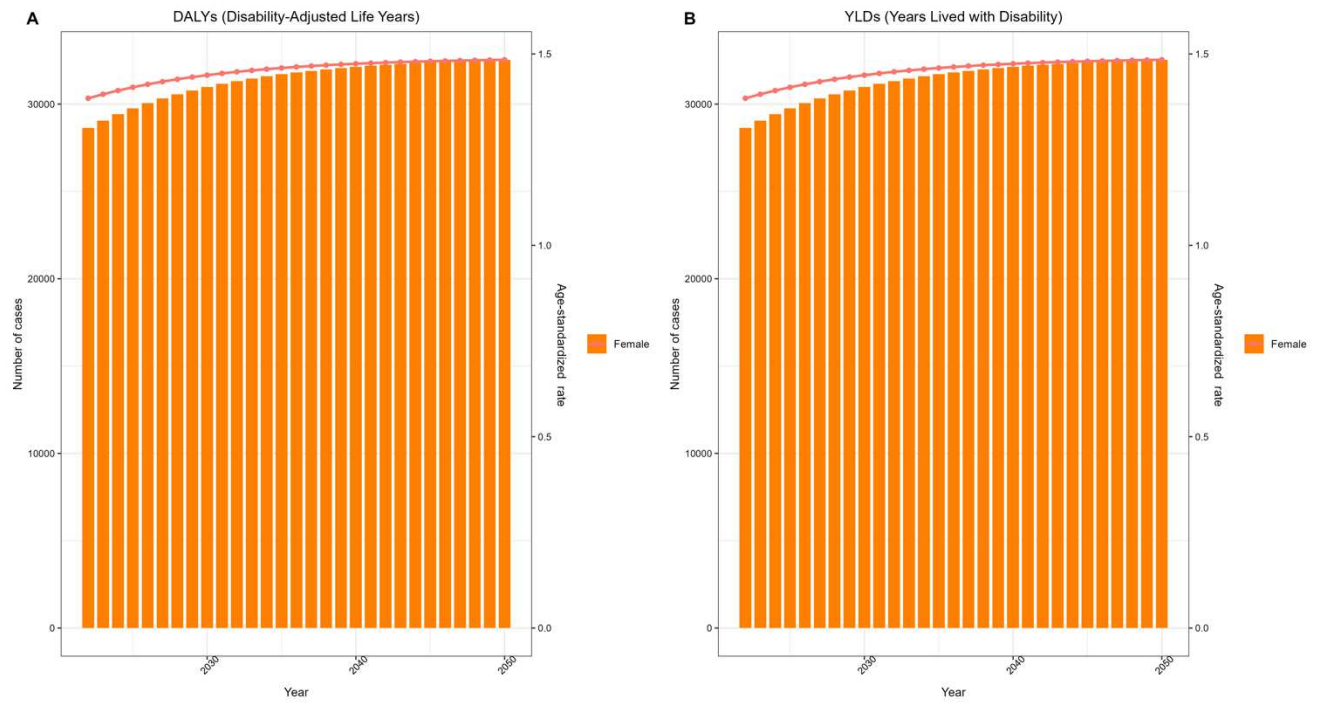


Figure 16

Cluster Dendrogram

— Minor increase

— Remained stable or minor decrease

— Significant decrease

— Significant increase

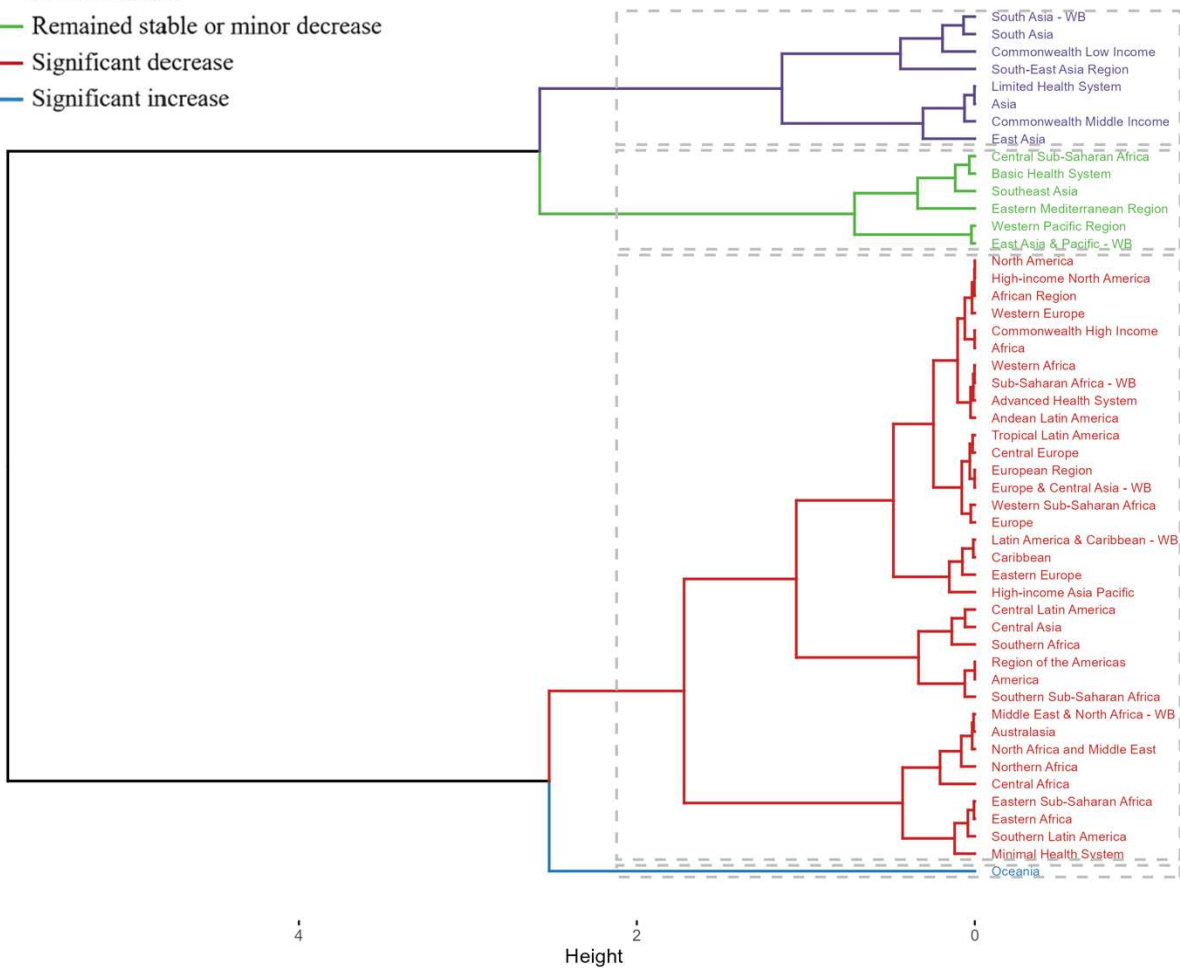


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