



International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE NUMBERS AND CHRONICLES OF MULTIPLE MYELOMA
INCIDENCE MORTALITY AND PREVALENCE ACROSS REGIONS:
REVIEW OF THE LITERATURE WITH SEER DATA ANALYSIS

DOI [https://doi.org/10.31435/ijitss.4\(48\).2025.4258](https://doi.org/10.31435/ijitss.4(48).2025.4258)

RECEIVED 21 October 2025

ACCEPTED 14 December 2025

PUBLISHED 24 December 2025

LICENSE



The article is licensed under a **Creative Commons Attribution 4.0 International License**.

© The author(s) 2025.

This article is published as open access under the Creative Commons Attribution 4.0 International License (CC BY 4.0), allowing the author to retain copyright. The CC BY 4.0 License permits the content to be copied, adapted, displayed, distributed, republished, or reused for any purpose, including adaptation and commercial use, as long as proper attribution is provided.

NUMBERS AND CHRONICLES OF MULTIPLE MYELOMA INCIDENCE MORTALITY AND PREVALENCE ACROSS REGIONS: REVIEW OF THE LITERATURE WITH SEER DATA ANALYSIS

Mateusz Kęska (Corresponding Author, Email: matteuszeska@gmail.com)
5 Military Clinical Hospital with Polyclinic SPZOZ, Kraków, Poland
ORCID ID: 0000-0003-0712-7613

Michael Platschek
Blessed Marta Wiecka Hospital in Bochnia, Bochnia, Poland
ORCID ID: 0009-0008-9085-4531

Anna Barbara Tuleja
University Hospital in Wrocław (USK), Wrocław, Poland
ORCID ID: 0009-0003-9185-9493

Michał Drabik
5 Military Clinical Hospital with Polyclinic SPZOZ, Kraków, Poland
ORCID ID: 0009-0004-0198-4926

Julia Kosmulska
University Hospital in Wrocław (USK), Wrocław, Poland
ORCID ID: 0009-0000-8770-3793

Klaudia Dybalska
Brzeziny Specialist Hospital, Brzeziny, Poland
ORCID ID: 0009-0006-9900-0167

Maksym Sikora
Hospital of the Order of the Brothers Hospitallers of St. John of God in Kraków, Kraków, Poland
ORCID ID: 0009-0008-4495-7732

Sylwia Wiktoria Kolano
Independent Public Healthcare Institution of the Ministry of the Interior and Administration in Kraków,
Kraków, Poland
ORCID ID: 0009-0000-1180-1135

Jakub Nowak
Independent Public Healthcare Institution of the Ministry of the Interior and Administration in Kraków,
Kraków, Poland
ORCID ID: 0009-0003-7097-0635

Karol Józef Szkarłat
Medical University of Silesia in Katowice, Faculty of Medical Sciences in Katowice, Katowice, Poland
ORCID ID: 0009-0004-2889-8382

Illia Lastovetskyi
5 Military Clinical Hospital with Polyclinic SPZOZ, Kraków, Poland
ORCID ID: 0000-0003-1520-3241

ABSTRACT

Global and regional data reveal a sustained rise in incident and prevalent multiple myeloma with crude deaths increasing through population ageing, while age standardized mortality has remained broadly stable. Men are affected more than women and ancestry strongly shapes risk, with the highest incidence and mortality in Black populations and the lowest in Asian and Pacific Islander groups. East Asia shows the fastest proportional growth, whereas the absolute burden is greatest in high income regions. Presentation remains dominated by organ damage and advanced stage in several Middle Eastern and African cohorts. Survival has improved across periods and age groups with wider use of proteasome inhibitors, immunomodulatory agents, autologous transplantation and anti CD38 antibodies, though early mortality persists in the oldest patients and outcomes vary by site and capacity of care. High body mass index is the only quantified modifiable contributor in global attribution analyses. Survivorship includes a measurable risk of second primary malignancies, enriched for hematologic cancers. Forecasts to mid century attribute most growth to demographics and anticipate increases in cases and deaths despite stable or falling age standardized rates in some settings. Treated epidemiology is shifting toward earlier use of lenalidomide and anti CD38 therapy, rising double refractoriness, and attrition between lines, highlighting the need for timely diagnosis, infection and renal management, equitable access, and planning for advanced immunotherapies.

