Clinical, Cosmetic and Investigational Dermatology

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ORIGINAL RESEARCH

Global Burden of Non-Melanoma Skin Cancer Among Elder Adults and Projections to 2071: A Systematic and Comprehensive Analysis of the Global Burden of Disease Study 2021

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Background: Non-melanoma skin cancer (NMSC) poses a significant health burden to the elderly globally. This study seeks to comprehensively assess the burden of NMSC among elderly adults in various regions and countries worldwide, covering the time frame from 1990 to 2021.

Methods: Using data from the Global Burden of Disease (GBD) 2021 study, we analyzed global trends in NMSC incidence, mortality, and disability-adjusted life years (DALYs) from 1990 to 2021. Joinpoint regression was used to evaluate temporal trends, and an Age-Period-Cohort (APC) model was applied to assess underlying influences. Future projections were made using the Bayesian Age-Period-Cohort (BAPC) model.

Results: Data indicates that among all assessment metrics, both the number of cases and age-standardized rates are higher in males than in females, suggesting a more pronounced increase in the disease burden of NMSC among men. Concurrently, the disease burden is significantly higher in the elderly population compared to younger age groups. Across the 21 GBD regions worldwide, the disease burden is heaviest in high-income North America, particularly evident in age-standardized incidence rates (ASIR): from 395.30 (336.70–456.10)/100,000 (95% UI) in 1990, it rose to 1251.80 (1158.40–1341.20)/100,000 (95% UI) in 2015. Additionally, the disease burden and mortality rates in Australasia and Western Europe were generally higher than in other regions. East Asia exhibited a high annual estimated percentage change (EAPC) in age-standardized incidence of 7.1 (6.2–7.9) (95% CI), indicating that NMSC in this region is undergoing a rapid rise, thereby increasing the urgency for prevention and control.

Conclusion: From 1990 to 2021, the global burden of NMSC has increased significantly. Elderly populations in various countries with high Standardized Disease Index values are facing a substantial disease burden.

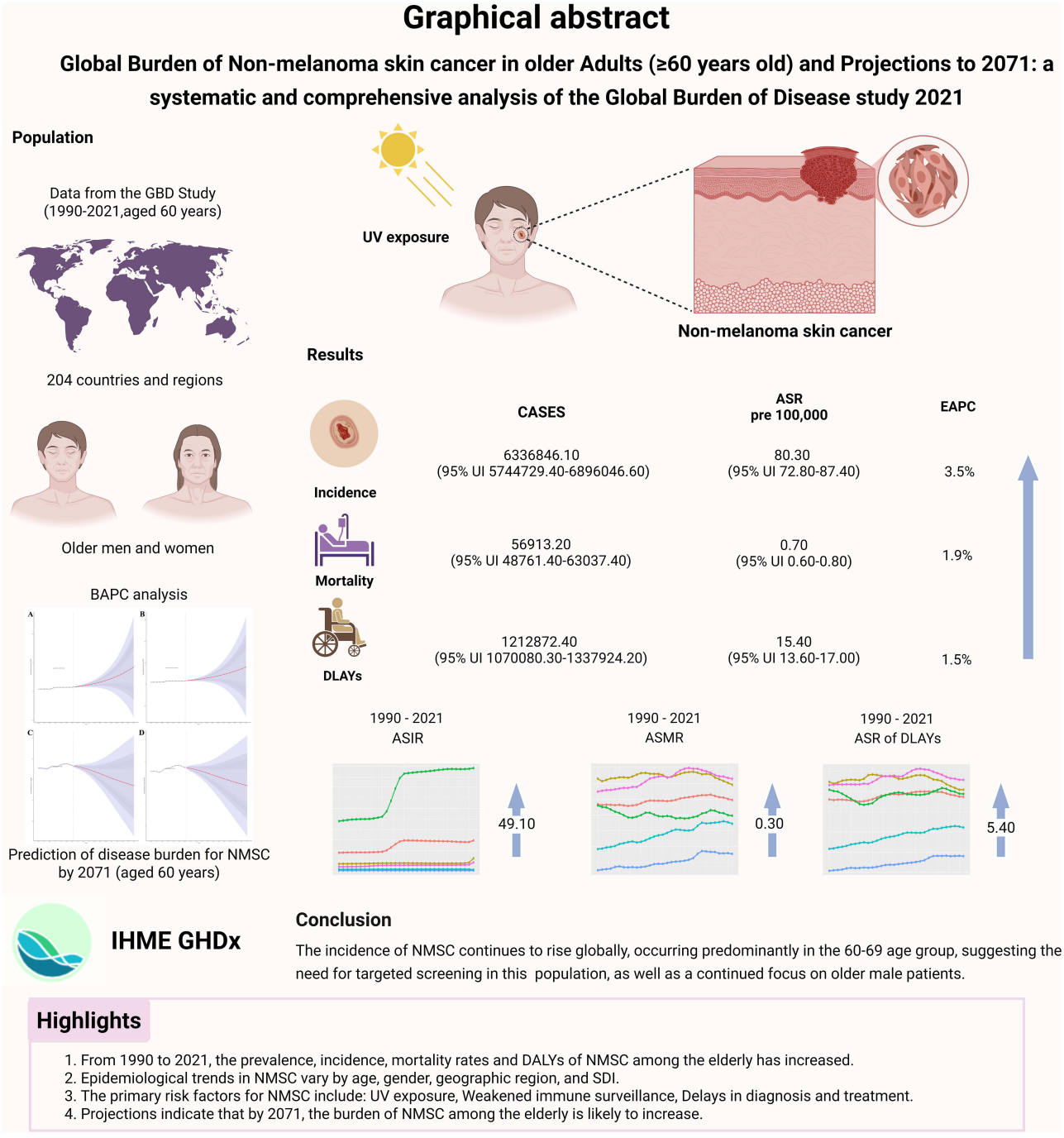
Keywords: NMSC, elderly population, Global Burden of Disease, Sociodemographic index, average annual percent change

Introduction

Non-melanoma skin cancer (NMSC) is a prevalent form of skin cancer, primarily encompassing basal cell carcinoma and squamous cell carcinoma.[1] In 2020, it was reported that NMSC constituted 78% of all skin cancer cases, with nearly 1.2 million instances recorded globally, leading to approximately 63,700 fatalities. In comparison, melanoma was responsible for around 57,000 deaths, thereby imposing a considerable burden on global economies and healthcare systems.[2,3]

Received: 23 September 2025
Accepted: 11 November 2025
Published: 20 November 2025