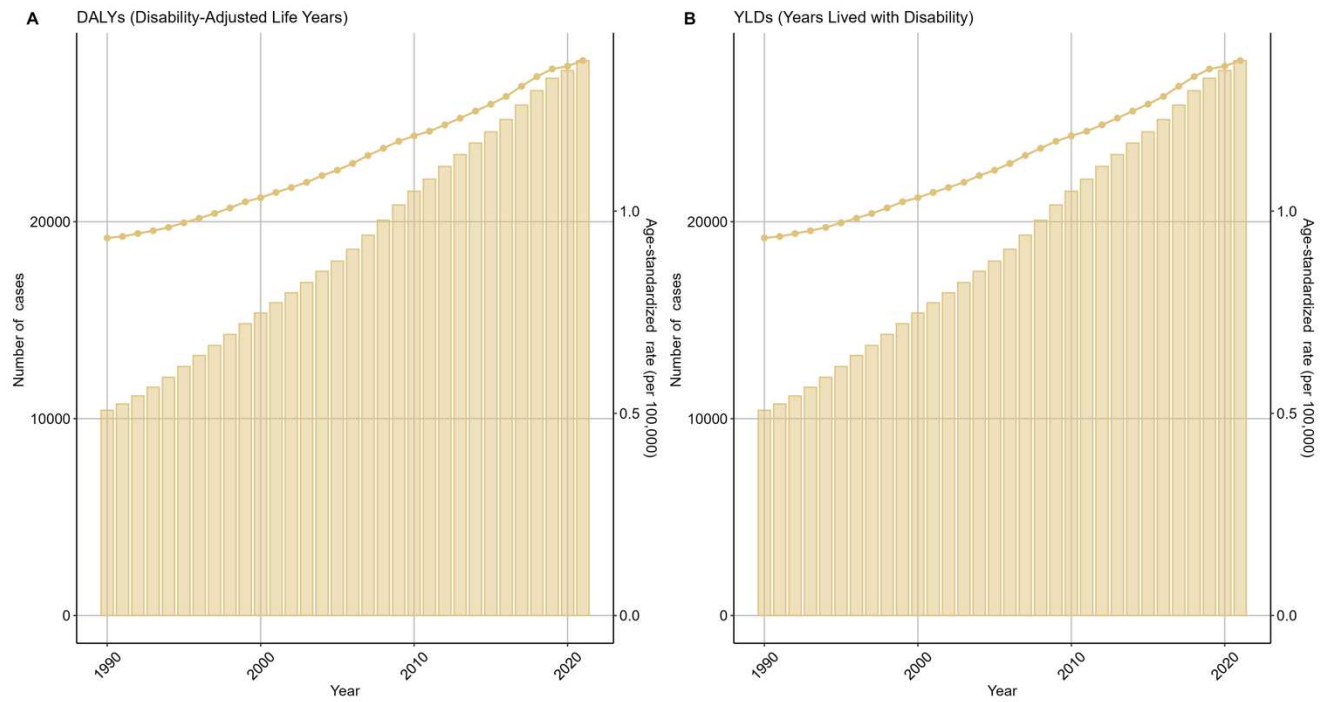
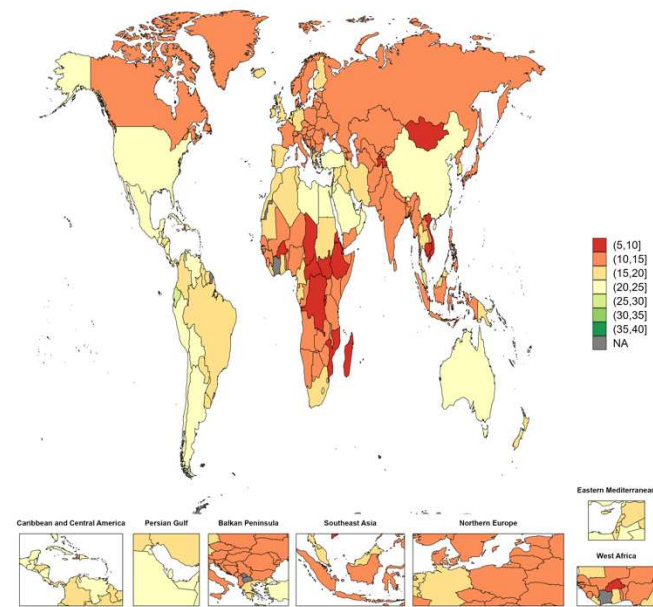
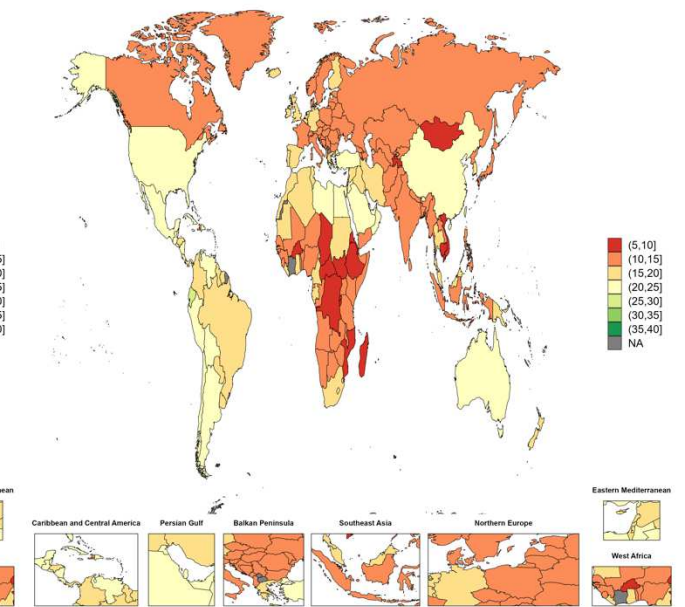


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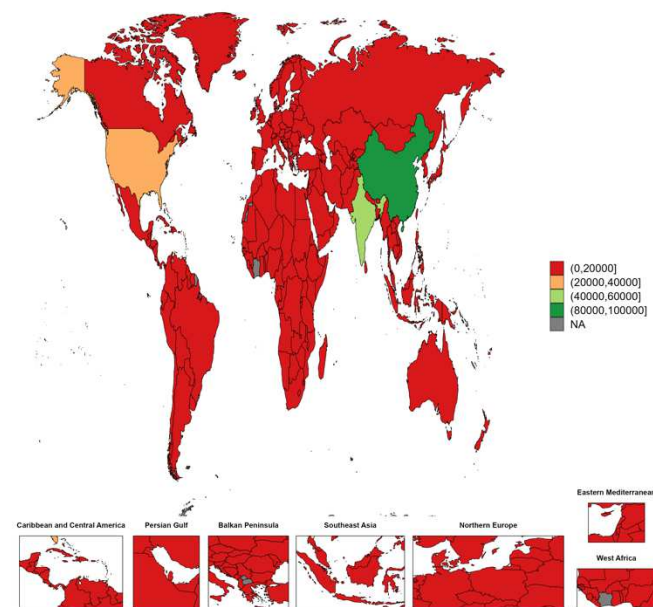
A Age-standardized DALYs rate