KEYWORDS

Multiple Myeloma, Epidemiology, Incidence, Mortality, Survival Analysis, Health Status Disparities

CITATION

Mateusz Kęska, Michael Platschek, Anna Barbara Tuleja, Michał Drabik, Julia Kosmulska, Klaudia Dybalska, Maksym Sikora, Sylwia Wiktoria Kolano, Jakub Nowak, Karol Józef Szkarłat, Illia Lastovetskyi (2025) Numbers and Chronicles of Multiple Myeloma Incidence, Mortality, and Prevalence Across Regions: Review of the Literature With SEER Data Analysis. *International Journal of Innovative Technologies in Social Science*. 4(48). doi: 10.31435/ijitss.4(48).2025.4258

COPYRIGHT

© The author(s) 2025. This article is published as open access under the **Creative Commons Attribution 4.0 International License (CC BY 4.0)**, allowing the author to retain copyright. The CC BY 4.0 License permits the content to be copied, adapted, displayed, distributed, republished, or reused for any purpose, including adaptation and commercial use, as long as proper attribution is provided.

Introduction

Multiple myeloma (MM) is a clonal plasma-cell malignancy characterized by marrow infiltration and the secretion of monoclonal immunoglobulins that drive the classic CRAB (hyperCalcemia, Renal impairment, Anemia, and Bone disease) features and a broad spectrum of infection-related complications (Cowan et al., 2022; Dimopoulos et al., 2023; Raje et al., 2022; Rajkumar & Kumar, 2016). MM predominantly affects older adults (median diagnosis in the mid-to-late 60s) with a slight male excess and marked variation by ancestry, including higher incidence among Black populations that is linked to the epidemiology of precursor states such as monoclonal gammopathy of undetermined significance (MGUS) (Cowan et al., 2022; Rajkumar & Kumar, 2016). Although still incurable for most, therapeutic advances over the last two decades have transformed the natural history of MM, extending survival and reshaping the treated epidemiology of the disease (Cowan et al., 2022; Hungria et al., 2024; Lin et al., 2024; Rajkumar & Kumar, 2016).

From a clinical standpoint, MM today is staged using the Revised International Staging System (R-ISS), which integrates tumor burden (β 2-microglobulin, albumin) with disease biology (lactate dehydrogenase and high-risk cytogenetics including t(4;14), del(17p), t(14;16)) to stratify prognosis and guide initial management (Cowan et al., 2022; Rajkumar & Kumar, 2016). Two organ-threatening complications are particularly consequential for population outcomes. First, infection remains the leading cause of early morbidity and mortality because of disease-related immunoparesis and treatment-induced immunosuppression; consensus guidance emphasizes vaccination, time-limited antimicrobial prophylaxis, infection-control measures, and immunoglobulin replacement in selected patients (Raje et al., 2022). Second, renal impairment, present in up to half of patients at diagnosis and occasionally requiring dialysis is both a marker of aggressive biology and a modifiable driver of early death; IMWG recommendations prioritize rapid institution of bortezomib-based therapy and supportive measures, with renal response incorporated into outcome assessment (Dimopoulos et al., 2023).

The therapeutic landscape continues to diversify, with direct epidemiologic consequences (e.g., rising prevalence through survival gains and changing patterns of refractoriness). Standard first-line therapy for transplant-eligible patients typically combines a proteasome inhibitor, an immunomodulatory agent, and dexamethasone, followed by autologous transplantation and maintenance; in non-transplant candidates, triplet or quadruplet regimens are now routine (Cowan et al., 2022; Rajkumar & Kumar, 2016). In the relapsed setting, randomized trials and meta-analyses highlight two additional themes with public-health relevance. First, deeper responses matter at the population level: minimal residual disease (MRD) negativity is strongly associated with progression-free survival (PFS) and is “reasonably likely” to predict clinical benefit, supporting its use as an intermediate endpoint that can accelerate availability of effective therapies (Landgren et al., 2024). Second, novel immune-based strategies are moving earlier in care. Anti-BCMA approaches—including antibody–drug conjugates and CAR T-cell therapy—have produced high response rates and prolonged PFS in refractory disease, with phase 3 data and consensus guidance now informing patient selection, toxicity mitigation, and real-world implementation (Hungria et al., 2024; Lin et al., 2024). In parallel, targets beyond BCMA such as GPRC5D have entered the clinic, broadening options for multi-refractory patients and potentially altering future patterns of treatment exposure and resistance (Rodriguez-Otero et al., 2024).

