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RESEARCH

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# The global, regional, and national burdens of maternal sepsis and other maternal infections and trends from 1990 to 2021 and future trend predictions: results from the Global Burden of Disease study 2021

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## Abstract

**Background** Maternal sepsis and other maternal infections (MSMIs) significantly contribute to maternal morbidity and mortality worldwide, posing critical challenges due to their rapid progression and severe outcomes.

**Methods** Data from the Global Burden of Disease (GBD) 2021 study, covering 204 countries and territories, were used to evaluate the incidence, death, and disability-adjusted life years (DALYs) of MSMI. Statistical methods included joinpoint regression, age-period-cohort analysis, decomposition analysis, frontier analysis, and ARIMA model forecasting.

**Results** From 1990 to 2021, global MSMI incidence decreased from 22.45 million to 19.05 million, with the age-standardized rate (ASR) dropping from 764.03 (95% UI: 573.01–970.54) to 494.19 (95% UI: 377.34–623.90) per 100,000 people. High-SDI regions saw significant reductions, while low-SDI regions experienced increases. Women aged 20–24 consistently had the highest incidence, death, and DALYs. Iron deficiency was a significant risk factor, especially in lower SDI regions. Decomposition analysis showed that epidemiological changes and population growth were major drivers, particularly in low-SDI regions. Age-period-cohort analysis revealed women aged 20–29 as the most vulnerable, with notable improvements after 2000 and progressively decreasing risks in younger cohorts. Frontier analysis revealed that higher-SDI countries had greater improvement potential. ARIMA forecasting suggests continued declines in MSMI cases and ASR through 2040.

**Conclusions** While significant progress has been made globally, challenges persist, including rising incidence in low-SDI regions, vulnerability of women aged 20–29, and the impact of iron deficiency. Efforts to address these and improve healthcare infrastructure are critical to further reduce MSMI and enhance maternal health outcomes.

**Keywords** Maternal sepsis, Maternal infections, Global burden of disease, Sociodemographic index, Trend

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## Introduction

Maternal sepsis and other maternal infections (MSMI) are significant contributors to maternal morbidity and mortality worldwide, presenting critical challenges in obstetric care [1]. The WHO described the latest dysfunction caused by maternal sepsis during pregnancy, childbirth, postabortion, or the postpartum period, which is particularly alarming due to its rapid progression and potential for severe outcomes [2]. It encompasses a spectrum of infections, including those of the genital tract, urinary system, and other systemic infections that may complicate pregnancy [3, 4]. Other maternal infections, such as those caused by bacteria, viruses, fungi, or parasites, can also have devastating effects on both the mother and the fetus, leading to complications such as preterm birth, low birth weight, and neonatal infections [5–7].

Pregnant women have a higher susceptibility to infections than nonpregnant women due to the physiological, immunological, and mechanical changes that occur during pregnancy. These alterations can also mask the typical signs and symptoms of infection and sepsis, leading to potential delays in recognition and treatment [8, 9]. Unlike typical sepsis, the onset of maternal sepsis can be insidious, with patients often appearing deceptively well before sudden and rapid deterioration into septic shock, multiple organ dysfunction syndrome, or even death [10].

Managing MSMI during the perinatal period presents unique challenges, requiring a balance between the mother's physiological changes and the fetus's well-being. A multidisciplinary approach, involving obstetricians, neonatologists, anesthesiologists, and other specialists, is often necessary, especially in high-risk pregnancies or when complications arise [11]. Understanding the global burden of MSMI is crucial for shaping healthcare strategies. Large-scale efforts like the Global Burden of Disease (GBD) study quantify the impact of these infections, identify data gaps, and guide effective interventions.

## Methods

### Data sources

The data spanning 1990 to 2021 were sourced from the GBD 2021 study, which was made available by the Institute for Health Metrics and Evaluation. The GBD 2021 study utilized the latest epidemiological data sources and enhanced standardized methods to provide comprehensive estimates of disease burden, including incidence, death, and disability-adjusted life years (DALYs), for 371 diseases and injuries in 204 countries and territories.

### Case definition

Maternal sepsis is defined as a temperature < 36 °C or > 38 °C and clinical signs of shock (systolic blood pressure < 90 mmHg and tachycardia > 120 bpm). Other maternal infections are defined as any maternal infection excluding HIV, sexually transmitted infection (STI), or not related to pregnancy.

### Measures of burden and data presentation

The measures of disease burden for MSMI include incidence, death, and DALYs from 1990 to 2021. The incidence refers to the occurrence of first-ever MSMI cases. DALYs, common indicators for measuring disease burden, consist of the burden caused by years lived with disability (YLDs) and years of life lost (YLLs). YLDs were calculated by multiplying the prevalence of MSMI by the associated disability weights, whereas YLLs were derived by multiplying the number of MSMI-related deaths by the remaining standard life expectancy at the time of death. The age categories included 10–14, 15–19, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, and 50–54 years. The sociodemographic index (SDI), reflecting overall development levels through educational attainment, lagged distributed income, and total fertility rate, was split into five levels: high, high-middle, middle, low-middle, and low. Additionally, the data were categorized by GBD region, allowing for regional comparisons and insights.

### Statistical analysis

We applied several statistical methods to analyze MSMI trends and burden from 1990 to 2021. The Estimated Average Percentage Change (EAPC) was used to assess trends in disease burden over a specific period. Joinpoint analysis uses segmented regression to divide longitudinal changes into distinct segments and identify statistically significant trends within each segment. The natural logarithm of disease burden is regressed over different time periods, and the Annual Percent Change (APC) along with its 95% confidence interval (CI) is calculated for each period. The APC reflects the rate of change within each specific segment of the time series, allowing for the identification of distinct trends over different periods. The Average Annual Percent Change (AAPC) provides the overall average trend over the specified period. If the 95% CI of the corresponding EAPC, APC, or AAPC estimate is greater than 0, the metric is considered to be increasing. If the 95% CI is less than 0, it indicates a decreasing trend. If the 95% CI includes 0, the trend is deemed stable.

To decompose the temporal trends, we employed the age-period-cohort model using the Intrinsic Estimator (IE) method. This approach allows us to separately estimate the effects of age, period, and cohort on disease burden. The IE method provides estimates of the coefficients for age, period, and cohort effects. These coefficients are then exponentiated ($\exp(\text{coef.}) = e^{\text{coef.}}$) to represent the relative risk (RR) of incidence or mortality

**Table 1** Numbers and ASR per 100 000 cases of incidence of MSMI in 1990 and 2021, along with the relative changes and EAPC in ASR per 100 000 cases from 1990 to 2021, categorized by global, SDI, and GBD regions