B Age-standardized YLDs rate



C Number of DALYs cases



D Number of YLDs cases

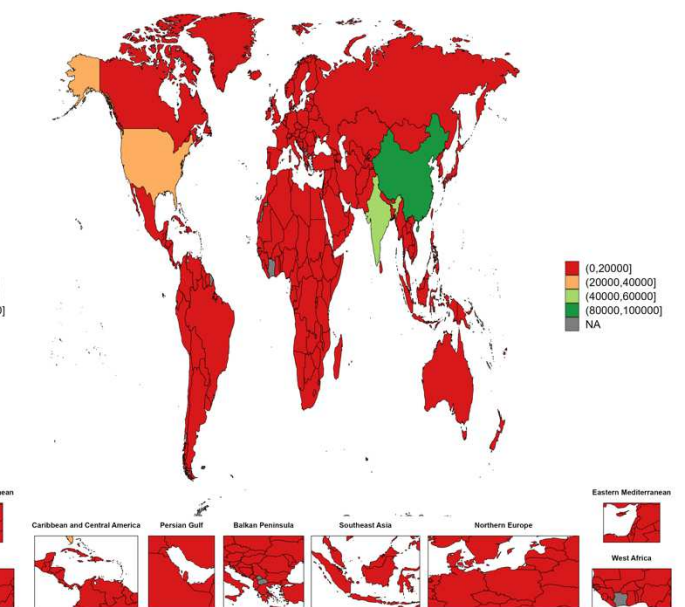


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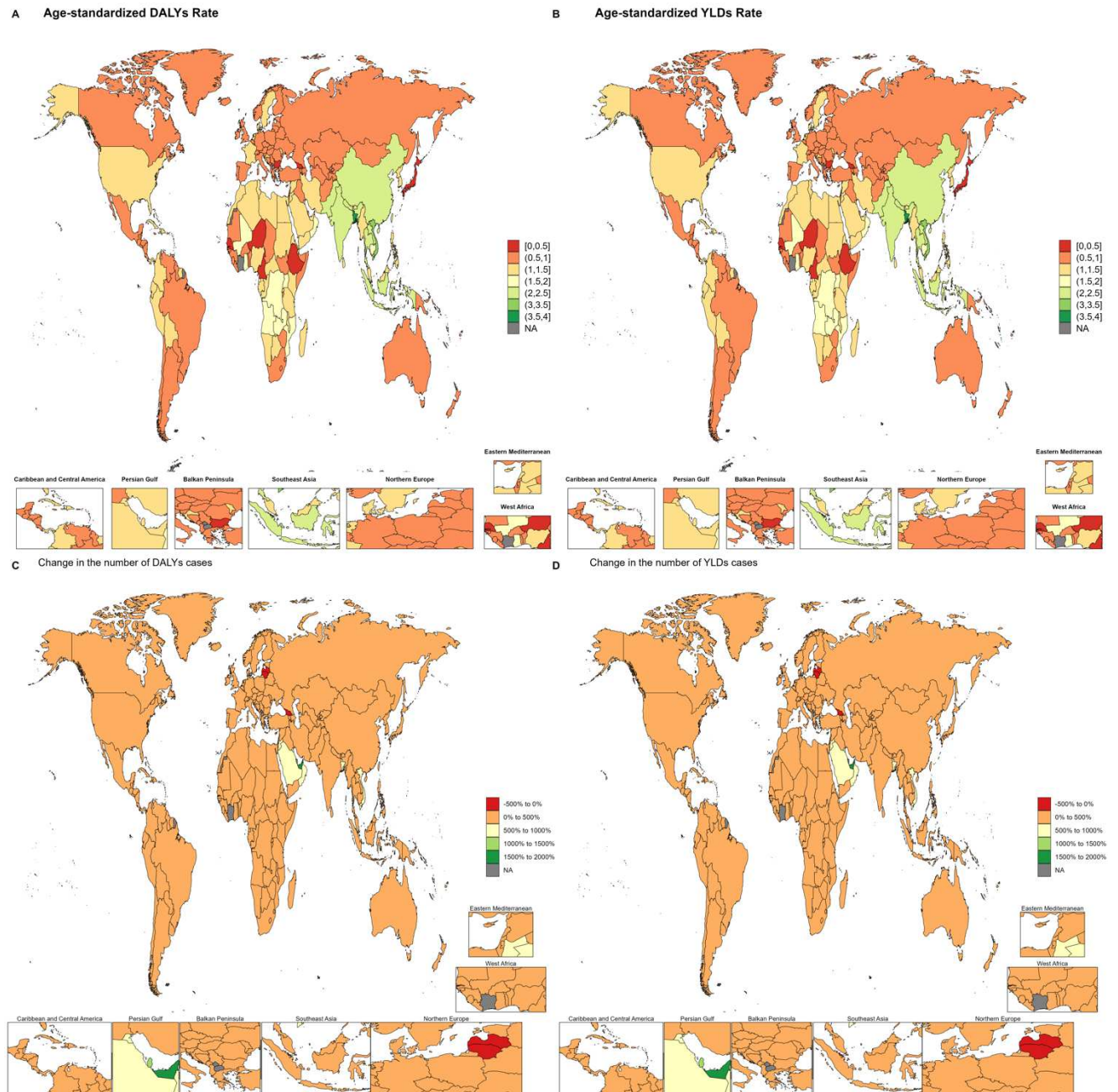


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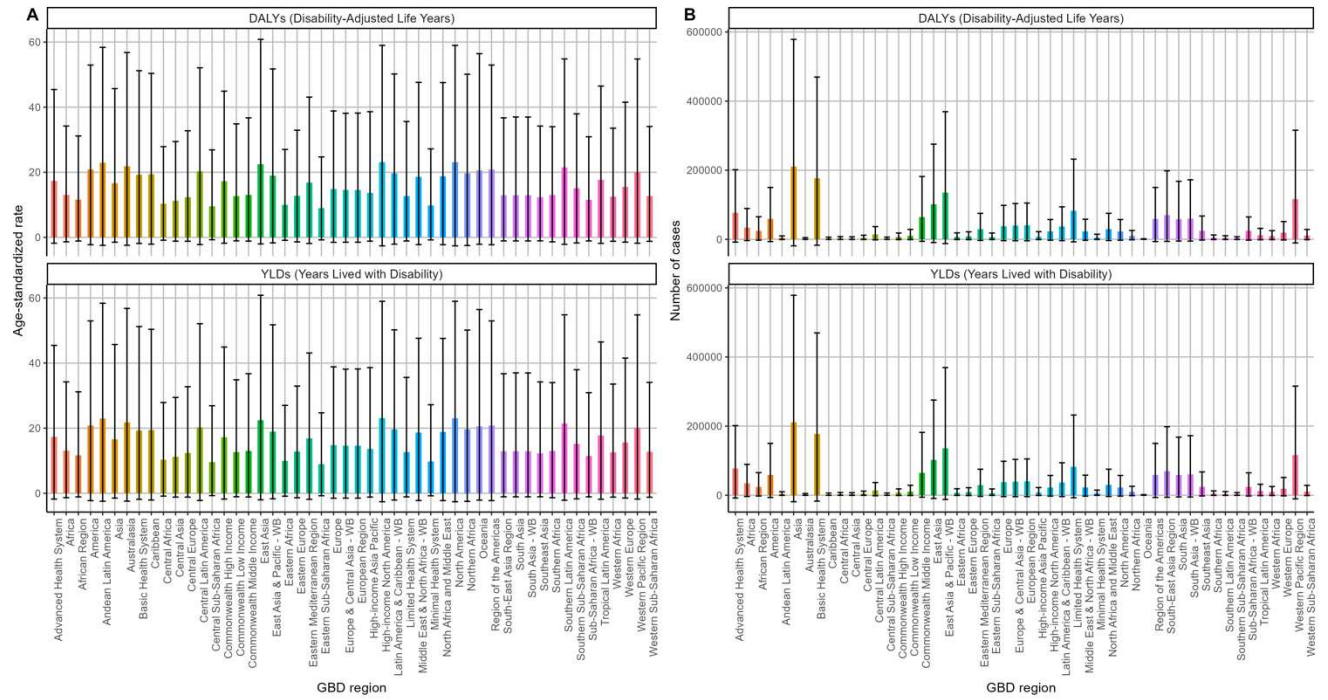


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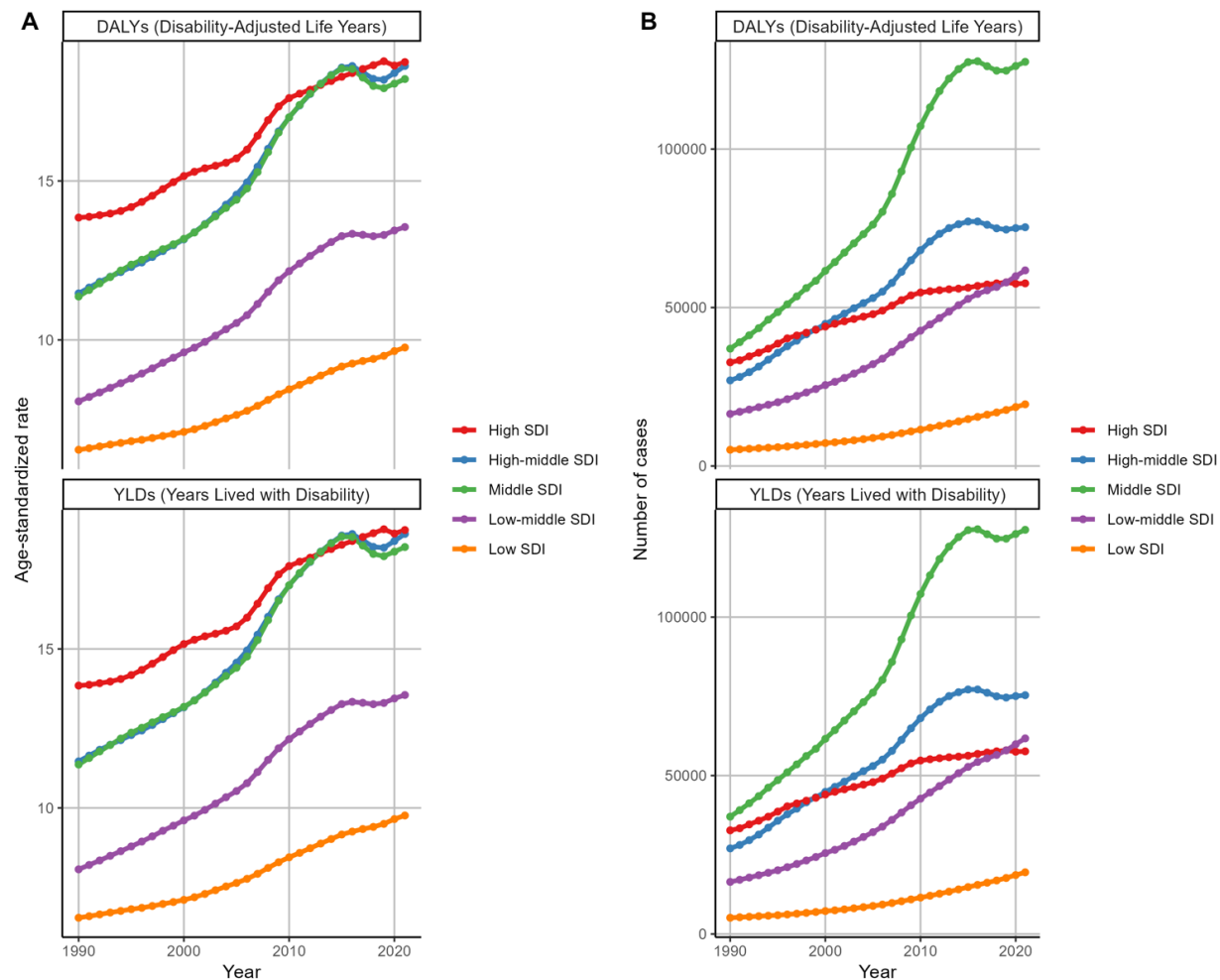