Graphical Abstract



The global population structure is undergoing an unprecedented transformation characterized by aging, with the proportion and number of individuals aged 60 and above continuously rising. This demographic shift presents social and economic challenges while significantly altering the distribution of the global disease spectrum, rendering age-related disease burdens a core issue in public health. A previous observational study indicated that the proportion of skin cancer patients aged 70 and above increased from 44% in 1989 to 74% in 2021.[4] The clinical management of skin cancers in the elderly is particularly challenging, often leading to higher rates of complications and skin cancer-specific mortality

compared to younger patients.[5] Although NMSC has a relatively lower mortality rate compared to melanoma, it's extremely high incidence and recurrence rates result in substantial consumption of medical resources. NMSC is strongly linked to long-term cumulative exposure to ultraviolet radiation, with its risk significantly increasing with age. The elderly population, due to greater cumulative sun exposure over their lifetimes, diminished cellular repair capacity, and decreased immune surveillance function, constitutes the highest-risk group for NMSC.[6] Furthermore, elderly patients with NMSC encounter numerous challenges, including subtle early symptoms, multiple comorbidities, nutritional deficiencies, significant psychological and emotional stress, and poor treatment tolerance.[7] Although the disease can achieve a favorable prognosis through effective treatment, if not diagnosed and treated promptly, it may lead to severe local tissue destruction, functional impairment, and disfigurement, profoundly impacting patients' quality of life and resulting in high medical costs.[8]

For a long time, the global disease burden (GBD) of NMSC has been significantly underestimated due to incomplete reporting in most cancer registry systems. Common reasons for this underreporting include the high incidence of NMSC, which may lead to incomplete registration, and the fact that many cases are treated in outpatient settings and are not included in hospital registry systems. The GBD study provides a unique opportunity to comprehensively and comparably assess the epidemiological characteristics of NMSC through systematic data modeling. Although there are existing studies exploring the overall burden of NMSC, research specifically targeting the expanding elderly population and conducting systematic analyses at global, regional, and national levels remains insufficient. Grasping the patterns of incidence, mortality, and disability-adjusted life years (DALYs) related to NMSC in older adults, along with observing its trends across different time periods, is essential for creating focused prevention approaches, improving resource distribution, and elevating the quality of skin health care for this age group.

This study aims to comprehensively assess the disease burden and trends of NMSC among the elderly population aged 60 and above at global, regional, and national levels from 1990 to 2021, utilizing the latest data from the 2021 GBD study. By revealing the heterogeneity in its epidemiological characteristics, this research seeks to provide critical scientific evidence for policy formulation and public health interventions aimed at reducing the global burden of NMSC in the elderly population.

Materials and Methods

Study Population and Data Collection

The GBD study, conducted by the Institute for Health Metrics and Evaluation (IHME), presents extensive and standardized metrics related to global health. This research utilizes data from the GBD 2021 dataset (https://ghdx.healthdata.org/gbd-2021), which delivers essential insights concerning mortality statistics, disease prevalence, and risk factors spanning different regions and population groups. This dataset functions as a comprehensive collection that documents the incidence, prevalence, and death rates associated with 371 diseases and injuries in 204 nations and regions, classified by age and gender.[9] We extracted epidemiological indicators of NMSC among individuals aged 60 and above from 1990 to 2021. This includes rates of prevalence, incidence, mortality, and DALYs, along with DALYs data related to various risk factors.

Statistical Analysis

This study employs descriptive epidemiological methods to analyze the temporal and demographic characteristics of NMSC incidence in the elderly population, providing detailed descriptions by gender and age groups. To mitigate the impact of varying population structures on the analysis results, this paper adopts the World Health Organization (WHO) population structure as the standard, calculating the standardized incidence rates of NMSC in the elderly population from 1990 to 2021 for comparative analysis.

The Estimated Annual Percentage Change (EAPC) value was utilized to represent the overall trend in incidence rates. In this analysis, the logarithm of incidence rates served as the dependent variable, while time (year) was treated as the independent variable within a regression framework. The EAPC coefficient was computed using the formula: $EAPC = 100 \times [\exp(\beta) - 1]$, where β denotes the linear regression coefficient. An upward trend is indicated when the lower limit of

the 95% confidence interval (CI) for the EAPC exceeds 0, whereas a downward trend is suggested when the lower limit is less than or equal to 0.[10]

Segment regression based on disease incidence trends divides the study period into distinct intervals, optimizing the trend for each interval. This approach allows for an evaluation of the specific characteristics of disease changes across different intervals. The Joinpoint Regression Software (version 5.2.0), developed by the National Cancer Institute, was utilized to calculate indicators such as the Annual Percentage Change (APC) and the Average Annual Percentage Change (AAPC) to assess the incidence trend. An APC greater than 0 indicates a year-on-year increase in the incidence rate; if no joinpoint is present, then APC equals AAPC, indicating that the overall data set exhibits a monotonically increasing or decreasing trend.[11,12]

The APC model, based on the Poisson distribution, breaks down the target analysis variables into three aspects: age, period, and cohort, which aids in examining the risk of disease occurrence or death across these dimensions. The age effect reflects influences stemming from internal factors, including individual physiological or social changes; the period effect encapsulates impacts arising from external factors, such as macro policies or social events; and the cohort effect signifies the interplay of internal and external factors, representing the cumulative or delayed effects experienced by individuals encountering various social events at different stages of life.[13] This study delineates the period from 1990 to 2021 into seven intervals of five years each: 1990–1994, 1995–1999, 2000–2004, 2005–2009, 2010–2014, 2015–2019, and 2020–2024, with the data for 2020–2021 represented by their mean value. Age is further segmented into nine groups, each encompassing five years. Utilizing the equation birth cohort = period - age, fifteen birth cohorts are calculated. An analysis is conducted using the median age, period, and cohort as the control group, employing the online analytical software developed by the National Cancer Institute, which is based on the R language.[14]

Prediction of NMSC Incidence in the Elderly Population Based on the Bayesian Age-Period-Cohort (BAPC) Model. The BAPC model integrates sample information with prior information on unknown parameters to estimate the posterior distribution, thereby inferring the unknown parameters.[15] This prediction process is implemented using the BAPC package and the INLA package in R.

Results

Global Burden and Trends of NMSC from 1990 to 2021

We obtained global statistics on NMSC patients from 1990 to 2021 using the GBD database to assess trends in the global disease burden associated with NMSC. Utilizing appropriate statistical methods, we calculated prevalence, incidence, and mortality rates, along with their respective age-standardized rates (ASR) and EAPC for NMSC across various regions, socioeconomic status groups, and genders (Table S1). This allowed us to demonstrate the trends in NMSC-related metrics from 1990 to 2021. Detailed results are presented in the Supplementary Tables. Our data indicate that males exhibit higher numbers and age-standardized rates than females across all indicators, including incidence, morbidity, mortality, and DALYs. Concurrently, the EAPC suggests faster growth among males, indicating a more pronounced increase in the burden of NMSC within this population. Among various SDI regions, the highest number of cases, incidence, deaths, and DALYs were observed in the High-income North America region, which also showed the highest prevalence EAPC of 4.5 (4.0, 5.0) (95% CI), indicating the heaviest burden. Conversely, the Low SDI region exhibited the lowest values for all indicators, with a prevalence EAPC of 0.30 (0.20–0.30) (95% CI), reflecting a lighter burden with slow growth. Among the 21 specific GBD regions, High-income North America bore the heaviest disease burden, particularly in ASIR: 395.30 (336.70–456.10) per 100,000 (95% UI) in 1990, increasing to 1251.80 (1158.40–1341.20) per 100,000 (95% UI). Additionally, Australasia and Western Europe exhibited higher disease and mortality burdens compared to other regions. In East Asia, the incidence EAPC reached 7.1 (6.2, 7.9) (95% CI), indicating a rapid increase in NMSC in this region and mounting pressure for disease prevention and control. In Central Europe, while the EAPC for incidence was positive, the EAPC for mortality and DALYs were −0.5 (−0.7, −0.4) (95% CI) and −1.0 (−1.2, −0.8) (95% CI), respectively, indicating effective treatment or prevention strategies in this region. Figure 1 provides a detailed visualization of ASR incidence rates, mortality rates, and DALYs for 204 countries and regions.