| Characteristic | Number in 1990 (95% UI) | ASR in 1990 (95% UI) | Number in 2021 (95% UI) | ASR in 2021 (95% UI) | Relative change of numbers from 1990 to 2021 | Relative change of ASR from 1990 to 2021 | EAPC (ASR, 95% CI) |
|---|---|---|---|---|---|---|---|
| Global | 22,450,868 (16778828 to 28812949) | 764.03 (573.01 to 970.54) | 19,047,404 (14608563 to 24086486) | 494.19 (377.34 to 623.9) | -15.16% | -35.32% | -1.18 (-1.25 to -1.12) |
| High SDI | 2,101,373 (1632187 to 2563348) | 471.73 (367.95 to 572.78) | 1,454,516 (1210068 to 1754445) | 316.19 (261.92 to 380.86) | -30.78% | -32.97% | -1.54 (-1.67 to -1.41) |
| High-middle SDI | 3,464,319 (2544071 to 4324952) | 577.47 (426.37 to 719.36) | 2,035,759 (1607902 to 2543159) | 365.81 (283.8 to 457.83) | -41.24% | -36.65% | -0.94 (-1.19 to -0.7) |
| Middle SDI | 7,230,604 (5277420 to 9435629) | 704.91 (520.39 to 910.87) | 4,951,604 (3759510 to 6269844) | 416.74 (315.72 to 528.61) | -31.52% | -40.88% | -1.23 (-1.4 to -1.07) |
| Low-middle SDI | 6,572,867 (4886463 to 8549073) | 1069.58 (802.61 to 1375.87) | 5,878,472 (4402325 to 7500139) | 549.86 (413.95 to 700.75) | -10.56% | -48.59% | -2.01 (-2.07 to -1.95) |
| Low SDI | 3,061,689 (2301567 to 4006663) | 1245.47 (951.98 to 1602.84) | 4,711,030 (3557613 to 6151574) | 793.64 (610.12 to 1026.92) | 53.87% | -36.28% | -1.49 (-1.58 to -1.41) |
| Andean Latin America | 313,100 (240477 to 389614) | 1513.92 (1202.36 to 1881.43) | 335,485 (265695 to 417156) | 938.27 (747.74 to 1163.11) | 7.15% | -38.02% | -1.52 (-1.57 to -1.46) |
| Australasia | 39,760 (26799 to 52324) | 368.49 (248.81 to 486.26) | 55,512 (44860 to 67998) | 381.4 (308.49 to 465.25) | 39.62% | 3.50% | 0.71 (0.52 to 0.9) |
| Caribbean | 196,356 (146846 to 250506) | 942.74 (707.72 to 1191.07) | 162,891 (124478 to 206226) | 678.56 (517.23 to 858.58) | -17.04% | -28.02% | -1.05 (-1.09 to -1.01) |
| Central Asia | 226,718 (158593 to 314176) | 583.44 (409.25 to 807.31) | 195,462 (136318 to 270654) | 421.29 (290.7 to 593.58) | -13.79% | -27.79% | -0.75 (-0.91 to -0.6) |
| Central Europe | 364,747 (295128 to 424420) | 637.3 (512.9 to 740.66) | 143,975 (122561 to 169480) | 338.89 (286.74 to 395.18) | -60.53% | -46.82% | -1.61 (-1.84 to -1.38) |
| Central Latin America | 1,026,704 (776867 to 1294541) | 1079.69 (833.67 to 1351.42) | 942,746 (726787 to 1182212) | 691.17 (532 to 865.97) | -8.18% | -35.98% | -1 (-1.19 to -0.81) |
| Central Sub-Saharan Africa | 332,480 (248697 to 446314) | 1227.93 (921.93 to 1611.28) | 529,429 (401012 to 683718) | 757.87 (578.67 to 975.32) | 59.24% | -38.28% | -1.39 (-1.59 to -1.19) |
| East Asia | 3,978,752 (2745642 to 5417721) | 508.84 (357.06 to 688.31) | 1,607,813 (1199217 to 2116220) | 275.07 (201.43 to 361.64) | -59.59% | -45.94% | -1.42 (-1.81 to -1.03) |
| Eastern Europe | 836,275 (623341 to 1029937) | 796.55 (590.82 to 981.16) | 567,219 (432837 to 703317) | 655.56 (498.45 to 813.04) | -32.17% | -17.70% | 0.36 (-0.07 to 0.79) |
| Eastern Sub-Saharan Africa | 1,177,090 (884838 to 1550421) | 1235.99 (957.97 to 1586.07) | 1,786,962 (1329131 to 2365074) | 770.44 (590.83 to 999.44) | 51.81% | -37.67% | -1.54 (-1.63 to -1.45) |
| High-income Asia Pacific | 166,434 (118001 to 223919) | 192.77 (136.51 to 259.77) | 85,924 (69955 to 105034) | 123.05 (99.79 to 150.96) | -48.37% | -36.17% | -1.64 (-1.82 to -1.46) |
| High-income North America | 908,568 (723333 to 1085244) | 639.03 (511.14 to 756.15) | 677,817 (577265 to 791933) | 419.87 (358.45 to 489.71) | -25.40% | -34.29% | -2.15 (-2.48 to -1.82) |
| North Africa and Middle East | 1,945,626 (1440451 to 2420003) | 1088 (814.38 to 1345.82) | 1,732,958 (1291203 to 2179750) | 545 (404.98 to 685.4) | -10.93% | -49.91% | -1.9 (-2.01 to -1.8) |

**Table 1** (continued)

| Characteristic | Number in 1990 (95% UI) | ASR in 1990 (95% UI) | Number in 2021 (95% UI) | ASR in 2021 (95% UI) | Relative change of numbers from 1990 to 2021 | Relative change of ASR from 1990 to 2021 | EAPC (ASR, 95% CI) |
|---|---|---|---|---|---|---|---|
| Oceania | 34,389 (25214 to 44497) | 985.72 (733.99 to 1266.68) | 56,511 (42019 to 73172) | 766.08 (573.04 to 985.67) | 64.33% | -22.28% | -0.83 (-0.87 to -0.79) |
| South Asia | 5,968,535 (4369709 to 7878055) | 1043.53 (768.34 to 1362.2) | 5,021,395 (3677490 to 6576976) | 481.95 (354.08 to 628.35) | -15.87% | -53.82% | -2.45 (-2.54 to -2.37) |
| Southeast Asia | 1,902,682 (1395358 to 2528530) | 701.92 (517.68 to 922.64) | 1,550,623 (1157963 to 2014588) | 428.81 (318.17 to 557.56) | -18.50% | -38.91% | -1.34 (-1.44 to -1.25) |
| Southern Latin America | 237,140 (185660 to 286041) | 926.14 (724.82 to 1116.7) | 206,821 (169788 to 249646) | 602.12 (496.3 to 727.12) | -12.79% | -34.99% | -0.94 (-1.2 to -0.68) |
| Southern Sub-Saharan Africa | 217,218 (165017 to 285936) | 736.39 (571.82 to 957.28) | 215,988 (165610 to 281935) | 484.22 (369.81 to 637.75) | -0.57% | -34.24% | -1.14 (-1.22 to -1.07) |
| Tropical Latin America | 838,219 (638348 to 1029681) | 947.39 (729.69 to 1164.66) | 721,246 (595287 to 857905) | 624.66 (515.32 to 739.21) | -13.95% | -34.07% | -0.51 (-0.77 to -0.25) |
| Western Europe | 752,932 (582458 to 944277) | 390.58 (301.86 to 487.71) | 567,968 (458617 to 712059) | 323.26 (259.66 to 404.98) | -24.57% | -17.24% | -0.24 (-0.37 to -0.1) |
| Western Sub-Saharan Africa | 987,146 (765297 to 1304769) | 1064.36 (849.11 to 1366.73) | 1,882,658 (1470745 to 2459095) | 748.2 (589.65 to 955.14) | 90.72% | -29.70% | -1.13 (-1.2 to -1.05) |

Abbreviations: ASR age-standardized rate; UI uncertainty interval; EAPC estimated annual percentage change; CI confidence interval

for specific ages, periods, or birth cohorts compared to their respective averages.

Decomposition analysis quantified factors driving changes in MSMI incidence. This approach disentangles the changes in the affected population into three key determinants at the group level: aging of the population, population growth, and epidemiological changes.

Frontier analysis helps determine the minimum attainable disease burden for each country or region, given their current SDI level. This approach serves as a standard for ideal performance by identifying the lowest possible burden that could theoretically be achieved based on the current SDI. We computed the 'effective differences' for each area, which indicate the discrepancy between the existing disease burden and the lowest possible burden. These differences provide a quantitative measure of how far each country or region is from the optimal performance benchmark.

The autoregressive integrated moving average (ARIMA) models were applied to forecast future trends in MSMI case numbers and age-standardized rates (ASR). Optimal model parameters (p, d, q) were selected through minimized Akaike information criterion (AIC) and Bayesian information criterion (BIC), alongside maximized $R^2$ values. The finalized model generated projections from 2021 to 2040, with 95% confidence intervals quantifying prediction uncertainty.

All data processing and statistical analyses were performed using the R (version 4.2.1) and joinpoint regression software (version 4.9.1.0), and were visualized using Origin 2024 software. Detailed descriptions of each method are provided in the supplementary materials.

## Results

### Trends in MSML incidence, death and dalys from 1990 to 2021

From 1990 to 2021, the global burden of MSMI underwent significant changes. Table 1 offers a detailed comparison of incidence, ASR, and relative changes by SDI levels and GBD regions over this period, including EAPC values. Globally, MSMI cases decreased from 22.45 million to 19.05 million, with the ASR dropping from 764.03 to 494.19 per 100,000 people, representing a reduction of 35.32%. The EAPC in ASR was – 1.18, indicating an overall downward trend.