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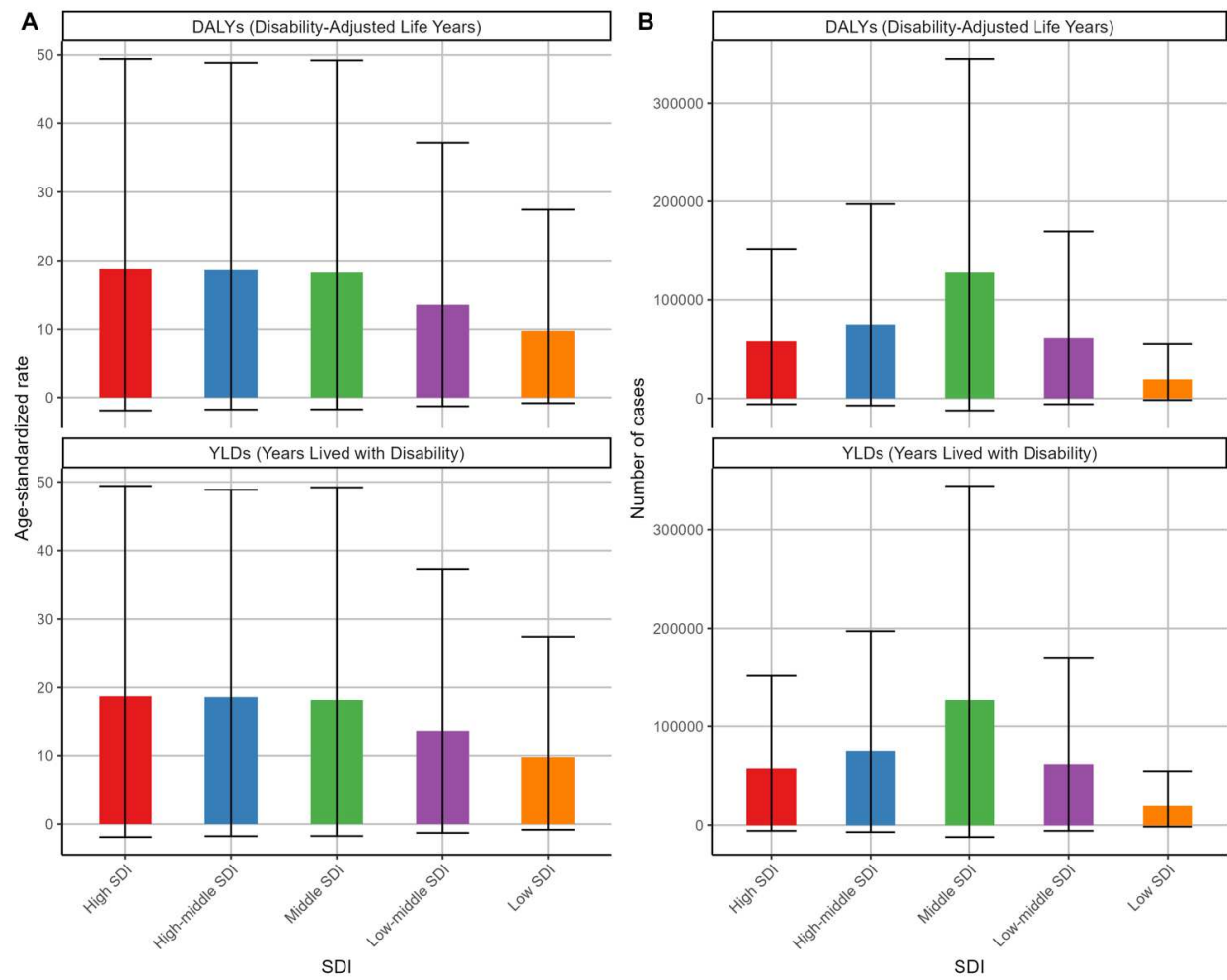


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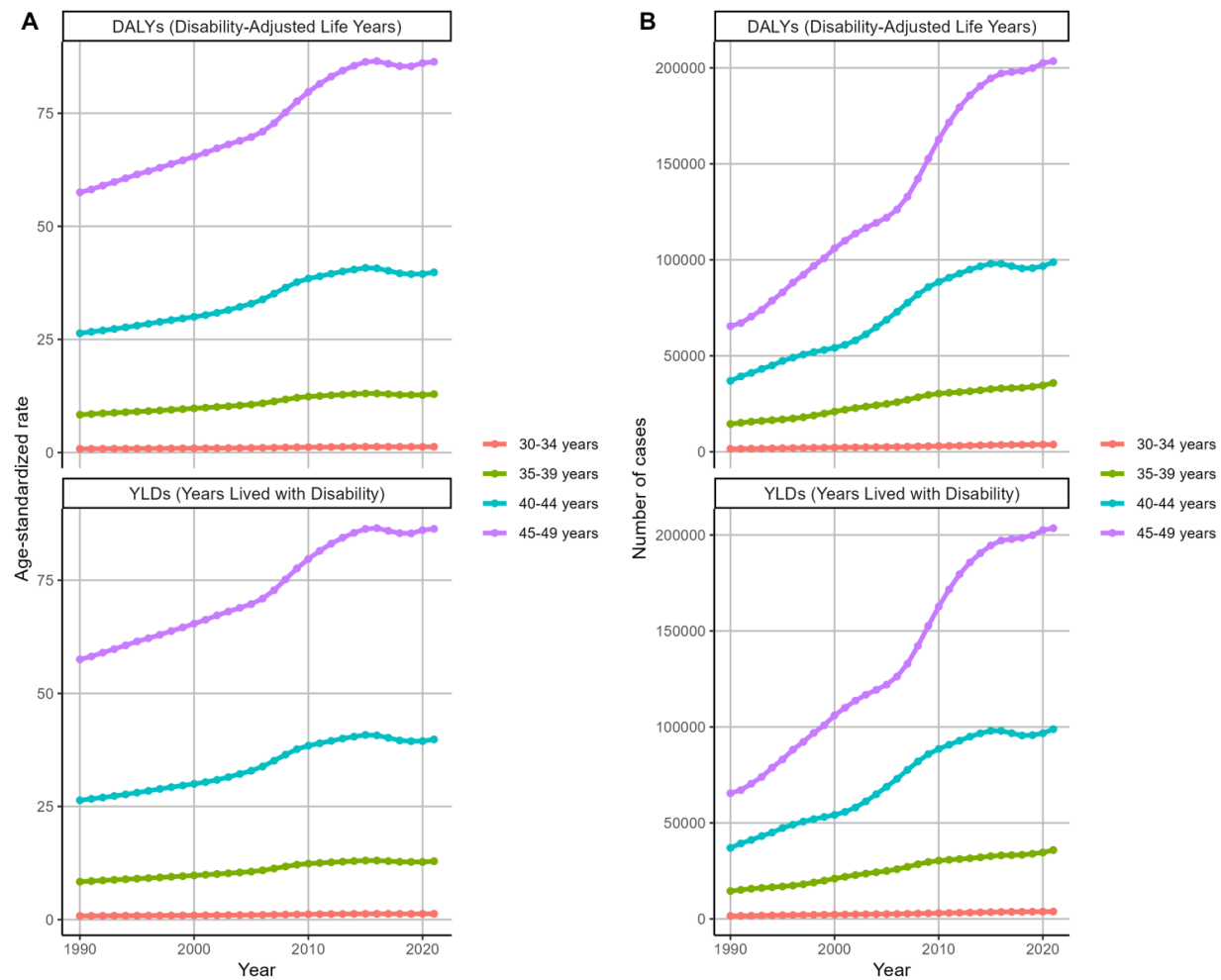