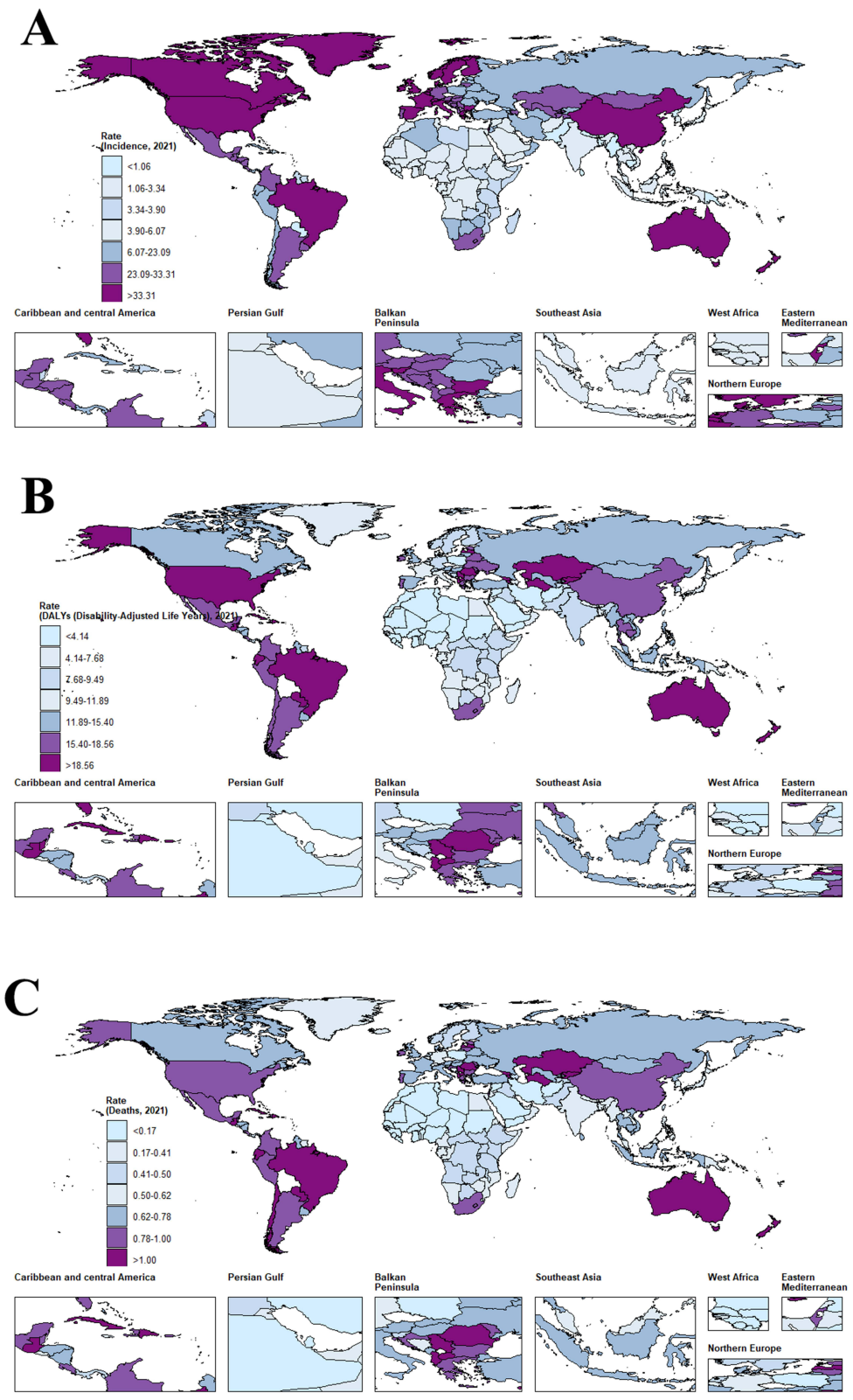


Figure 1 Age-standardized disease burden and estimated annual percentage change of NMSC across 204 countries and territories from 1990 to 2021. (**A**) ASIR of NMSC across 204 countries and territories from 1990 to 2021. (**B**) Age-standardized DALYs of NMSC across 204 countries and territories from 1990 to 2021. (**C**) ASDR of NMSC across 204 countries and territories from 1990 to 2021.

Abbreviations: ASDR, age-standardized death rate; DALYs, disability-adjusted life years; EAPC, estimated annual percentage change.

https://doi.org/10.2147/CCID.S569517

Global Trends by SDI Stratification and Gender

Figure 2 organizes data according to socioeconomic development levels and gender groups, providing a visual representation of the ASRs for overall incidence, prevalence, DALYs, and mortality from 1990 to 2021. Notably, the graphical representations of DALYs and mortality display similar patterns (Figure 2A and B), while incidence and prevalence exhibit comparable trends (Figure 2C and D). In medium to high SDI regions, despite elevated baseline levels, mortality rates and DALYs have shown stable or declining trends. Conversely, high SDI regions have experienced rapid increases in ASPR and ASIR between 2000 and 2005, while maintaining well-controlled mortality and DALYs within these populations. In low and lower-middle SDI regions, the disease burden has remained relatively low but is exhibiting an upward trajectory. Data visualization highlights significant gender disparities: the global female DALY rate consistently remains lower than that of males. This gender gap is most pronounced in high-SDI regions, whereas the disparity is smaller in low-SDI regions.