Notwithstanding these advances, MM remains biologically heterogeneous and adept at immune escape. Genomic subtypes (e.g., hyperdiploid vs. IgH translocation), secondary events (MYC dysregulation, MAPK and NF- κ B pathway lesions), and a profoundly immunosuppressive marrow microenvironment all contribute to clonal persistence, drug resistance, and relapse—key determinants of long-term population burden (Wang et al., 2024). These disease-inherent and host-environmental factors intersect with health-system determinants (diagnostic capacity, access to novel agents, supportive care), shaping cross-regional differences in incidence, survival, and cause-specific mortality.

Against this backdrop, an updated epidemiologic synthesis is needed to contextualize global and regional trends, quantify demographic and clinical patterns at diagnosis, describe outcome disparities in the era of modern therapy, and highlight how evolving treatments (triplets/quadruplets, MRD-driven strategies, BCMA and GPRC5D-directed immunotherapies) are likely to influence the future burden of MM. The present review integrates contemporary clinical knowledge with population-scale observations to map where MM epidemiology stands today and where it is heading, while anchoring interpretation in the realities of infection prevention, renal management, and immune-escape biology that continue to shape outcomes across health systems.

Multiple Myeloma Epidemiology

Multiple myeloma is a globally expanding malignancy. Contemporary analyses that integrate Global Burden of Disease and cancer registry data converge on a sustained rise in incident cases, prevalent cases and disability over the last three decades, with only modest change in age standardized mortality at the global level. In 2021 there were about 148,700 incident cases, 394,500 prevalent cases and 116,400 deaths worldwide, with the age standardized mortality rate near 1.37 per 100,000, and all indicators except mortality showed clear upward trends since 1990 (Hou et al., 2025; L. Zhou et al., 2021; P. Zhou et al., 2025; Zhuge et al., 2025). The absolute burden is highest in high income regions, while the fastest relative growth has occurred in middle social development settings and particularly in East Asia, where increases in age standardized incidence, prevalence and mortality have been among the most pronounced since 1990 (Hou et al., 2025; L. Zhou et al., 2021; P. Zhou et al., 2025; Zhuge et al., 2025). Forecasting studies that decompose drivers attribute most future growth to population expansion and ageing rather than to unfavorable epidemiologic change, and they predict continued increases in cases and deaths through 2040 to 2050, with age standardized rates remaining stable or slowly declining in many settings (Hou et al., 2025; Mousavi et al., 2025; L. Zhou et al., 2021; P. Zhou et al., 2025; Zhuge et al., 2025).