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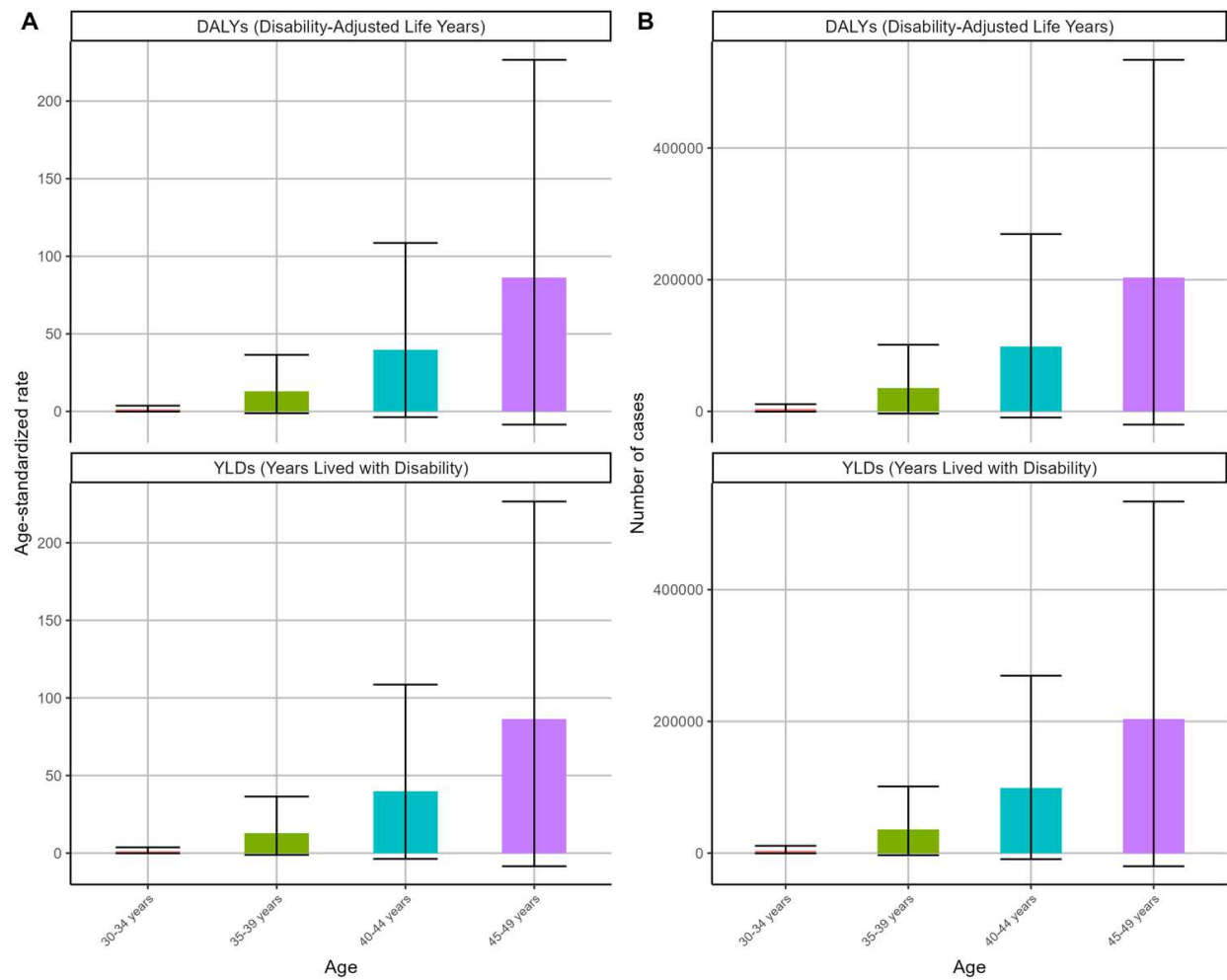


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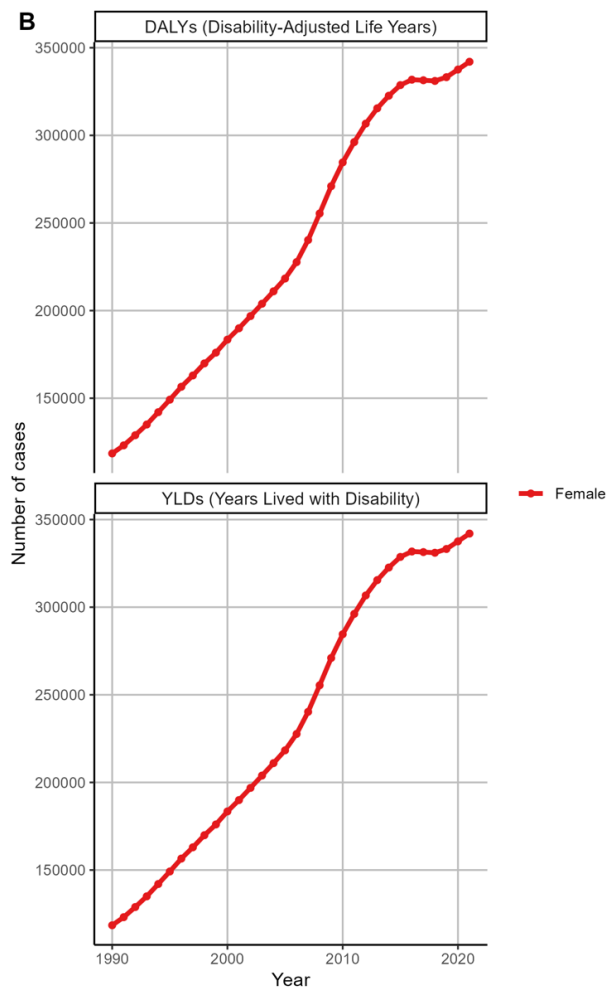
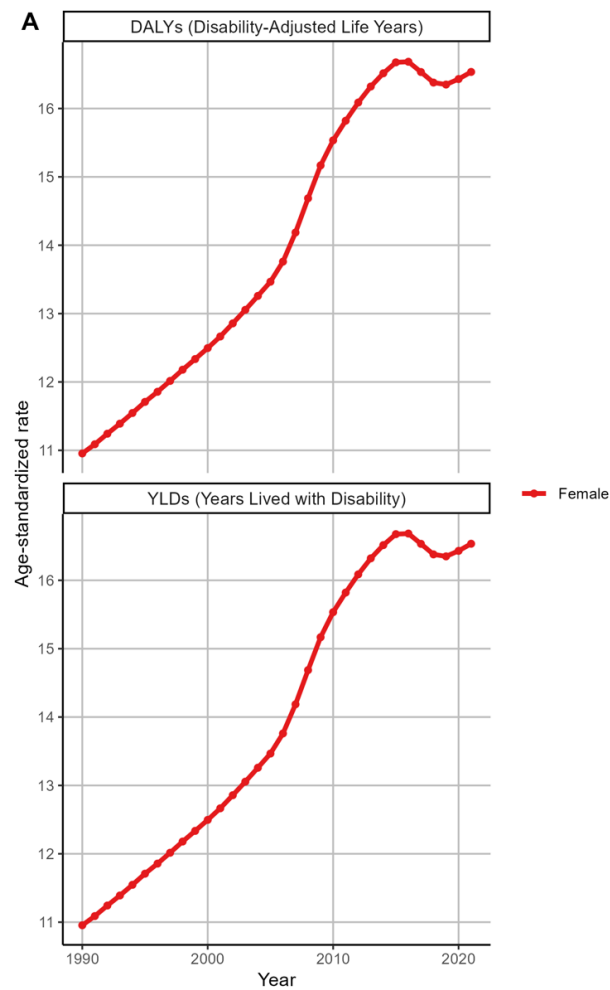