Disease Distribution Among Older Adults (Aged 60 to 95+) in 21 GBD Regions

Globally, the incidence and prevalence of NMSC among individuals aged 60 and older from 1991 to 2021 exhibited a similar significant upward trajectory. Moreover, the distribution patterns across various regions were notably consistent (Figure 3A and B). The global age-standardized incidence rate in 2021 demonstrated a significant increase compared to 1991, indicating a persistent rise in the disease burden. Regional analysis revealed substantial disparities in incidence rates, with the most severe burdens occurring in Australasia, North America, Western Europe, and Central Europe. Incidence rates in these high-income regions were markedly higher than the global average. In stark contrast, Africa exhibited the lightest disease burden, with incidence rates of 58.09 per 100,000 in the 90–94 age group and 57.09 per 100,000 in the 95+ age group, which are significantly lower than those in all other regions (Table S1). The concepts of DALYs and mortality rates exhibit similarities and will be discussed together in the subsequent sections (Figure 3C and D). Globally, the disease

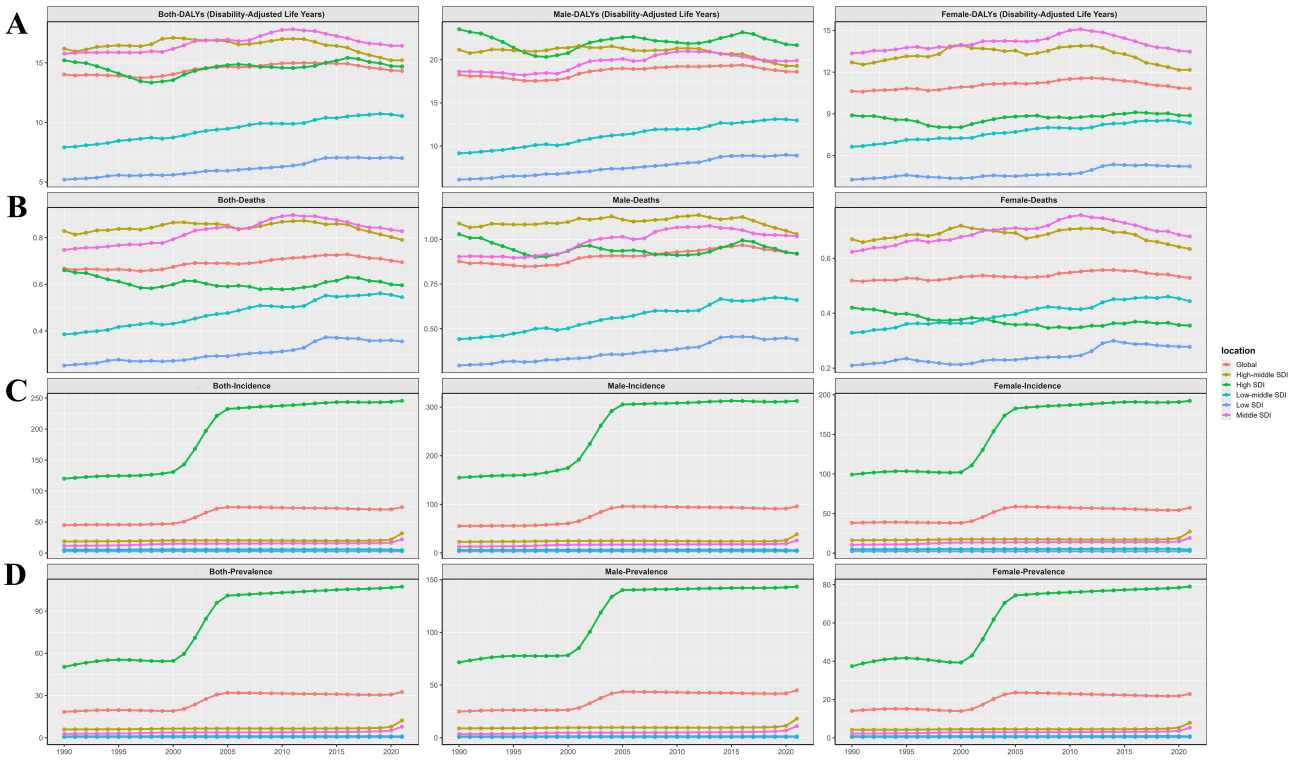


Figure 2 Trends in the disease burden of NMSC from 1990 to 2021 by different SDI level regions and gender. (**A**) Trends in ASRs for DALYs of NMSC from 1990 to 2021 by different SDI level regions and gender. (**B**) Trends in ASMR of NMSC from 1990 to 2021 by different SDI level regions and gender. (**C**) Trends in ASIR of NMSC from 1990 to 2021 by different SDI level regions and gender. (**D**) Trends in ASPR of NMSC from 1990 to 2021 by different SDI level regions and gender. Trends in ASPR, ASIR, ASMR and age-standardized DALYs of NMSC from 1990 to 2021 by different SDI level regions.

Abbreviations: ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; DALYs, disability-adjusted life years; SDI, socio-demographic index.