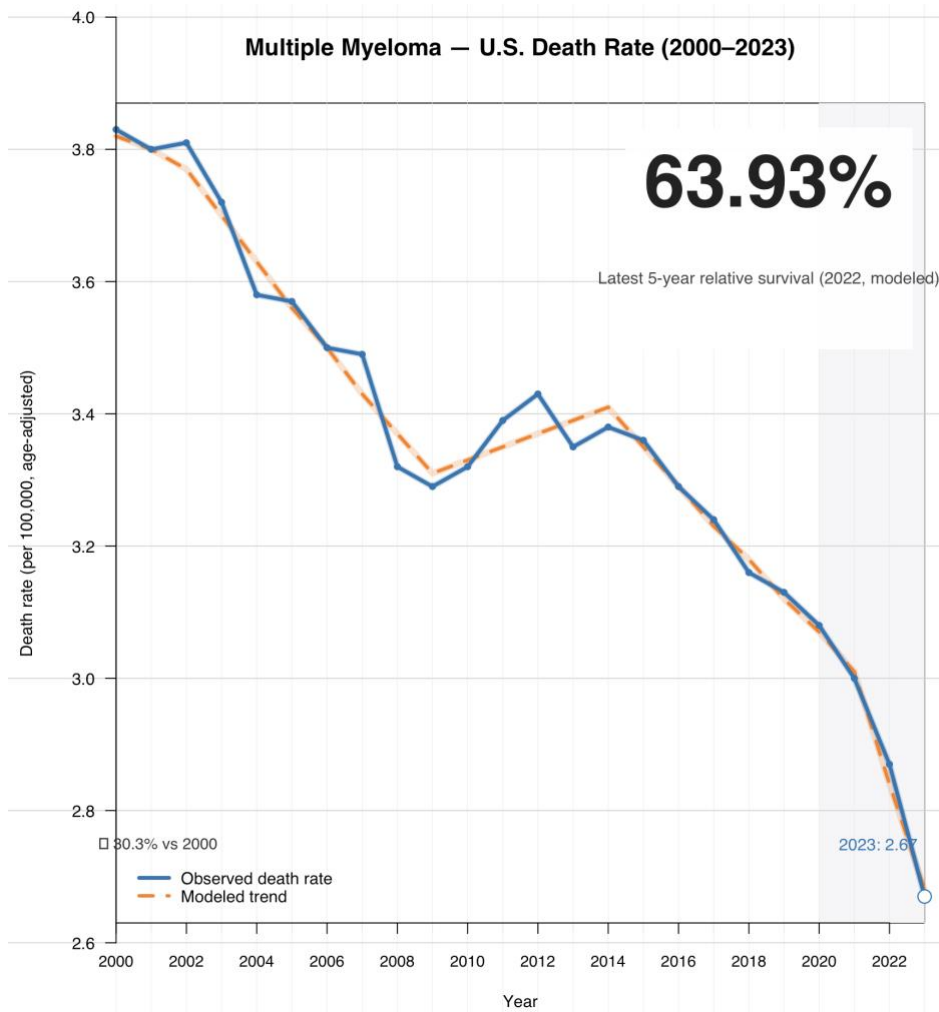


Fig. 1. Multiple Myeloma related mortality. Source: SEER & CDC (<https://seer.cancer.gov/statfacts/> last accessed on October 2025)

When analyzing the age and sex patterns, men have higher incidence, prevalence and mortality than women, and this gradient is evident in global and regional data as well as in country specific studies in Asia, the Americas and Europe (Hou et al., 2025; Mousavi et al., 2025; Oliveira et al., 2024; Park et al., 2024; L. Zhou et al., 2021; Zhu et al., 2024; Zhuge et al., 2025). The disease is concentrated in older adults, with incidence and mortality peaking around ages 70 to 74 years in global series and with age specific incidence rising most steeply in the 60 to 69 and 70 years and older strata in national data from South Korea (Hou et al., 2025; Park et al., 2024; L. Zhou et al., 2021; Zhuge et al., 2025). Very early onset disease is uncommon. In a large French Belgian cohort, diagnosis before age 40 represented fewer than two percent of cases and, despite generally favorable baseline International Staging System distribution, survival remained inferior to the age matched general population, with bone disease, International Staging System stage 3 and high risk cytogenetics independently adverse (Caulier et al., 2021).

Marked geographic heterogeneity reflects both demography and health system capacity. Western Europe, high income North America and Australasia report the highest age standardized incidence and prevalence, while Central Africa and parts of South Asia exhibit the lowest recorded rates, acknowledging under ascertainment in several low resource countries (Hou et al., 2025; L. Zhou et al., 2021; Zhuge et al., 2025). East Asia has experienced the fastest proportional rise across multiple indicators since 1990, and pan Asian synthesis further documents subregional variation with the highest age standardized incidence and mortality currently in Western Asia, a male predominance, and mortality to incidence ratios that are highest in South Eastern and South Central Asia, indicating poorer outcomes in those subregions (Hou et al., 2025; Mousavi et al., 2025; Zhuge et al., 2025). Country level outliers in Asia include Israel and the Gaza Strip and West Bank with leading sex specific age standardized incidence and mortality, and several high development

settings in East and Southeast Asia with relatively high five year prevalence (Mousavi et al., 2025). In the Middle East and Africa, collated national and institutional series show rising incidence and late stage at presentation, with limited diagnostic capacity and access to novel agents repeatedly cited as contributors to outcome disparities; across cohorts IgG myeloma predominates and advanced International Staging System stage at diagnosis is frequent (Mattar et al., 2024). A Qatar population based program found incident rates increasing between 2007 and 2021 with a median age of 57 years, pronounced skeletal morbidity at diagnosis and frequent anemia, renal impairment and hypercalcemia; overall survival approached 103 months, with hypercalcemia independently associated with higher mortality and autologous transplantation associated with longer survival (Elsabah et al., 2024). In Brazil, three decades of national data reveal increasing age standardized incidence, prevalence and mortality in both sexes, with steeper growth in low and low middle development areas and greater absolute burden in high development states (Oliveira et al., 2024). In Puerto Rico, incidence increased in both men and women across age groups from 2001 to 2019, while mortality did not decline as it did among several comparator racial and ethnic groups in the United States; five year overall survival for Puerto Rican men was the lowest among the male strata examined (Castañeda-Avila et al., 2024). United States analyses demonstrate that age adjusted incidence has increased while age adjusted mortality has declined since 1999, yet large disparities persist, with non Hispanic Black populations having the highest incidence and mortality and Asian American and Pacific Islander populations the lowest; disparities are modulated by geography and urbanicity, with the highest mortality for non Hispanic Black individuals in the South and in small metropolitan areas (Zhu et al., 2024).