Performance varied significantly across SDI groups. Most SDI categories showed declines, with high-middle SDI regions experiencing the largest decrease (-41.24%), while low SDI regions saw a 53.87% increase in cases. The ASR consistently decreased across all SDI groups, with the largest decline in low-middle SDI regions (-48.59%). Despite the overall reduction, significant disparities remain between SDI regions.

Among GBD regions, MSMI cases exhibited both increases and decreases. Western Sub-Saharan Africa had the most notable increase (90.72%), whereas Central Europe and East Asia saw the most significant decreases (-60.53% and −59.59%). ASR mostly decreased across regions, with South Asia showing the largest decline (-53.82%), while Australasia experienced a slight increase (3.50%). The EAPC results showed that South Asia and North Africa and the Middle East had the greatest decreases, whereas Eastern Europe and Australasia showed a persistent upward trend in ASR.

We used bar charts and line graphs to visualize the analysis. Figure 1A illustrates the trends in MSMI incidence from 1990 to 2021, showing a steady decline in cases from approximately 22 million in 1990 to 12 million in 2021. The ASR similarly decreased from 764 to 494 per 100,000, reflecting the impact of improved healthcare interventions and preventive measures globally. Figure 1B shows MSMI-related deaths, which rose from 20,000 in 1990 to 30,000 in the early 2000s, before declining to 10,000 by 2021. This trend suggests an initial worsening followed by significant improvements in MSMI management. The ASR peaked at 1.0 per 100,000 in the early 2000s, then dropped to 0.5 per 100,000 by 2021, highlighting advancements in care and the effectiveness of interventions. Figure 1C presents the burden of MSMI in DALYs, which increased from 1 million in 1990 to 2 million in the early 2000s before falling back to 1 million in 2021. The ASR halved, decreasing from 60 to 30 per 100,000, indicating significant progress in reducing long-term health impacts and improving quality of life for those affected.

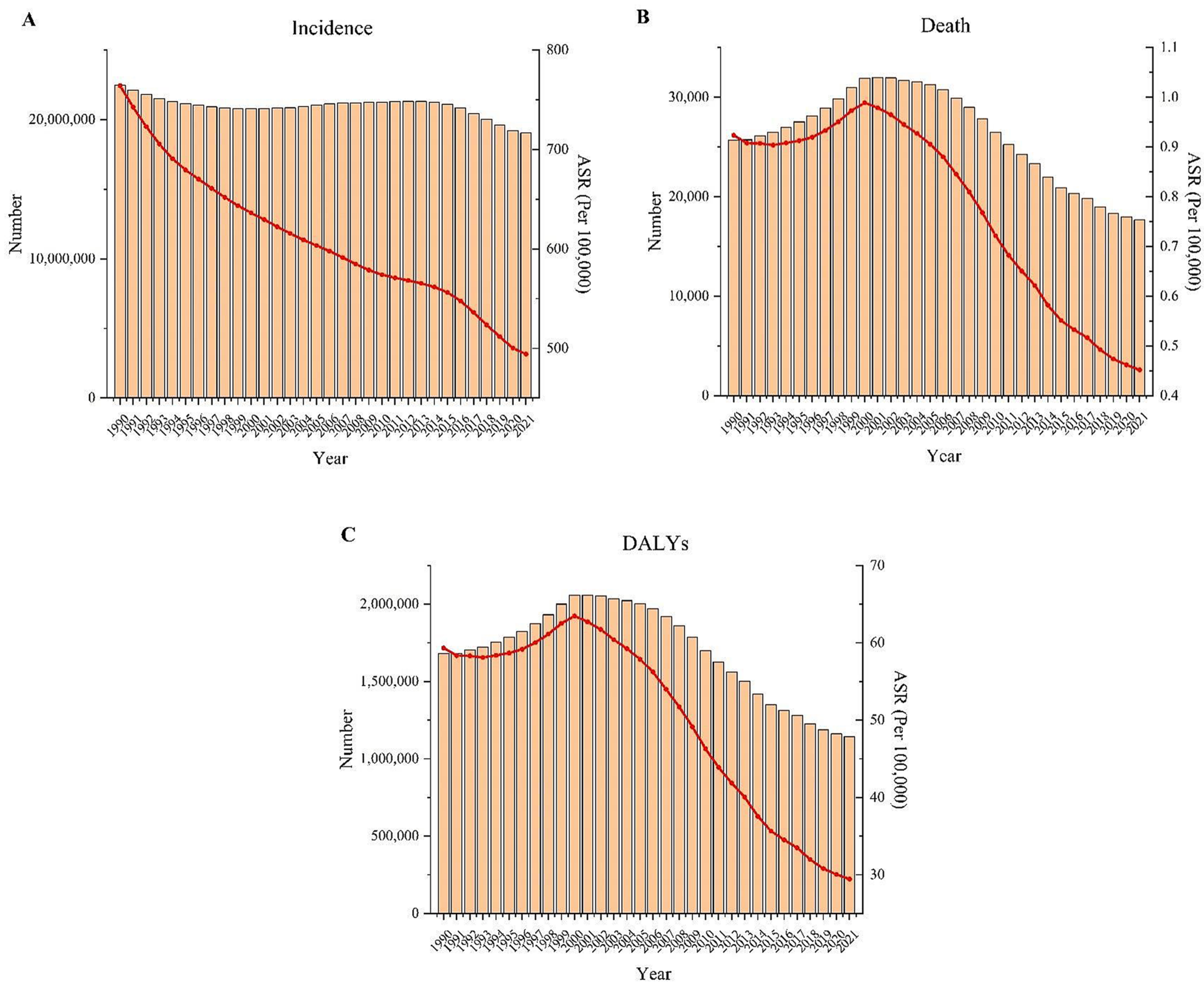


**Fig. 1** Global trends for age-standardized rates (per 100,000 people) and absolute numbers of MSMI from 1990 to 2021. (**A**) Burden of MSMI measured in incidence; (**B**) Burden of MSMI measured in death; (**C**) Burden of MSMI measured in DALYs. The bar graph represents the number of cases, while the red line represents the ASR per 100,000 people. Abbreviations: DALYs disability-adjusted life-years; ASR age-standardized rate

### Burden of MSMI based on age

The analysis of MSMI burden by age group from 1990 to 2021 revealed that women aged 20–34 consistently experience high incidence, death, and DALYs, with the highest burden observed in the 20–24 age group. The incidence of MSMI peaked in this age group, with approximately 6 million cases and an ASR exceeding 2,000 per 100,000 (Fig. 2A). Similarly, the number of deaths peaks in the 20–24 age group, with around 4,000 deaths and an ASR exceeding 1.4 per 100,000 (Fig. 2B). The DALYs are also highest in this age group, with approximately 300,000 DALYs and an ASR exceeding 100 per 100,000 (Fig. 2C). The results indicate that targeted interventions for women in these age groups are crucial.

### Joinpoint regression analysis of MSMI

The joinpoint regression analysis indicated significant improvements in MSMI incidence, death, and DALYs, particularly after 2000 (Table 2). Specifically, MSMI incidence showed a significant decline over the study period, with an AAPC of -1.40% (95% CI, -1.45 to -1.35). The decline was most pronounced from 1990 to 1994 (APC −2.50%) and from 2015 to 2021 (APC −2.07%). Death due to MSMI also demonstrated a notable reduction, with an AAPC of -2.29% (95% CI, -2.50 to -2.08). Following a slight increase from 1995 to 2000 (APC 1.86%), substantial declines were observed, especially from 2007 to 2015 (APC −5.28%). Similarly, DALYs decreased significantly, with an AAPC of -2.24% (95% CI, -2.44 to -2.04). Although there was a temporary increase from 1995 to 2000 (APC 1.80%), the period from 2007 to 2015 saw the sharpest decline (APC −5.12%). Overall, the data indicate that despite periods of slower progress and setbacks, the long-term trends in MSMI incidence, death, and DALYs were consistently positive, reflecting improvements in healthcare and intervention measures globally.