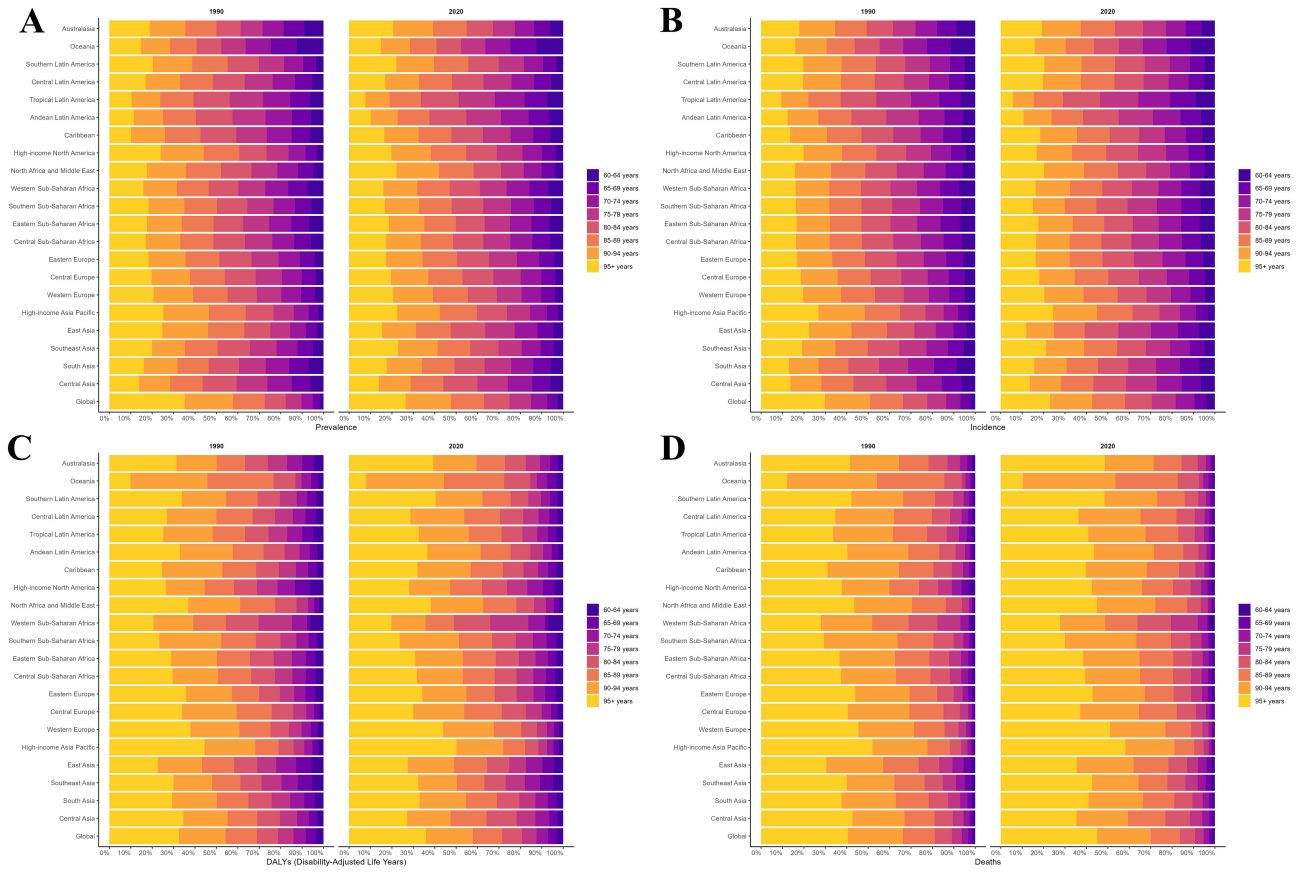


Figure 3 Distribution of NMSC Among Older Adults (Aged 60 to 95+) in 21 GBD Regions. (**A**) Distribution in ASPR of NMSC from 1990 to 2021 by different SDI level regions. (**B**) Distribution in ASIR of NMSC from 1990 to 2021 by different SDI level regions. (**C**) Distribution in ASRs for DALYs of NMSC from 1990 to 2021 by different SDI level regions. (**D**) Distribution in ASMR of NMSC from 1990 to 2021 by different SDI level regions. Distribution of ASPR, ASIR, ASMR and age-standardized DALYs of NMSC Among Older Adults (Aged 60 to 95+) in 21 GBD Regions.

Abbreviations: ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; DALYs, disability-adjusted life years; SDI, socio-demographic index.

burden of NMSC among individuals aged 60 and older, as measured by both the ASR of DALYs and mortality rates, demonstrated significant changes between 1991 and 2021. The overall global DALY rate increased in 2021 compared to 1991, indicating a persistent rise in the health impact of NMSC within this age group. Regional analyses revealed pronounced patterns of disease burden inequality. The regions with the highest burden included Australasia, North America, Western Europe, and Southern Europe, all characterized by high levels of population aging and historically elevated ultraviolet radiation exposure. In stark contrast, Sub-Saharan Africa, particularly Western and Eastern Sub-Saharan Africa, exhibited the lightest burden. The DALY rate in the oldest age group was less than one-fifth of that in high-burden regions, primarily due to the photoprotective effects of racial skin pigmentation and relatively limited life expectancy. An analysis of temporal trends reveals significant regional heterogeneity in the EAPC of age-standardized DALY rates globally. Regions with negative EAPC values, such as certain high-income countries, indicate declining disease burden rates, likely to benefit from decades of successful sun protection campaigns, early screening, and widespread effective treatments. Conversely, many low- and middle-income regions, particularly in parts of Latin America and Asia, exhibit positive EAPC values, signifying a steady increase in their NMSC burden rates.

Burden Trends by Sex and Age (≥60 Years Old)

Based on the prevalence data of NMSC from 1990 and 2021, categorized by age cohort, sex, and SDI region (Figure 4A), it was found that the prevalence peaked in the 70–74 age group for men. In contrast, for women, the peak shifted from the 75–79 age group in 1990 to the 70–74 age group in 2021. Notably, male prevalence remained significantly higher than that of females, with a difference of approximately 50%. Areas with high SDI exhibited the highest prevalence,