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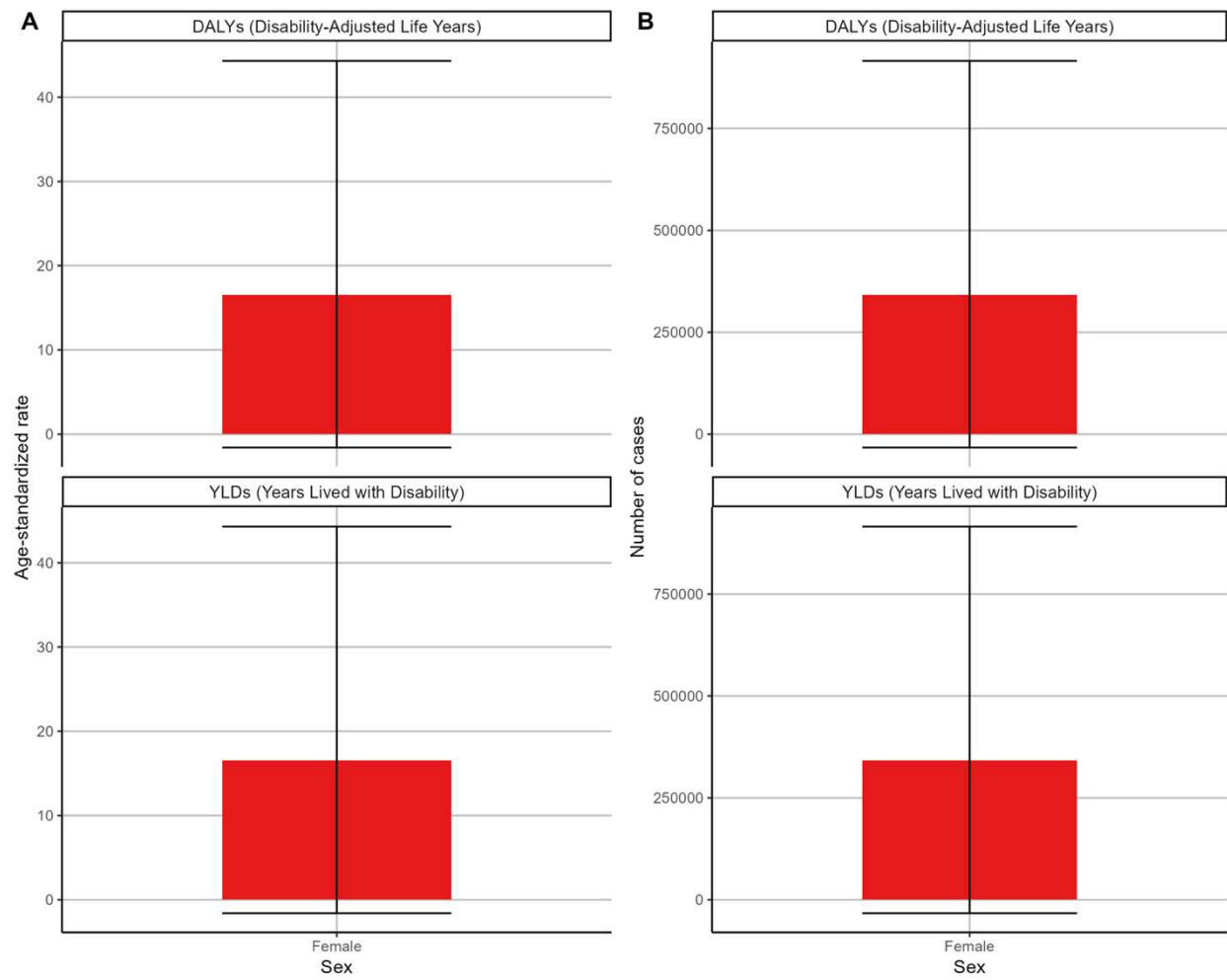


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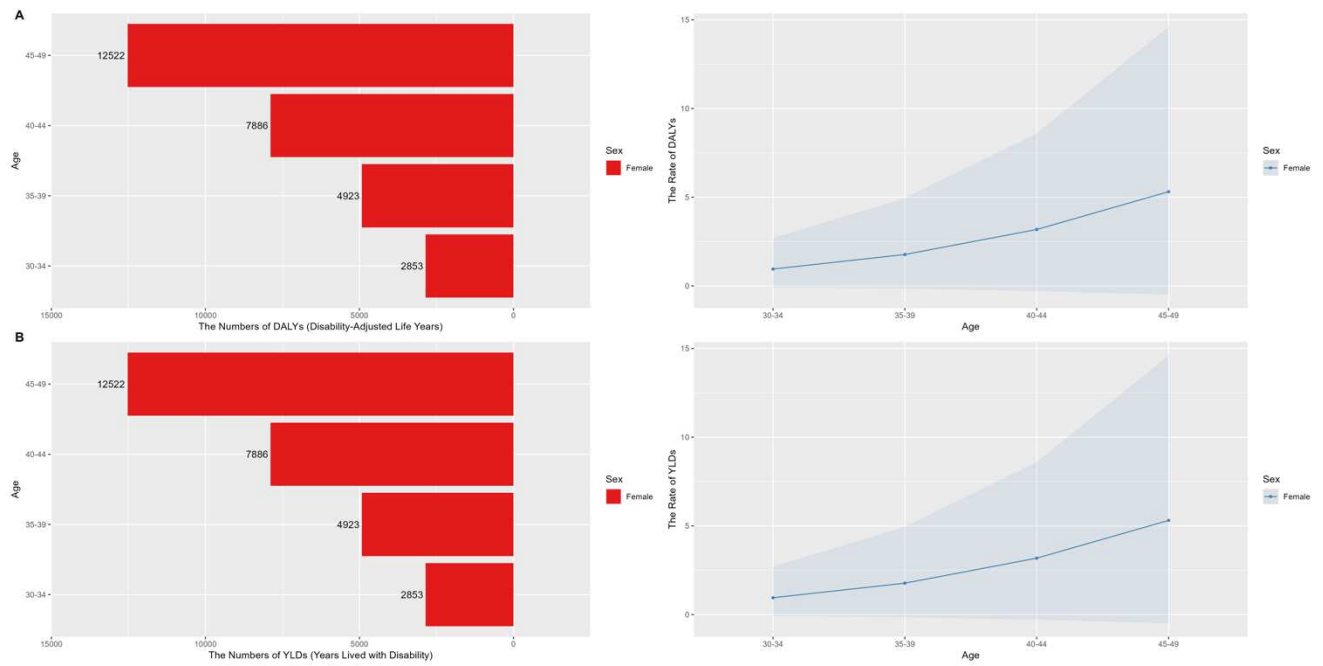


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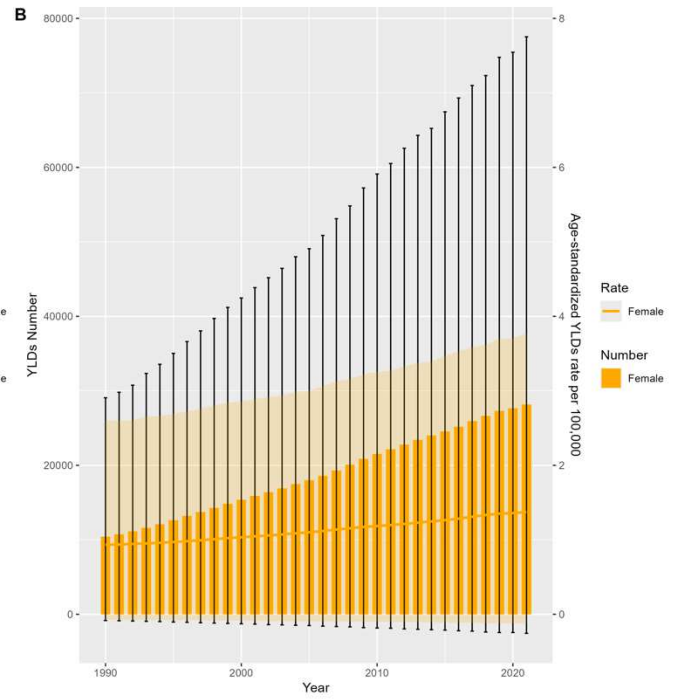
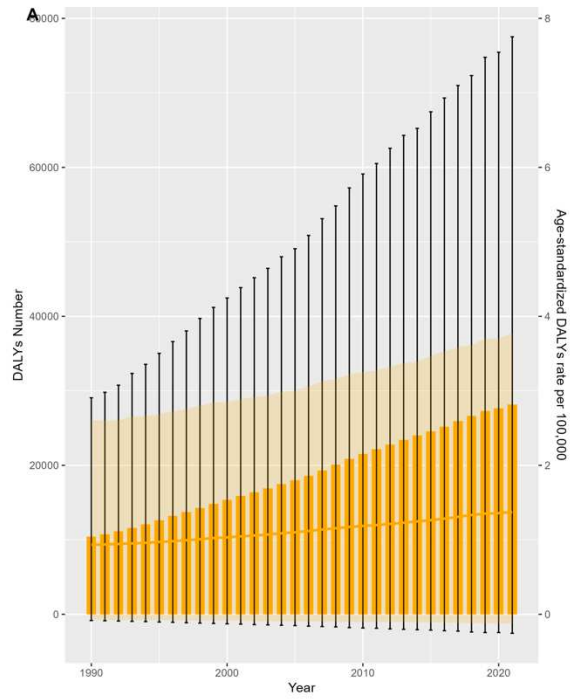