Risk attribution analyses identify high body mass index as the only quantified modifiable risk factor within the Global Burden of Disease framework. The proportion of deaths and disability attributable to high body mass index has increased since 1990 and is highest in high income North America, with generally higher attributable fractions in women than in men in several regions (L. Zhou et al., 2021; P. Zhou et al., 2025; Zhuge et al., 2025). Although this factor explains a minority of the burden, its sustained rise underscores the intersection between population level metabolic health and myeloma risk (L. Zhou et al., 2021; P. Zhou et al., 2025; Zhuge et al., 2025).

Projections converge on continued growth in absolute burden. Modeling studies foresee increases in incident cases, prevalent cases and deaths through 2040 to 2050 across most regions, with growth largely explained by demographic forces. East Asia and several middle development regions are expected to contribute disproportionately to new cases, whereas some high income regions may experience stable or decreasing age standardized incidence and mortality due to improvements in early diagnosis and treatment (Hou et al., 2025; Mousavi et al., 2025; L. Zhou et al., 2021; P. Zhou et al., 2025; Zhuge et al., 2025). In Italy, a health system level model that tracks patients by line of therapy estimates an expanding treated population and a shift of the prevalent pool toward earlier lines because of wider use of lenalidomide and anti CD38 monoclonal antibodies in the front line. The same model anticipates a rapid rise in lenalidomide and anti CD38 refractoriness, including a growing double refractory population, and documents substantial attrition between successive lines of therapy that may shape treated epidemiology over time (Mina et al., 2025).

Interesting aspect is also clinical presentation at diagnosis that remains dominated by symptomatic end organ damage. Across Middle Eastern and African cohorts, International Staging System stage 2 or 3 is common at diagnosis, with IgG isotype the most frequent and with typical cytogenetic lesions including deletion 13q, translocation t(11;14), translocation t(4;14) and deletion 17p as reported across multiple single center series (Mattar et al., 2024). The Qatar registry confirms high frequencies of osteolytic disease, anemia and renal impairment, and documents extramedullary plasmacytomas in more than a quarter of patients at presentation (Elsabah et al., 2024). In very young adults, bone disease is also frequent at diagnosis and high risk cytogenetics, including t(4;14) and deletion 17p as well as 1q gains and 1p deletions, portend inferior progression free and overall survival despite intensive therapy (Caulier et al., 2021). Limited biomarker work in Middle Eastern and African cohorts has described higher circulating interleukin 6, interleukin 10, B cell activating factor and beta 2 microglobulin in patients versus controls, and has suggested that decreases in the serine threonine phosphatase inhibitor CIP2A after bortezomib based therapy correlate with better responses, observations that require validation in larger populations but that illustrate the heterogeneity of immune and signaling milieus across regions (Mattar et al., 2024).

Age standardized mortality has been largely stable at the global level since 1990, with declines in some high income regions, while crude mortality rises with ageing populations. National data from South Korea showed increasing crude mortality with stable age standardized mortality, and improving one year and three year survival during an era of rapid adoption of proteasome inhibitor and immunomodulatory agent

combinations as first line therapy (Park et al., 2024; Zhuge et al., 2025). In the United States, mortality has declined overall but remains highest among non Hispanic Black populations, highlighting the need for targeted strategies in high risk communities (Zhu et al., 2024). In the Middle East and Africa, later stage at diagnosis and limited access to diagnostics and novel agents likely contribute to inferior outcomes, aligning with the higher mortality to incidence ratios observed in several Asian subregions with constrained resources (Mattar et al., 2024; Mousavi et al., 2025).

Table 1. Selected studies allowing meaningful cross-region comparisons. Metrics and abbreviations are defined below. Note: Values use the authors' age-standardization where specified.