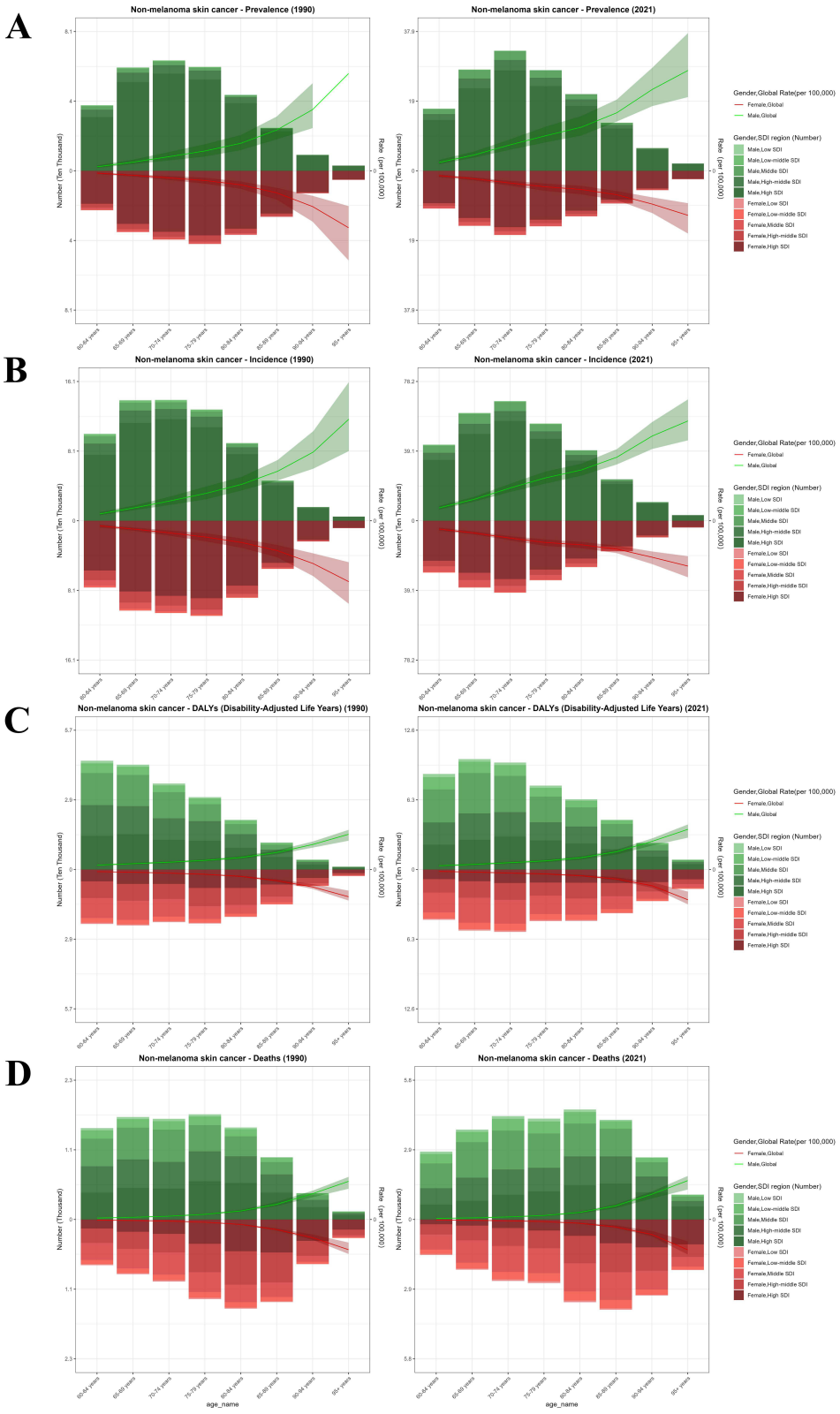


Figure 4 Trends in ASPR, ASIR, ASMR, age-standardized DALYS for NMSC in different age groups (60 to 95+, 5-year interval) by gender, 1990 and 2021. (**A**) Trends in ASPR for NMSC in different age groups by gender. (**B**) Trends in ASIR of NMSC in different age groups by gender. (**C**) Trends in ASR for DALYs of NMSC in different age groups by gender. (**D**) Trends in ASMR of NMSC in different age groups by gender.

Abbreviations: ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; DALYs, disability-adjusted life years; SDI, socio-demographic index.

consistent with previous analyses. The incidence of NMSC demonstrated a similar trend from 1990 to 2021 (Figure 4B). An analysis of DALYs between 1990 and 2021 revealed that the age group with the highest burden among men shifted from 60–64 years in 1990 to 65–69 years in 2021. For women, the peak burden age group transitioned from 60–64 years in 1990 to 70–74 years in 2021 (Figure 4C). In examining mortality rates, minimal differences were observed among male cohorts under 90 years of age. However, for women, the peak mortality rate shifted from the 80–84 age group in 1990 to the 85–89 age group in 2021, reflecting a similar trend to that observed in the incidence peak (Figure 4D).

The Trends for the Burden of NMSC by 21 SDI Regions

We compiled and analyzed trends in ASPR, ASIR, ASDR, and age-standardized DALYs for NMSC globally and across 21 GBD regions from 1990 to 2021, generating corresponding fitted curves. These fitted curves illustrate local differences in the connection between age-standardized disease burden metrics and the SDI. (Figure 5). ASPR and ASIR exhibit considerable similarity, while the remaining regions align more closely with the fitted curve, demonstrating that a higher SDI correlates with increased ASPR and ASIR values. However, high-income North America significantly deviates above the fitted curve, with calculated correlations exhibiting statistical significance ($p < 0.05$) (Figure 5A and B). For the ASRs of Death and DALYs, both trends are similar. When the SDI is below 0.7, both metrics increase as the SDI rises; beyond 0.7, they decrease as the SDI increases. Notably, Australasia consistently exceeds the fitted curve (Figure 5C and D).

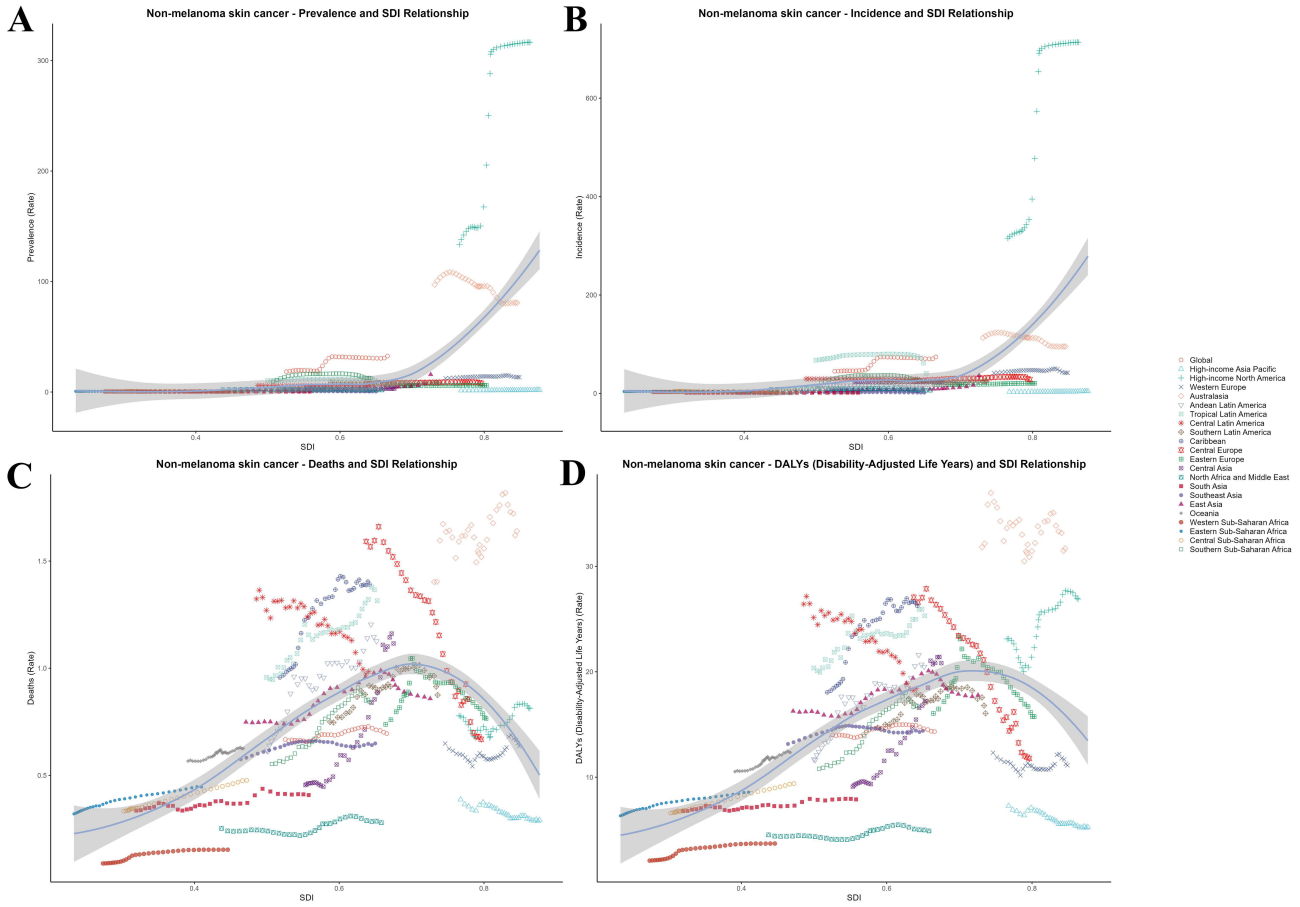


Figure 5 Trends in ASPR, ASIR, ASMR, age-standardized DALYS for the burden of NMSC across Global and 21 GBD regions by SDI from 1990 to 2021. (**A**) Trends in ASPR for NMSC across 21 GBD regions by SDI. (**B**) Trends in ASIR of NMSC across 21 GBD regions by SDI. (**C**) Trends in ASR for DALYs of NMSC across 21 GBD regions by SDI. (**D**) Trends in ASMR of NMSC across 21 GBD regions by SDI.
Abbreviations: ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; DALYs, disability-adjusted life years; SDI, socio-demographic index.

https://doi.org/10.2147/CCID.S569517

BAPC Analysis

To forecast trends in ASPR, ASMR, ASIR, and age-standardized DALYs for NMSC among the elderly population (aged 60 and above) beyond 2021, we employed a BAPC model. This model was utilized to project global incidence rates from 2021 to 2071. The projections indicate an upward trend in global ASPR and ASIR (Figure 6A and B). Conversely, both the age-standardized rates for deaths and for DALYs demonstrate a declining trend (Figure 6C and D).