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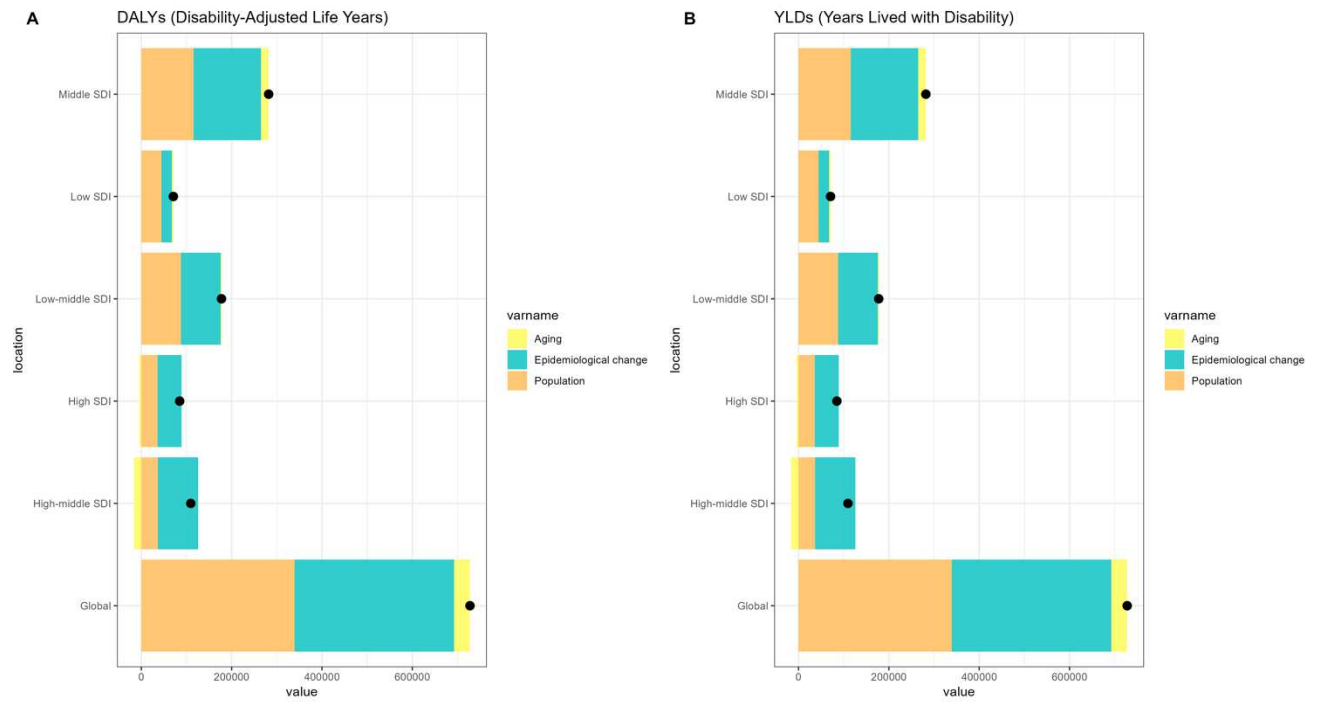


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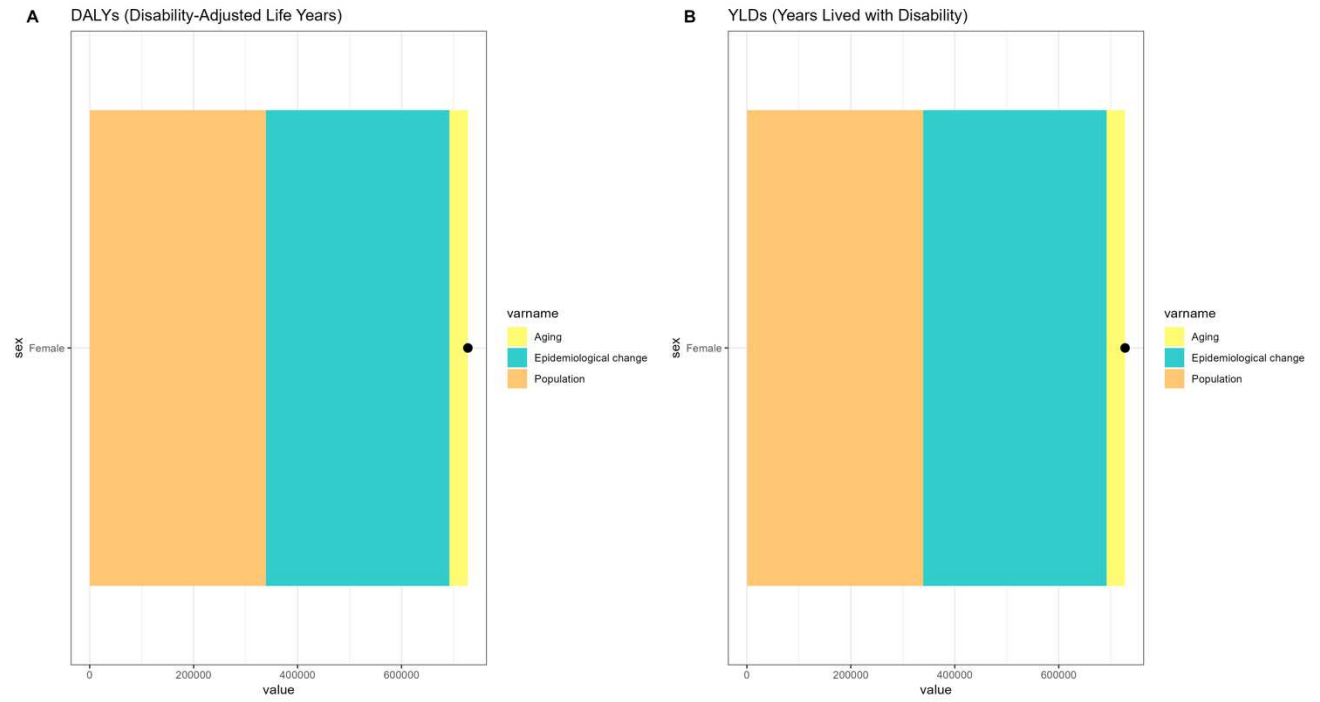