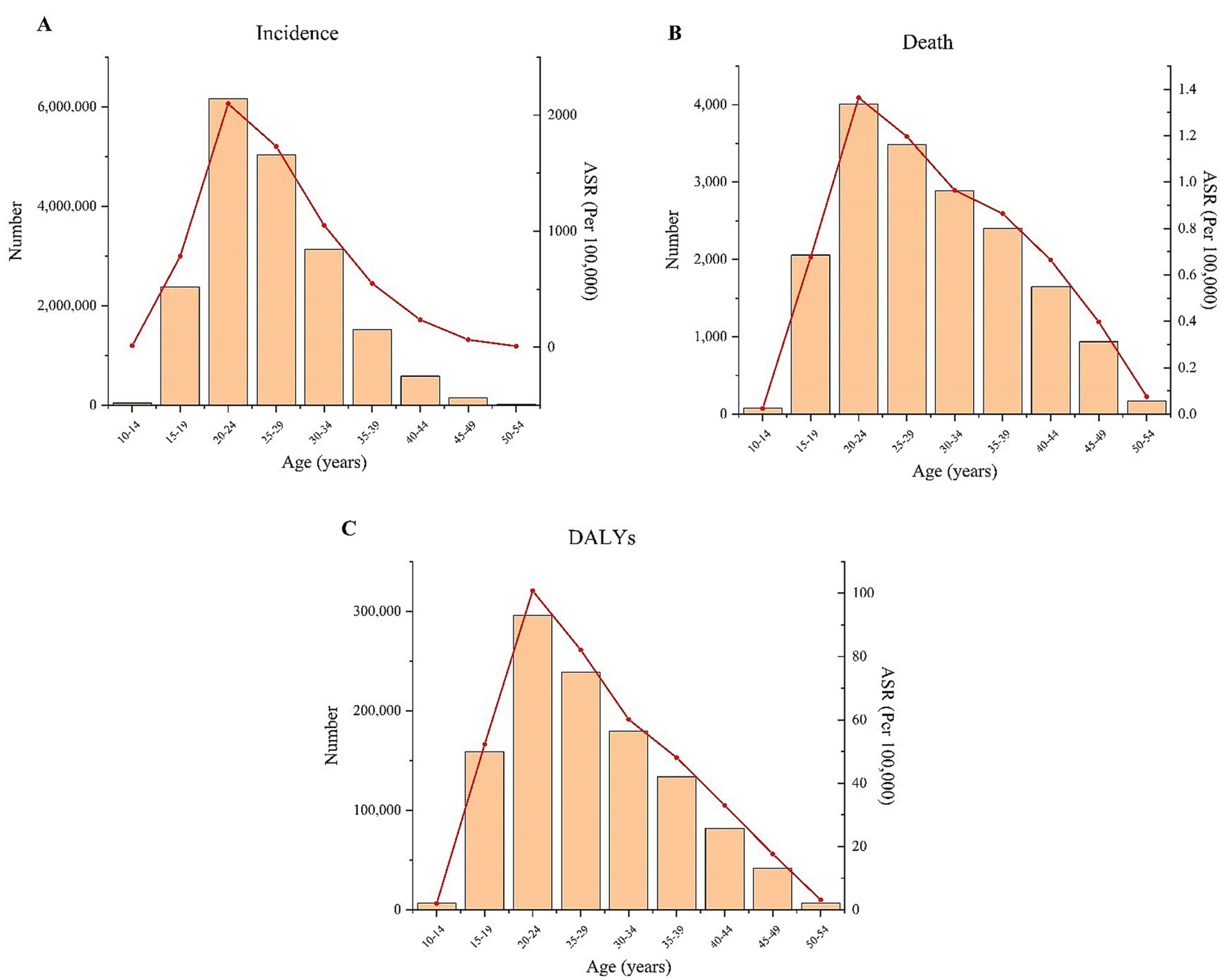


**Fig. 2** Global burden of MSMI according to age. (**A**) Incidence of MSMI by age group. (**B**) Deaths due to MSMI by age group. (**C**) DALYs due to MSMI by age group. Abbreviations: DALYs disability-adjusted life-years; ASR age-standardized rate

**Table 2** The joinpoint regression analysis of MSMI incidence, death, and dalys from 1990–2021

| Incidence | | Death | | DALYs | |
|---|---|---|---|---|---|
| **Period** | **APC** | **Period** | **APC** | **Period** | **APC** |
| **1990–2021 (AAPC)** | **-1.40* (-1.45 to -1.35)** | **1990–2021 (AAPC)** | **-2.29* (-2.50 to -2.08)** | **1990–2021 (AAPC)** | **-2.24* (-2.44 to -2.04)** |
| 1990–1994 | -2.50* (-2.69 to -2.32) | 1990–1995 | -0.27 (-0.67 to 0.13) | 1990–1995 | -0.23 (-0.63 to 0.17) |
| 1994–1999 | -1.37* (-1.56 to -1.18) | 1995–2000 | 1.86* (1.33 to 2.39) | 1995–2000 | 1.80* (1.27 to 2.34) |
| 1999–2009 | -1.05* (-1.1 to -1) | 2000–2004 | -1.53* (-2.30 to -0.75) | 2000–2004 | -1.65* (-2.39 to -0.90) |
| 2009–2015 | -0.60* (-0.73 to -0.48) | 2004–2007 | -2.94* (-4.46 to -1.40) | 2004–2007 | -2.95* (-4.37 to -1.50) |
| 2015–2021 | -2.07* (-2.17 to -1.98) | 2007–2015 | -5.28* (-5.51 to -5.04) | 2007–2015 | -5.12* (-5.34 to -4.90) |
| | | 2015–2021 | -3.48* (-3.84 to -3.12) | 2015–2021 | -3.35* (-3.69 to -3.00) |

Abbreviations: DALYs disability-adjusted life-years; APC annual percent change; AAPC average annual percent change. * $p < 0.05$

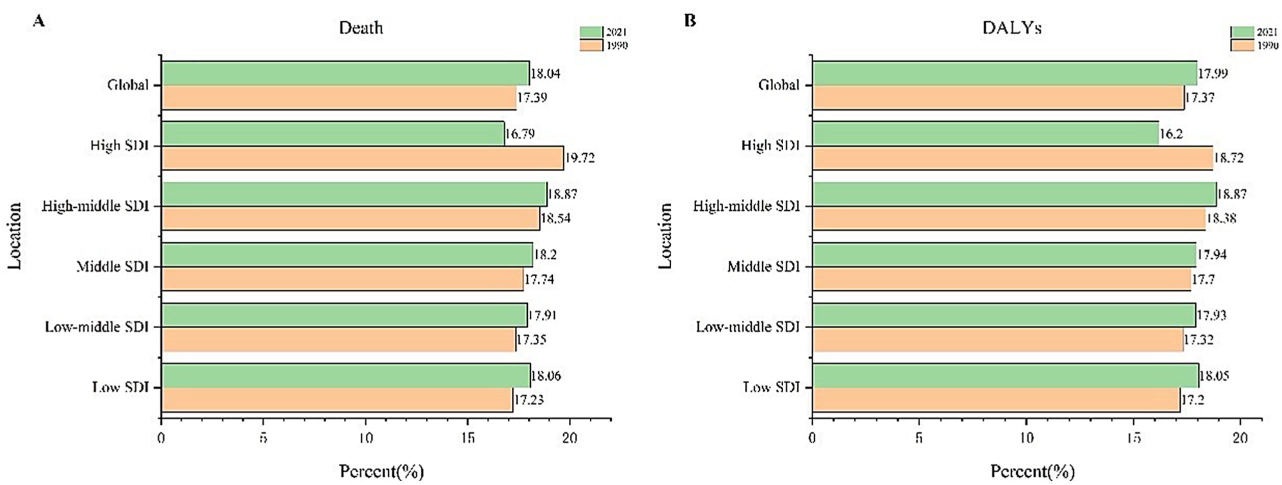


**Fig. 3** Iron deficiency is the leading risk factor contributing to MSMI-related deaths and DALYs worldwide, with its impact across different SDI categories between 1990 and 2021. (**A**) The percentage of death due to MSMI attributable to iron deficiency. (**B**) The percentage of DALYs due to MSMI attributable to iron deficiency. Abbreviations: DALYs disability-adjusted life-years; SDI sociodemographic index

### Analysis of MSMI attributable to iron deficiency as a risk factor

Figure 3A and B compare the percentages of death and DALYs due to MSMI attributable to iron deficiency across different SDI categories between 1990 and 2021, respectively. Globally, the percentage of death attributable to iron deficiency in MSMI increased slightly from 17.39% in 1990 to 18.04% in 2021. High SDI regions experienced a notable decrease from 19.72 to 16.79%, reflecting effective interventions and improvements in healthcare. Conversely, low and low-middle SDI regions experienced an increase in iron deficiency, highlighting ongoing challenges in addressing iron deficiency. High-middle and middle SDI regions showed relatively stable percentages with only minor increases. For DALYs, the global percentage attributable to iron deficiency rose from 17.37% in 1990 to 17.99% in 2021. The trends across different SDI regions were similar to those observed for deaths: high SDI regions experienced significant reductions, indicating improved quality of life and reduced long-term health impacts due to better iron management. However, low and low-middle SDI regions experienced increases. High-middle and middle SDI regions slightly increased, indicating a persistent issue.