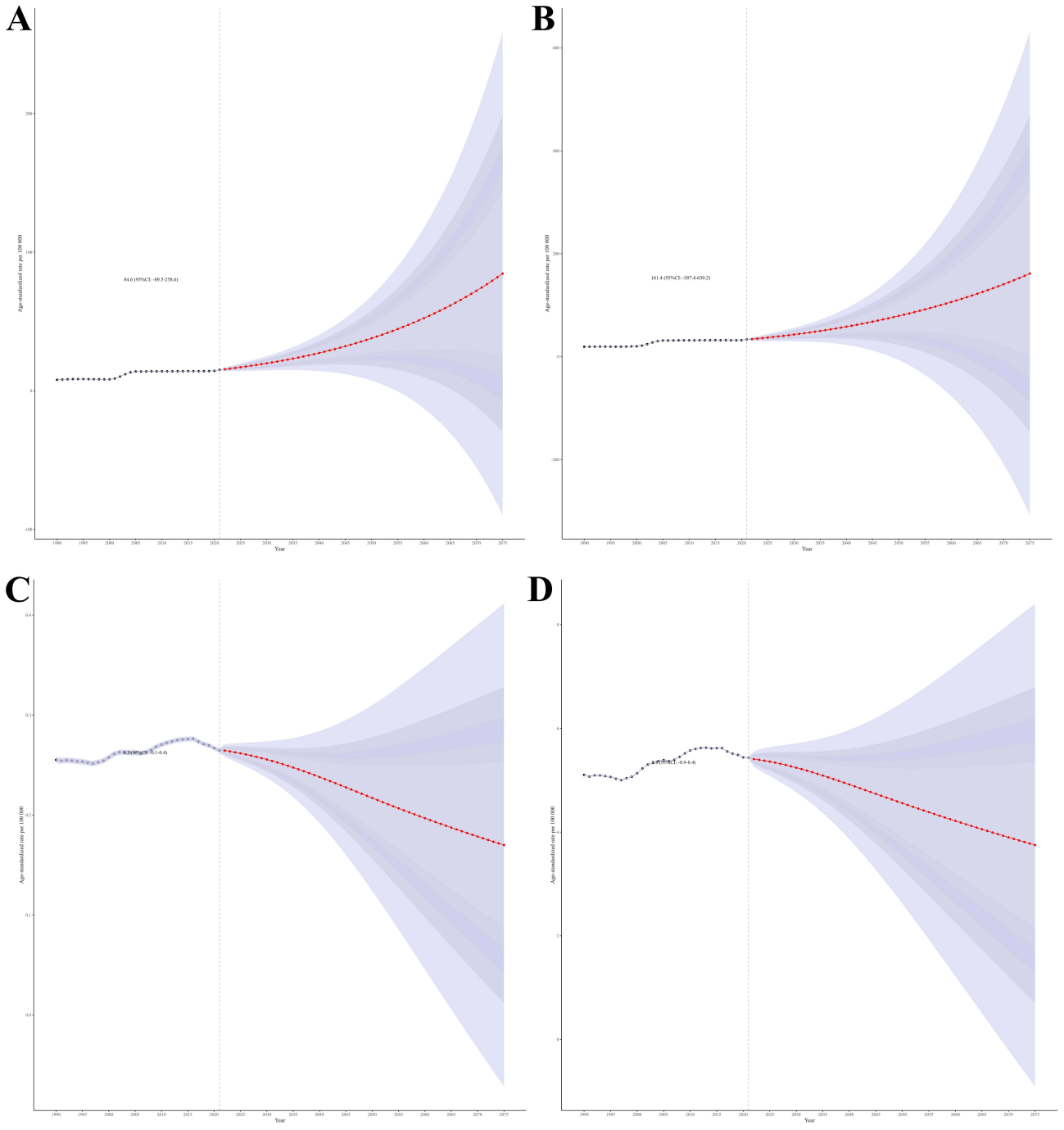


Figure 6 The global trends in ASPR (**A**), ASMR (**B**), ASR of DALYs (**C**) and ASMR (**D**) from 2021 to 2071 for NMSC were predicted using Bayesian age-period-cohort (BAPC) models.

Abbreviations: ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; DALYs, disability-adjusted life years; SDI, socio-demographic index.

Discussion

This study employed the GBD 2021 database alongside historical data to classify global NMSC cases by GBD region, SDI, gender, and age. It provides a comprehensive analysis of the prevalence, incidence, DALYs, deaths, age-standardized rates, and EAPC among individuals aged 60 years and older worldwide.

Research indicates a significant global increase in the burden of NMSC, with notable rises in the number of cases, incidence, deaths, and DALYs in 2021 compared to 1990. The global EAPC predominantly reflects a positive trend, suggesting that the disease burden of NMSC continues to escalate in most regions worldwide. Furthermore, substantial regional and national variations in NMSC are evident, particularly among fair-skinned populations with high SDI indices. While the disease burden is most pronounced in high-SDI regions (eg, North America, Australia, Western Europe), growth rates are more rapid in middle- and low-SDI regions, especially in East Asia, South Asia, and Southeast Asia. This escalating trend is likely multifactorial, driven not only by genuine increases in ultraviolet radiation exposure due to behavioral changes and ozone depletion but also significantly enhanced by heightened skin cancer awareness, the widespread adoption of dermatological screening programs, and the improved sensitivity of diagnostic technologies. The dramatic surge in incidence in regions such as High-income North America (ASIR rising from 395.30 to 1251.80 per 100,000), coupled with stable or declining mortality, strongly suggests that this "epidemic of detection" includes a substantial component of overdiagnosis of indolent lesions. This disparity is attributed to the strong association between ultraviolet radiation exposure and NMSC incidence and mortality, highlighting distinct regional patterns and geographic distributions in the global disease burden.[16,17] Consequently, there is an urgent need to develop targeted prevention and control policies that are informed by the regional distribution of disease burden, particularly focusing on areas where the burden has escalated in recent years.