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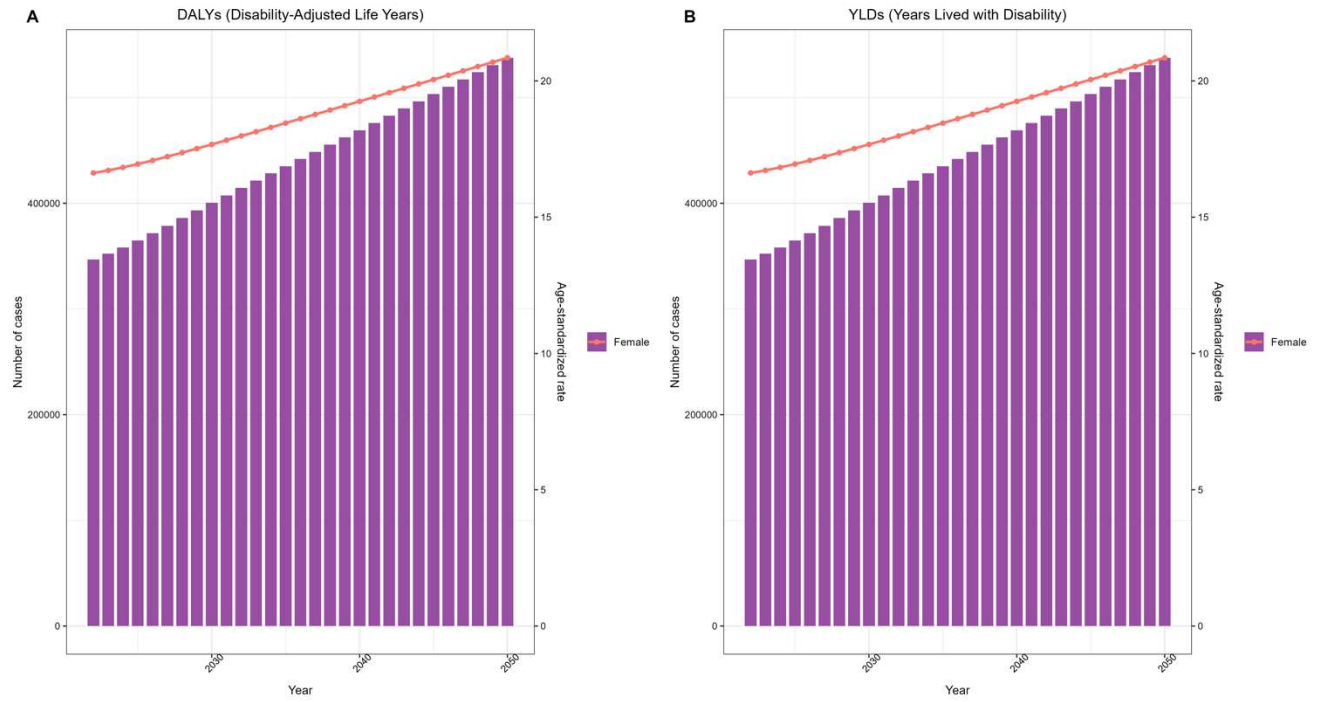
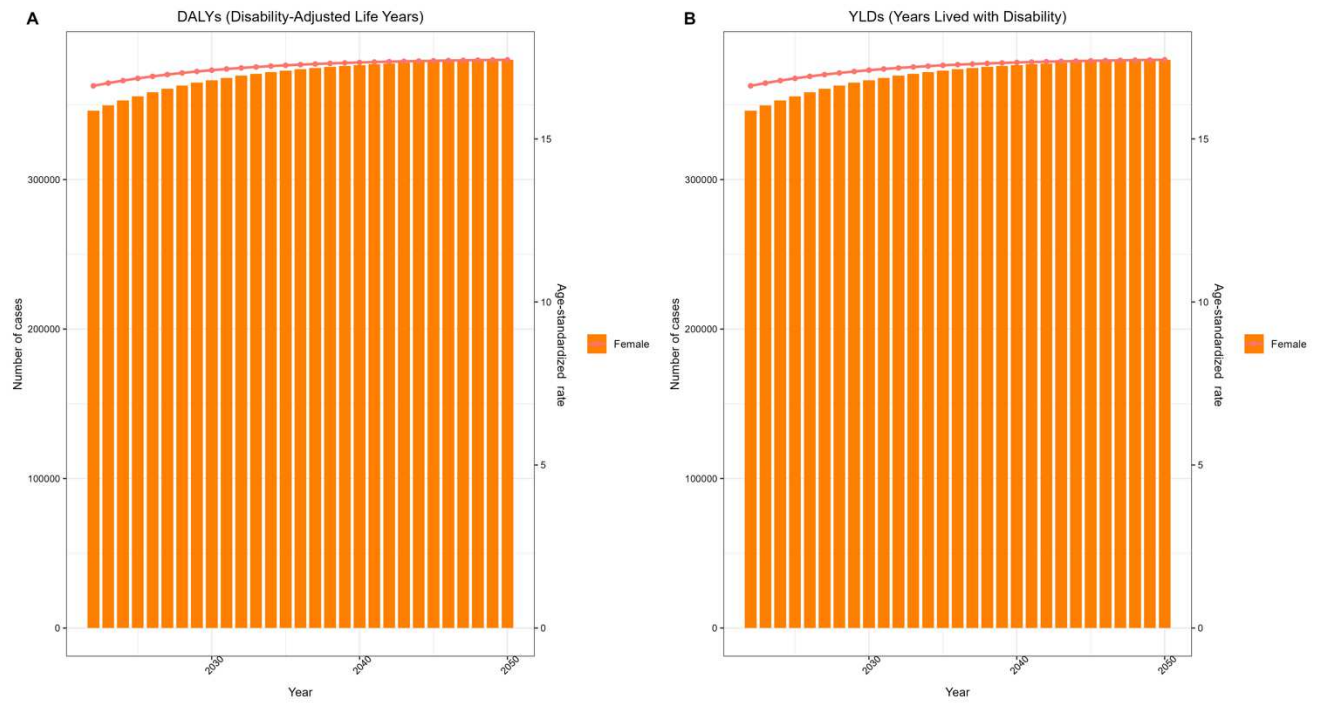


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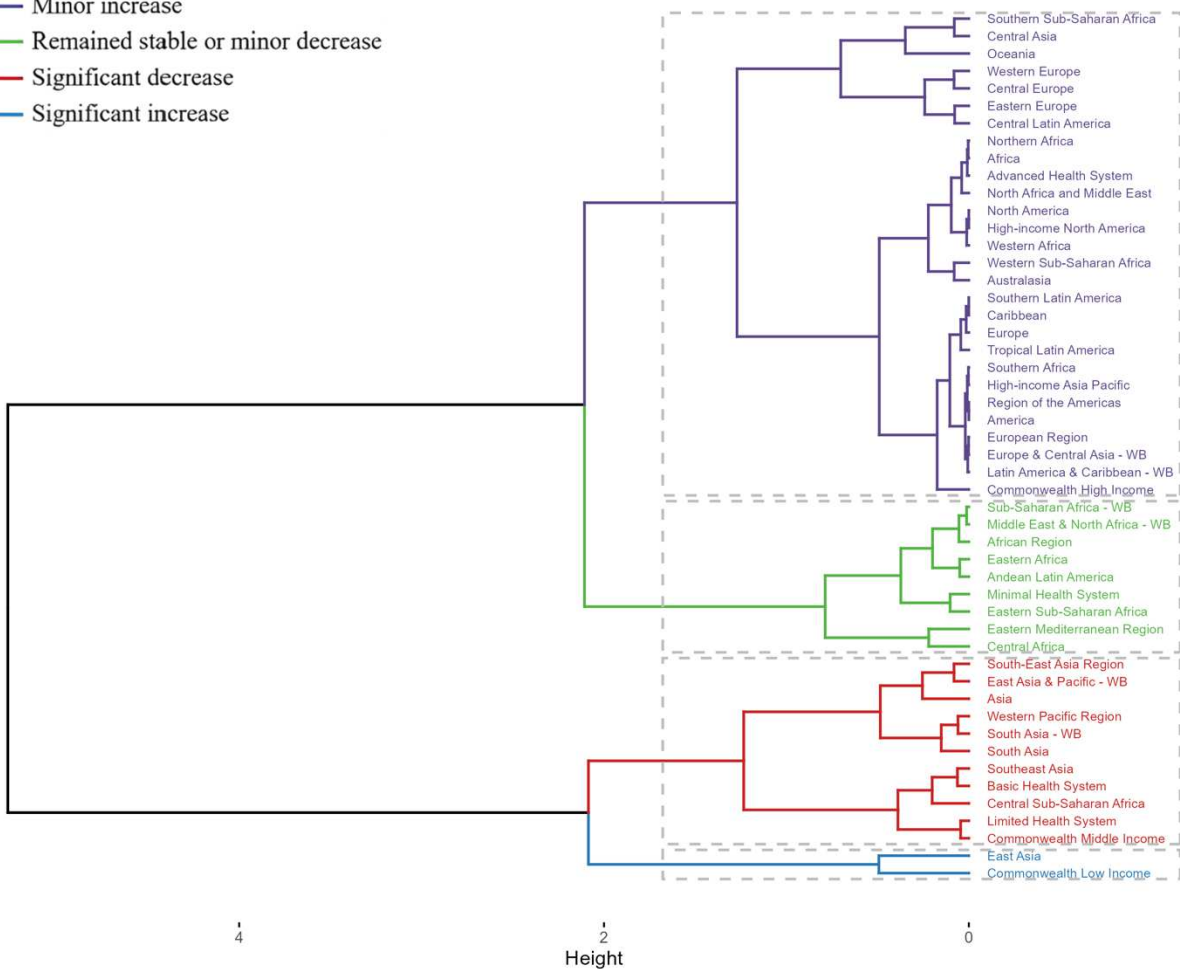


100

101 **Figure 33**

Cluster Dendrogram

- Minor increase
- Remained stable or minor decrease
- Significant decrease
- Significant increase



102

103 **Figure 34**

Supplementary Files

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

- [table1Hip.xlsx](#)
- [table2Knee.xlsx](#)