### The effect of age, period, and cohort on the incidence, death, and dalys of MSMI

#### *Age effects*

After controlling for period and cohort effects, the age effect showed significant variations in the risk of MSMI and related outcomes. Incidence and death peaked in the 20–29 age group, with relative risks (RRs) of up to 9.103 for incidence and 3.460 for death, identifying these age groups as the most vulnerable to MSMI. Risks declined significantly for individuals over 30, with the lowest risks observed in the 50–54 age group.(Table 3).

#### *Period effects*

Period effects indicate the impact of healthcare improvements and public health interventions. From 1992 to 2021, the RRs for both incidence and death demonstrated a general downward trend, with significant declines especially after the early 2000s. The incidence RR decreased from 1.241 in 1992–1996 to 0.884 in 2017–2021,

**Table 3** Age-period-cohort analysis of MSMI incidence, death, and dalys from 1990–2021

| Factor | Incidence | | Death | | DALYs | |
|---|---|---|---|---|---|---|
| RR | 95%CI | RR | 95%CI | RR | 95%CI | |
| **Age (years)** | | | | | | |
| 10–14 | 0.057 | 0.057 to 0.057 | 0.072 | 0.068 to 0.077 | 0.091 | 0.09 to 0.092 |
| 15–19 | 3.758 | 3.753 to 3.763 | 1.886 | 1.847 to 1.927 | 2.329 | 2.323 to 2.336 |
| 20–24 | 9.103 | 9.093 to 9.113 | 3.46 | 3.4 to 3.521 | 4.129 | 4.119 to 4.138 |
| 25–29 | 6.343 | 6.337 to 6.349 | 3.056 | 3.006 to 3.106 | 3.399 | 3.392 to 3.406 |
| 30–34 | 3.564 | 3.561 to 3.568 | 2.391 | 2.351 to 2.433 | 2.456 | 2.451 to 2.462 |
| 35–39 | 1.951 | 1.949 to 1.954 | 1.938 | 1.902 to 1.976 | 1.827 | 1.823 to 1.832 |
| 40–44 | 0.895 | 0.893 to 0.896 | 1.354 | 1.323 to 1.385 | 1.166 | 1.163 to 1.17 |
| 45–49 | 0.301 | 0.3 to 0.302 | 0.745 | 0.724 to 0.766 | 0.584 | 0.582 to 0.587 |
| 50–54 | 0.043 | 0.043 to 0.043 | 0.148 | 0.141 to 0.157 | 0.11 | 0.109 to 0.111 |
| **Period** | | | | | | |
| 1992–1996 | 1.241 | 1.24 to 1.243 | 1.129 | 1.112 to 1.147 | 1.17 | 1.168 to 1.173 |
| 1997–2001 | 1.089 | 1.088 to 1.09 | 1.213 | 1.198 to 1.229 | 1.235 | 1.233 to 1.237 |
| 2002–2006 | 0.99 | 0.989 to 0.99 | 1.194 | 1.181 to 1.208 | 1.194 | 1.192 to 1.196 |
| 2007–2011 | 0.928 | 0.927 to 0.928 | 1.033 | 1.021 to 1.045 | 1.021 | 1.02 to 1.023 |
| 2012–2016 | 0.912 | 0.911 to 0.913 | 0.831 | 0.82 to 0.843 | 0.817 | 0.815 to 0.819 |
| 2017–2021 | 0.884 | 0.882 to 0.885 | 0.712 | 0.699 to 0.725 | 0.694 | 0.693 to 0.696 |
| **Cohort** | | | | | | |
| 1938–1942 | 1.063 | 1.05 to 1.076 | 1.288 | 1.131 to 1.467 | 1.159 | 1.136 to 1.183 |
| 1943–1947 | 1.01 | 1.004 to 1.015 | 1.178 | 1.107 to 1.255 | 1.084 | 1.074 to 1.094 |
| 1948–1952 | 0.888 | 0.884 to 0.891 | 1.106 | 1.056 to 1.159 | 1.035 | 1.027 to 1.042 |
| 1953–1957 | 0.876 | 0.873 to 0.879 | 1.094 | 1.052 to 1.138 | 1.037 | 1.031 to 1.043 |
| 1958–1962 | 0.883 | 0.88 to 0.885 | 1.063 | 1.027 to 1.099 | 1.021 | 1.016 to 1.026 |
| 1963–1967 | 0.952 | 0.95 to 0.954 | 1.038 | 1.007 to 1.069 | 1.01 | 1.006 to 1.015 |
| 1968–1972 | 1.045 | 1.043 to 1.046 | 1.068 | 1.04 to 1.096 | 1.055 | 1.052 to 1.059 |
| 1973–1977 | 1.101 | 1.1 to 1.103 | 1.083 | 1.057 to 1.109 | 1.087 | 1.083 to 1.09 |
| 1978–1982 | 1.14 | 1.138 to 1.141 | 1.018 | 0.994 to 1.042 | 1.041 | 1.038 to 1.044 |
| 1983–1987 | 1.132 | 1.131 to 1.133 | 0.91 | 0.888 to 0.932 | 0.952 | 0.949 to 0.954 |
| 1988–1992 | 1.094 | 1.093 to 1.095 | 0.857 | 0.834 to 0.88 | 0.913 | 0.911 to 0.916 |
| 1993–1997 | 0.991 | 0.99 to 0.992 | 0.844 | 0.818 to 0.87 | 0.909 | 0.906 to 0.912 |
| 1998–2002 | 0.89 | 0.889 to 0.892 | 0.79 | 0.757 to 0.824 | 0.859 | 0.855 to 0.864 |
| 2003–2007 | 0.995 | 0.986 to 1.005 | 0.808 | 0.66 to 0.988 | 0.887 | 0.867 to 0.908 |

Abbreviations: RR Relative Risk

reflecting the positive influence of enhanced healthcare services.

#### *Cohort effects*

Cohort effects reveal higher risks for older birth cohorts, such as those born between 1938 and 1942, with RRs of 1.063 for incidence and 1.288 for death. In contrast, younger cohorts, particularly those born after 1980, experienced notable risk reductions, with cohorts born between 1998 and 2002 showing RRs of 0.89 for incidence and 0.79 for death, reflecting improvements due to modern healthcare interventions.

### Decomposition analysis of the augmented incidence cases

The decomposition analysis assessed the increase in MSMI incidence from 1990 to 2021 by incorporating epidemiological changes, population growth, and aging (Fig. 4). Globally, epidemiological changes contributed the most to the rise in incidence across all SDI quintiles. Population growth was a major driver, especially in low and low-middle SDI regions, while population aging had a notable impact in high and high-middle SDI regions. The largest increases were observed in low and low-middle SDI regions, driven by both population growth and epidemiological changes. In high SDI regions, the contributions from all three factors were more balanced, indicating better control over incidence rates. These findings emphasize the need for targeted interventions to manage rising incidence, particularly in lower SDI regions.