Conversely, the observed decline in mortality and DALYs in regions such as Central Europe, despite an increase in incidence, highlights the effectiveness of treatment and prevention strategies. This pattern reflects the documented outcomes of long-term, nationally coordinated public health initiatives. For example, Australia's renowned "Slip, Slop, Slap" campaign, followed by the "SunSmart" initiative, has been remarkably successful in raising public awareness about sun protection, resulting in a reduction of melanoma incidence among younger generations and a shift in societal norms.[18] In parallel, countries such as Switzerland have exemplified excellence in skin cancer management by providing widespread access to and standardization of highly effective treatments, including Mohs micrographic surgery. This approach maximizes tissue preservation, minimizes recurrence, and subsequently reduces disease-specific mortality.[19] The experience from these nations provides a compelling model for other regions seeking to control NMSC mortality.

NMSC exhibits significant disparities across different SDI regions, with a heavier burden observed in high-SDI areas. This observation aligns with the increased awareness of NMSC among affluent populations, which may drive more intensive screening efforts. Consequently, these screening practices can lead to more comprehensive case documentation and reporting. Furthermore, higher living standards facilitate better access to healthcare, allowing individuals diagnosed with NMSC to receive more extensive medical services. This correlation is supported by the higher DALYs recorded among high-SDI populations. Additionally, occupational factors and leisure-related UV exposure, as well as HPV exposure, are associated with the disease burden of NMSC. This association is also linked to socioeconomic transitions.[20–24]

The incidence and biological behavior of NMSC exhibit a distinct gender bias. Males not only have higher incidence rates but also tend to present with tumors that grow more rapidly and are more aggressive. This disparity arises from the interplay of multiple factors. Behaviorally, men have historically engaged more in outdoor occupations, such as agriculture and construction, resulting in greater cumulative sun exposure. Furthermore, cultural norms contribute to this issue, as men are less likely to adopt sun protection measures, such as using sunscreen or seeking shade, during leisure activities, thereby further elevating their risk.[20] At the biological level, researchers hypothesize that estrogen may confer protective effects on female skin by delaying tumor development through antioxidant mechanisms and enhancing DNA damage repair. Concurrently, differences in immune surveillance and the aging skin microenvironment in males may also accelerate tumor progression.[25] NMSC exhibits a profound gender disparity, with males consistently bearing a higher burden across all metrics. While behavioral factors such as occupational and recreational sun exposure

contribute to this disparity, growing evidence suggests a biological underpinning. The hypothesis that estrogen may exert a protective effect in females is supported by mechanistic studies. Basic research has demonstrated that estrogen signaling through estrogen receptors can enhance the repair of UV-induced DNA damage in skin cells, which is a critical line of defense against carcinogenesis. Furthermore, in vivo studies have indicated that estrogen can act via specific pathways to suppress the progression of squamous cell carcinoma, one of the major subtypes of NMSC, thereby providing a direct link between hormonal status and tumor growth.[26] These findings suggest that the relative deficiency of protective mechanisms in male skin contributes to their heightened susceptibility and more aggressive disease progression.

Another finding of this study is that individuals over the age of 60 bear a heavier disease burden. The significant burden of non-melanoma in the elderly population can be attributed to the long-term combined effects of several factors, with cumulative lifetime UV exposure being the most critical.[27] This group generally exhibited a lack of sun protection awareness during their youth, resulting in the cumulative effects of decades of sun damage becoming particularly pronounced in older age. Concurrently, the age-related decline in immune system function significantly diminishes the body's capacity for "immune surveillance", which is crucial for the elimination of precancerous cells.[28] Additionally, the reduced barrier function and diminished DNA repair efficiency resulting from structural aging of the skin further increase the risk of cancer. Furthermore, delayed diagnosis in the elderly often arises from impaired vision, mobility limitations, or neglect of early symptoms. Individuals with chronic conditions who have been on long-term immunosuppressive medications face significantly heightened risks. Therefore, the substantial disease burden in the elderly is an inevitable consequence of historical exposure, physiological decline, and behavioral factors.[20]

The findings hold significant implications for public health policy. To effectively address disease burdens, resource allocation should prioritize low-SDI regions, with tailored intervention strategies designed according to the characteristics of different SDI areas. Concurrently, policy formulation must address gender-specific health needs, particularly by advancing gender equality and health equity in low-SDI regions. Furthermore, prevention should remain the foremost priority, actively managing modifiable risk factors through strengthened primary prevention measures. At the global level, international cooperation must be continuously enhanced to jointly tackle cross-border health threats and elevate overall health governance standards.

This research presents various limitations. The considerable variability in the quality of cause-of-death records and disease monitoring systems across different regions could impact the comparability and accuracy of the data. The rapid increase in incidence rates in high socioeconomic status regions—illustrated by the age-standardized incidence rate per 100,000 population in North America rising from 395.30 to 1251.80—occurs concurrently with stable or declining mortality rates. This trend strongly suggests changes in diagnostic practices and the potential for overdiagnosis. Conversely, our systematic analysis reveals a significant potential for large-scale underreporting in regions with low social development indices, providing a more realistic and critical perspective on the disparities in the global burden of non-melanoma skin cancer. Additionally, as an analysis based on the GBD research framework, the statistical modeling methods relied upon inherently carry certain model uncertainties. The study also failed to fully control all potential socioeconomic and environmental confounding factors, which may introduce bias into the results. Notably, the COVID-19 pandemic caused exceptional disruptions to data collection and reporting in 2021,[29] potentially affecting the accuracy of data for that year. Furthermore, despite employing comprehensive metrics such as DALYs, these indicators remain insufficient to fully capture the broad socioeconomic impact dimensions associated with disease.

Conclusion

In summary, over the past three decades, the global burden of disease has exhibited a marked upward trend, accompanied by significant inequalities across regions, genders, and age groups. These disparities are evident not only in core indicators such as disease incidence, mortality rates, and DALYs, but also reflect the profound influence of social determinants of health. These findings underscore the urgent need for targeted public health interventions that incorporate socioeconomic context analysis and address gender disparities. Particular attention must be given to the unique health needs and healthcare barriers faced by vulnerable populations, especially older adults, to promote more equitable, inclusive, and sustainable health outcomes.

Data Sharing Statement

Data resources from the GBD study 2021 could be accessed online through the Global Health Data Exchange (GHDx) query tool (http://ghdx.healthdata.org/gbd-results-tool).

Ethics Statements

According to Article 32 of the Ethical Review Measures for Life Science and Medical Research Involving Human Beings of the People's Republic of China, the data used in this study will not cause any form of harm to human beings, nor will it touch sensitive personal privacy or trade secrets, so the ethical review can be exempted. In addition, the database used in this study was publicly available and legally available.

Acknowledgments

We acknowledge the BioRender (https://www.biorender.com/) for their illustration services.

Funding

There is no funding to report.

Disclosure

The authors declare no competing interests.

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