### Relationships between the SDI and the disease burden of MSMI

The relationship SDI and age-standardized DALYs rate (ASDR) for MSMI across various countries and territories in 2021 demonstrated a significant inverse correlation ($r$ = -0.715, $p < 0.001$) (Fig. 5A). Countries with

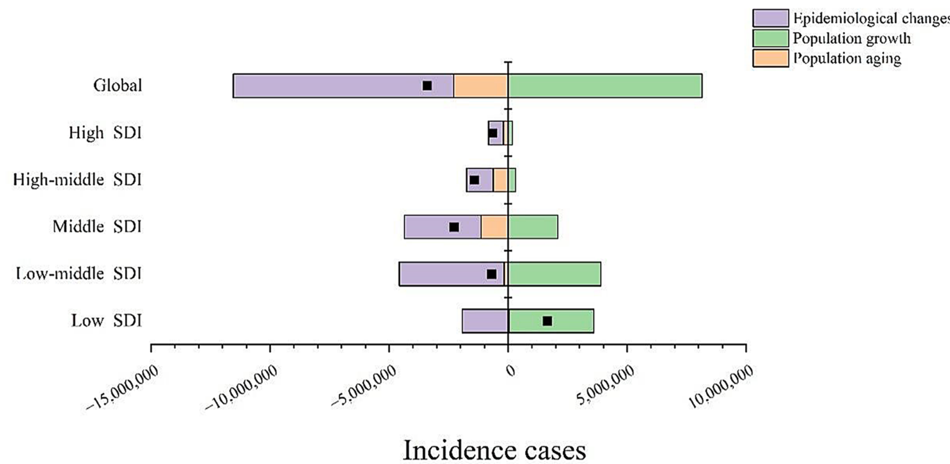


**Fig. 4** Decomposition analysis of MSMI incidence cases across different SDI categories in 2021. Alterations in MSMI-related incidence cases based on population-level determinants of epidemiological changes, population growth, and population aging from 1990 to 2021 at the global level and by the SDI quintile. The black square represents the overall alteration induced by all three components. Positive values indicate an increase in incidence cases associated with the respective component, while negative values indicate a reduction. The purple, green, and orange bars represent changes due to epidemiological factors, population growth, and population aging, respectively. The global trend demonstrates significant impacts from epidemiological changes and population growth, with varying contributions from population aging across different SDI quintiles. Abbreviations: SDI sociodemographic index; DALYs disability-adjusted life-years

lower SDI values, such as Somalia, Chad, and the Central African Republic, had the highest ASDRs, exceeding 400 per 100,000 people, reflecting inadequate healthcare infrastructure and poor socio-economic conditions. Middle-SDI countries like Afghanistan, Madagascar, and Zimbabwe had moderate ASDRs (100–300 per 100,000), showing improvements in healthcare and socio-economic conditions but still facing significant disease burdens. High-SDI countries, such as those in Western Europe, North America, and East Asia, had the lowest ASDRs (below 50 per 100,000), benefiting from advanced healthcare systems and better maternal care.

Similarly, the SDI-ASR relationship from 1990 to 2021 also showed a significant inverse correlation ($r$ = -0.744, $p<0.001$), except for regions like Central and Southern Sub-Saharan Africa, which experienced fluctuations (Fig. 5B). Low-SDI countries, particularly in Central and Sub-Saharan Africa, had the highest ASRs, exceeding 300 per 100,000, while middle-SDI countries, including those in South Asia and Latin America, had moderate ASRs (100–300 per 100,000). High-SDI countries, including those in Western Europe, North America, and East Asia, exhibited the lowest ASRs, often below 50 per 100,000.

#### Frontier analysis involving the SDI and MSMI burden

Figure 6A illustrates the ASR for MSMI across various countries from 1990 to 2021, plotted against SDI. The frontier line represents the expected ASR based on SDI, serving as a benchmark for comparison. As SDI increases, the ASR generally decreases and becomes more stable, with the frontier trend stabilizing once SDI exceeds 0.5, indicating more consistent ASR values in countries above this threshold.

Figure 6B highlights disparities in ASR among countries with similar SDI levels in 2021. For instance, Albania (SDI 0.71) had an ASR of 1.75, much lower than American Samoa (SDI 0.72, ASR 14.58). Similarly, the Central African Republic (SDI 0.31, ASR 337.35) had a much higher ASR than Mozambique (SDI 0.32, ASR 50.38). The top five countries with the largest effective difference (EF) from the frontier, ranging from 138.91 to 66.72, were Chad, the Central African Republic, the Democratic Republic of the Congo, Eritrea, and Mali, indicating urgent need for health interventions. Notably, only five countries—Australia, Niue, American Samoa, Kiribati, and the Marshall Islands—saw an increase in ASR. Australia, with an EF of 0.99, showed the smallest deviation between observed and expected ASR, suggesting relatively effective healthcare interventions. The other four countries had higher EF values (ranging from 10.96 to 98.25), reflecting significant public health challenges.

#### ARIMA forecasting of MSMI to 2040

The analysis of the provided data revealed significant epidemiological trends. In Fig. 7A, the number of cases starts at approximately 20 million in 1990 and fluctuates until 2021. After 2021, the forecasted number of cases has shown a downward trend, reaching approximately 15 million by 2040. This decrease suggests a reduction in the burden of the condition, likely influenced by effective public health measures and improvements in disease management. Moreover, Fig. 7B shows the ASR, which begins at approximately 600 per 100,000 people in 1990

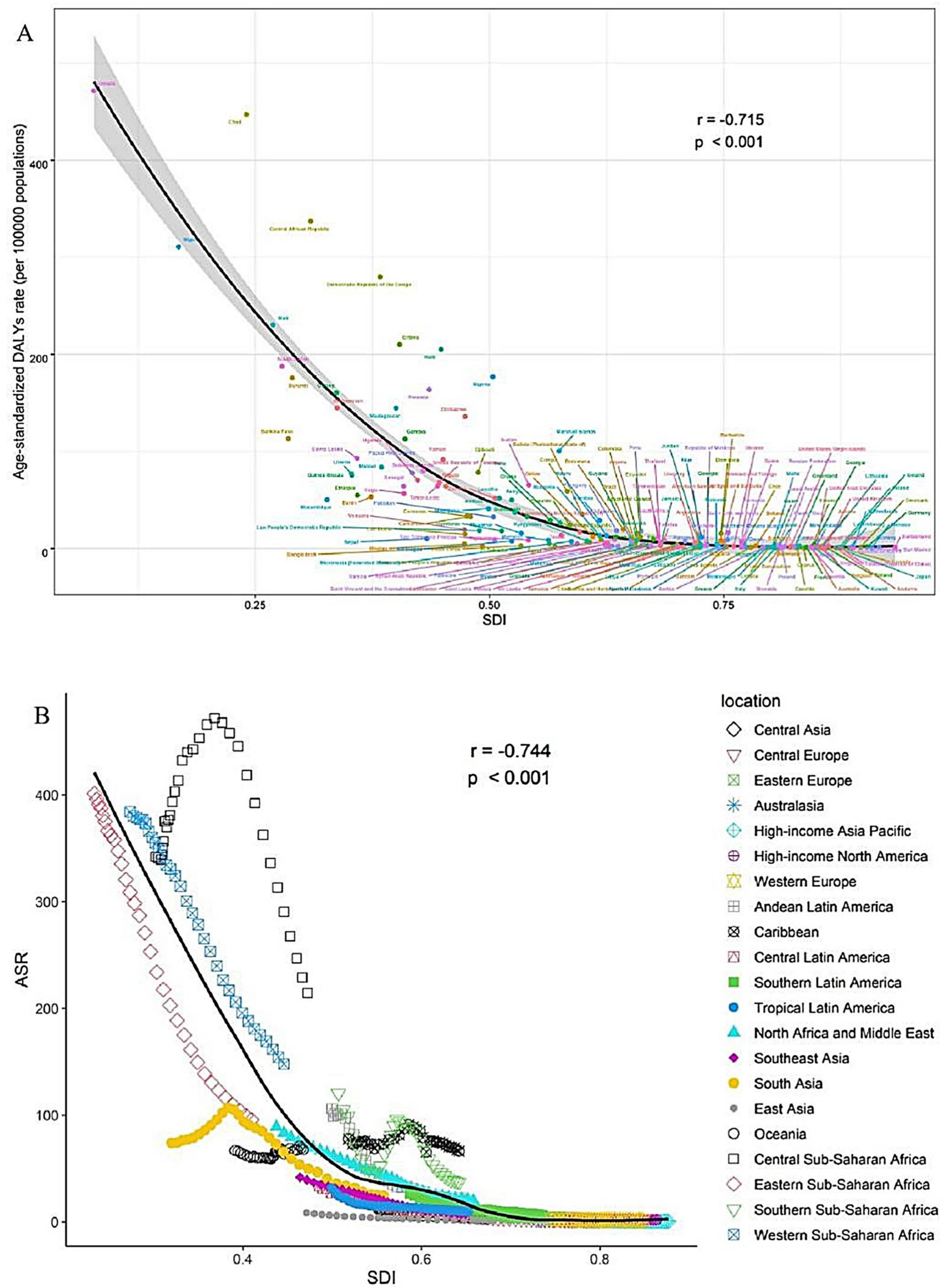


**Fig. 5** Relationships between the SDI and disease burden of MSMI. (**A**) SDI and ASDR across various countries and territories. The grey shaded area represents the 95% UI. (**B**) SDI and ASR across different SDI and GBD regions. For each region, points from left to right depict estimates from each year from 1990 to 2021. The bold solid line represents general inverse relationship between SDI and ASR for MSMI. Abbreviations: SDI sociodemographic index; DALYs disability-adjusted life-years; ASR age-standardized rate

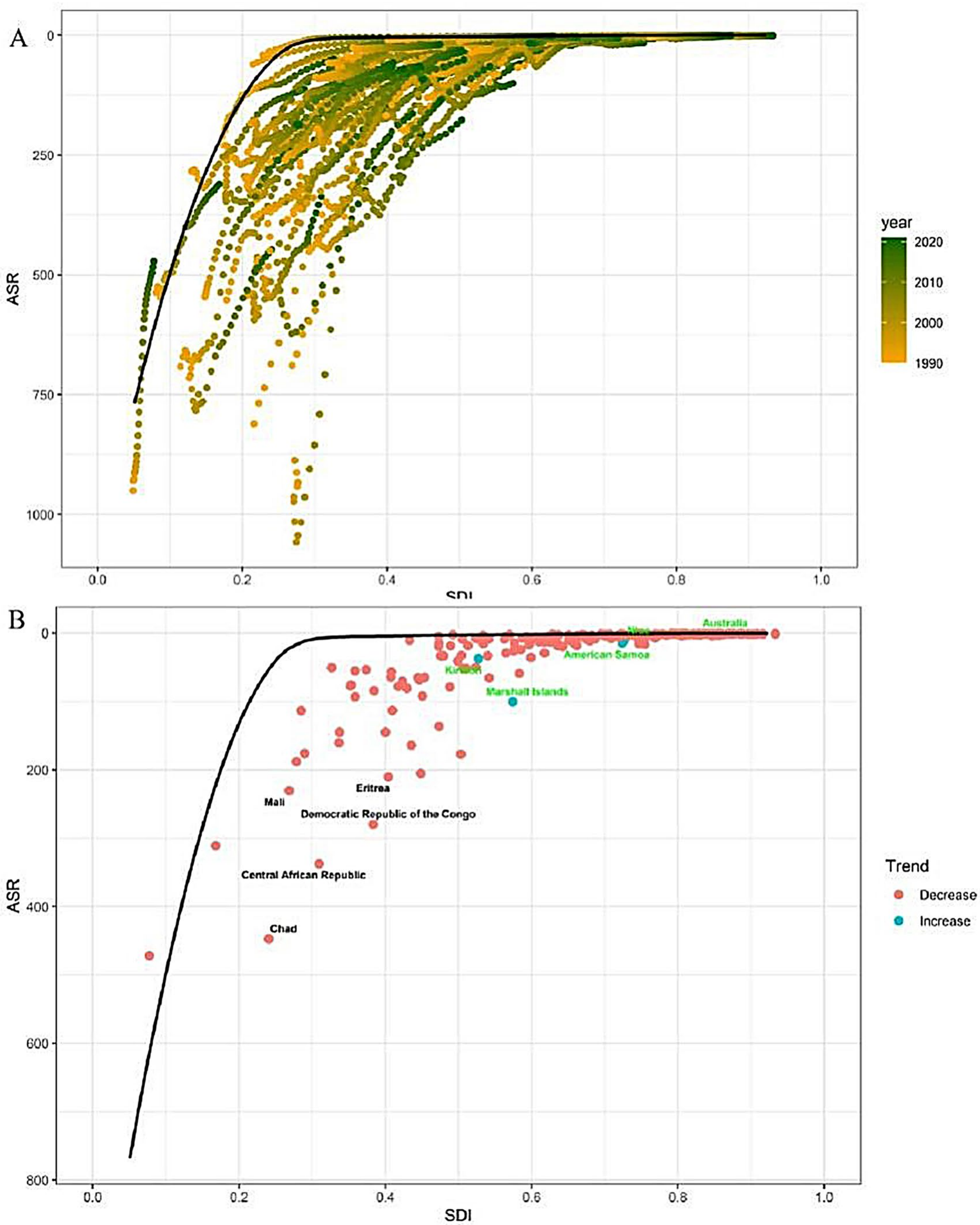


**Fig. 6** Frontier analysis involving the SDI and MSMI burden. (**A**) Frontier analysis of global trends for ASR of MSMI with ASR from 1990 to 2021. The color gradient indicates the year of the data, with darker colors representing more recent years. (**B**) Frontier analysis of MSMI with ASR in 2021. The frontier is marked in solid black, and countries and territories are presented as dots. The 15 leading countries with the most effective differences (the highest ASR of MSMI gap from frontier) are marked in black. Red dots represent a reduction in MSMI burden between 1990 and 2021. The blue dots represent an increase in MSMI burden during the same duration, and those countries are marked in green. Abbreviations: SDI sociodemographic index; ASR age-standardized rate

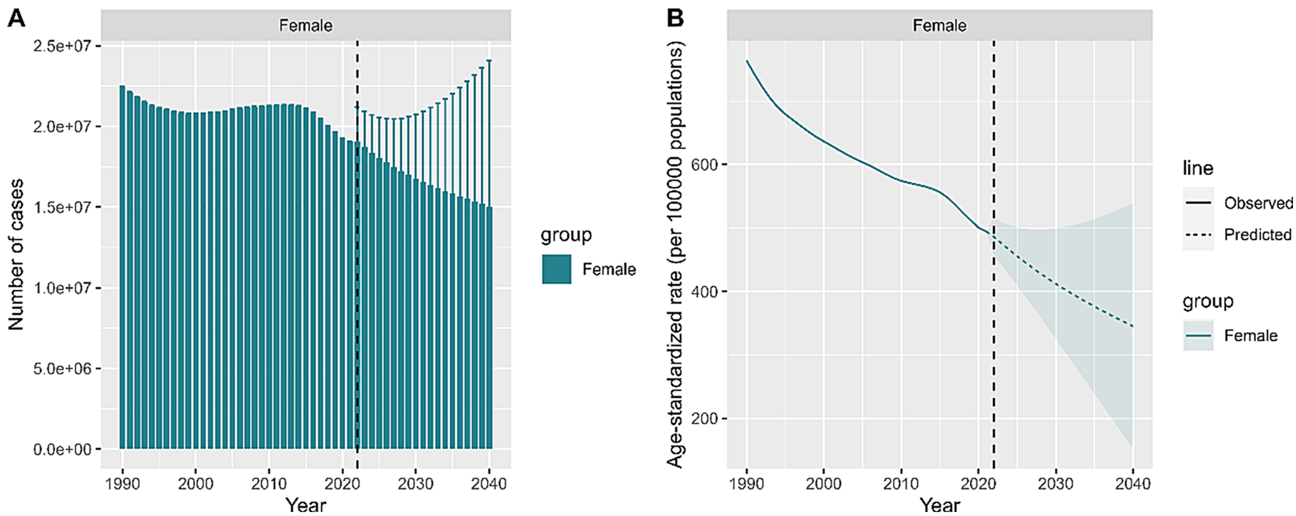


**Fig. 7** ARIMA forecasting of MSMI burden from 1990 to 2040. The vertical line separates the data into true values (1990–2021) and predicted values (2020–2040). (**A**) Observed and predicted number of cases of MSMI from 1990 to 2040. The bars represent the number of cases each year, and the lines on top of the bars from 2021 to 2040 indicate the upper limits of the 95% UI range of the predictions. (**B**) Observed and forecasting ASR of cases of MSMI from 1990 to 2040. The solid lines represent the observed data, while the dashed lines indicate the predicted data. The light-green shaded area represents the 95% UI of the predicted values

and steadily declines to approximately 494 per 100,000 people by 2021. The forecasting data after 2021 continue to show a downward trend, with the ASR decreasing to approximately 200 per 100,000 by 2040. This declining ASR indicates that when adjusting for the age structure of the population, the risk of developing the disease is decreasing, which suggests effective public health interventions and improvements in disease management.

## Discussion

Based on the latest GBD data, we conducted a comprehensive analysis of MSMI from 1990 to 2021, using advanced statistical methods to explore trends across SDI regions, countries, and age groups, and provided forecasts for trends up to 2040. Significant disparities persist among SDI regions, consistent with previous studies [12–14]. Moreover, our analysis identified several novel insights.

The observed and forecasted trends indicate a decrease in both the absolute number of cases and ASR, demonstrating the effectiveness of current public health measures. Although fewer resources may be required as case numbers decline, continuous monitoring and efficient resource allocation remain essential to sustaining progress. The declining ASR underscores the importance of maintaining preventive measures and enhancing treatments to further reduce disease incidence. This comprehensive approach ensures that public health strategies remain effective and resources are utilized optimally.

Age-period-cohort analysis further indicated that MSMI burden peaks among women aged 20–29, primarily due to increased exposure during pregnancy and childbirth [15]. However, these rates have declined in recent decades, particularly among younger cohorts. The possible causes of this situation include the impact of global health initiatives, particularly the United Nations Millennium Development Goals (MDGs) of 2000, which emphasized reducing global maternal mortality and the Surviving Sepsis Campaign [16–18]. During this period, the widespread promotion of preventive antibiotic use and the standardization of infection management also played crucial roles, significantly reducing perinatal infections and related severe complications [19].

Based on the findings from the decomposition analysis, substantial investments in healthcare infrastructure and improved access to services are needed in low and low-middle SDI regions. In regions where healthcare systems are particularly strained, managing population growth through family planning and enhancing reproductive health services can be effective [20–22]. Middle and high SDI regions should focus on age-specific maternal health services and managing chronic conditions, as population aging in these areas increases the risk of MSMI [23, 24].

Frontier analysis highlights inefficiencies in healthcare delivery, identifying regions or providers needing interventions and guiding better resource allocation. Findings align with previous research, indicating that regions with higher SDI tend to achieve more stable and lower ASR for MSMI, underscoring the importance of socio-economic development in improving health outcomes [25]. However, significant differences remain between countries with similar SDI levels, highlighting that healthcare effectiveness, policy implementation, and resource availability are also key factors in determining health outcomes [26–29].

Our findings indicate that iron deficiency plays a critical role, particularly in low-SDI regions. Previous research links iron deficiency to an increased risk of sepsis, as it impairs hemoglobin synthesis and immune function, both crucial for sepsis patients [30–34]. Pregnant women have a significantly increased demand for iron due to increased blood volume and fetal growth, often finding it challenging to supplement adequate iron through their diet [35]. Addressing iron deficiency can therefore be a critical component of MSMI treatment. Iron deficiency is the most common cause of anemia during pregnancy [36]. As the end stage of the iron-deficiency process, iron deficiency anemia (IDA) affects a large number of pregnant women worldwide, especially in developing countries with lower SDI [37, 38]. The adverse effects of maternal iron deficiency reported in previous studies have focused primarily on the next generation, including fetal growth restriction, preterm birth, low birth weight, fetal brain development, and neurodevelopmental sequelae in infancy and toddlerhood [39–41]. However, there is a paucity of research on iron deficiency and MSMI, highlighting the need for further studies to understand and address this gap in maternal health research. This disparity between different SDI regions highlights the need for tailored public health interventions. In low and low-middle SDI regions, efforts should focus on improving iron intake through fortified foods and supplements, and enhancing prenatal care to monitor and manage iron levels. Public health policies should also prioritize education on iron intake during pregnancy and develop infrastructure to support supplementation programs.

Addressing the challenges in screening and diagnosing MSMI, as well as refining the understanding and management of maternal sepsis, is crucial for improving outcomes. Current screening tools for MSMI are inadequate, with no optimal tool available, making early identification challenging [42]. Maternal sepsis often presents with vague symptoms, complicating timely diagnosis and risk stratification [43]. While systems like MEOWS have been developed, their global adoption remains limited, reducing early intervention opportunities [44]. Physiological changes during pregnancy can mimic sepsis, delaying recognition and management. Additionally, laboratory reference values differ for obstetric patients, and many sepsis criteria used in the general population have not been fully validated for pregnancy [45, 46]. As the concept of sepsis evolves with updates to its definitions and guidelines, similar advancements should be applied to MSMI [47–49]. Burden estimates empower stakeholders to identify gaps, assess unmet needs, and implement targeted interventions effectively [50].

The study has several strengths. First, it uses the latest GBD 2021 data, ensuring accurate and reliable findings. Second, by applying multiple advanced statistical methods, we provide a comprehensive and actionable understanding of MSMI across various demographics and regions, aiding public health decision-making. Third, the study emphasizes iron deficiency as a key risk factor for MSMI, guiding targeted interventions, particularly in low and low-middle SDI regions. However, the study has limitations. It does not differentiate between specific infection sources, focusing on the clinical state of MSMI, which may obscure variations in etiology and outcomes. Additionally, results are interpreted at the population level, potentially leading to ecological fallacies. Large cohort studies are needed to determine relative risks for specific locations and time periods.

## Conclusion

Overall, the global burden of MSMI has significantly declined from 1990 to 2021, with marked improvements in high SDI regions, whereas low SDI regions experienced an increase in cases, highlighting ongoing disparities. Women aged 20–24 are the most affected, emphasizing the need for targeted healthcare interventions. Iron deficiency is a critical factor, underscoring the importance of nutritional interventions and enhanced prenatal care. While epidemiological improvements have reduced MSMI incidence, population growth has offset these gains in low SDI regions, and population aging has notably impacted middle and high SDI regions. Forecasts suggest continued improvements in MSMI incidence and ASR through 2040, but sustained investment in healthcare infrastructure and public health strategies is essential to further reduce the MSMI burden and improve maternal health outcomes globally.

### Abbreviations

| | |
|---|---|
| MSMI | Maternal sepsis and other maternal infections |
| GBD | Global Burden of Disease |
| SDI | Sociodemographic index |
| YLDs | Years lived with disability |
| YLLs | Years of life lost |
| AAPC | Average annual percent change |
| APC | Annual percent change |
| EAPC | Estimated annual percentage change |
| DALYs | Disability-adjusted life years |
| RR | Relative risk |
| DEA | Data envelopment analysis |
| ASR | Age-standardized rate |
| ASDR | Age-standardized disability-adjusted life years rate |
| UI | Uncertainty interval |
| CI | Confidence interval |
| EF | Effective difference |
| ARIMA | Autoregressive integrated moving average |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12884-025-07409-2 .

Supplementary Material 1

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**Author contributions**
QH: Conceptualization, Data curation, Formal analysis, Methodology, Writing–original draft. LW: Methodology, Formal analysis. QC: Data curation, Formal analysis, Software. ZW: Funding acquisition, Project administration, Writing–review & editing. All authors contributed to the article and approved the submitted version.

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**Data availability**
The datasets generated and analysed during the current study are available in the GBD repository, https://www.healthdata.org/research-analysis/gbd.

## Declarations

**Ethics approval and consent to participate**
This study did not require ethical approval as it utilized publicly available data. The research was conducted in accordance with the Guidelines for Accurate and Transparent Health Estimates Reporting for cross-sectional studies.

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare no competing interests.

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