Ref	Geography/ Scope	Data Source / Period / N	Core epidemiology metrics	Trends / Projections	Disparities / SDI / Geography Survival conclusions
(Zhuge et al., 2025)	Global / Regional / National (GBD 2021) harmonized age-standardized rates.	GBD 2021; 1990–2021; 204 countries; ARIMA projections	Inc 148.76k (ASIR 1.74/100k) Prev 394.48k (ASPR 4.55/100k) Deaths 116.36k (ASMR 1.37/100k) DALYs 2.60M (ASDR 30/100k).	1990–2021: ASIR +0.48 (EAPC); ASPR +1.24; ASMR +0.09 (ns); ASDR +0.06 (ns). Next 15y: incidence & prevalence rise; mortality & DALYs ~flat.	ASIR highest in Western Europe (4.30/100k), lowest Central Africa (0.35/100k); fastest growth East Asia. High BMI PAF 7.96% globally (highest in High-income N. America ~11.5%).
(Mousavi et al., 2025)	Asia (continental, subregional & national) Regionally comparable age-standardized rates within Asia.	GLOBOCAN 2020; projections to 2040	2020 — ASIR 1.10/100k; ASMR 0.86/100k; 5-yr prevalence 3.20/100k; MIR 0.79. Eastern Asia 5-yr prev 4.80/100k; Western Asia ASIR 2.10, ASMR 1.60/100k.	To 2040 (no rate change assumed): incident +67.5%; deaths +73.8%.	MIR highest in SE Asia (0.88) & South-Central Asia (0.85). HDI positively correlated with ASIR/ASMR and negatively with MIR.
(Zhu et al., 2024)	United States (national) National registry-based, subgroup-comparable rates.	SEER-12 incidence (delay-adjusted) & CDC WONDER mortality; 1999–2020; 53,527 cases; 252,005 deaths	Age-adjusted incidence ↑; mortality ↓ overall. Highest incidence & mortality in NH Black; lowest in AAPI/AIAN.	1999–2020: incidence increased; mortality declined (age-adjusted).	Mortality highest in the South for NH Black & AIAN; among NH Black, highest in small metro areas (MRR 2.59).
(Park et al., 2024)	South Korea (nationwide adults ≥20y) Claims-based national study with age-standardized incidence.	NHIS-NHID + death certificates; 2010–2018; incident N=10,835	ASIR 2.42→2.71/100k (APC 1.86%/yr); crude incidence 2.42→3.49/100k; ASMR stable; prevalence doubled (3,487→6,947).	Significant rise in ages 60–69 and ≥70; women APC 2.70% vs men 1.13% (ns).	Median OS 3.36y; 1-yr survival 65.3%→76.2%; 3-yr 45.7%→50.8% (larger gains in women).
(Oliveira et al., 2024)	Brazil (national + 27 states)	GBD 2019; 1990–2019; age-standardized (≥40y)	Inc/100k — men 4.40→6.78, women 3.97→5.50. Prev/100k — men 8.45→15.10, women 8.58→14.12. Mort/100k — men 3.93→5.68, women 3.42→4.38. DALYs/100k — men 96.18→131.18, women 82.38→99.22.	Upward in all SDI quintiles; faster growth in low/low-middle SDI areas.	State heterogeneity: steepest incidence rise in Bahia (men); lowest in Distrito Federal (men).
(Castañeda-Avila et al., 2024)	Puerto Rico vs U.S. SEER (comparison) Comparable population-based rates for territory vs mainland.	PR Central Cancer Registry & SEER; trends 2001–2019; rates 2015–2019	Males higher incidence & mortality than females. PR males <65: incidence higher than NHW & U.S. Hispanics. ≥65 mortality in PR lower than NHW, NHB, U.S. Hispanics, & U.S. overall.	PR incidence APC — males <65 +4.3; ≥65 +3.1; females <65 +6.3; ≥65 +2.6. Mortality in PR ~stable; U.S. subgroups decreased.	PR males 5-yr OS — <65: 54.6% (95% CI 47.2–61.5); ≥65: 34.5% (95% CI 29.2–39.9).

Abbrev: ASIR = age-standardized incidence rate (per 100,000); ASMR = age-standardized mortality rate; ASPR = age-standardized prevalence rate; ASDR = age-standardized DALY rate; DALYs = disability-adjusted life years; MIR = mortality-to-incidence ratio; HDI = Human Development Index; PAF = population-attributable fraction; APC/EAPC = (estimated) annual percent change; NHB/NHW = non-Hispanic Black/White; AAPI = Asian American & Pacific Islander; AIAN = American Indian & Alaska Native; PR = Puerto Rico; SEER = Surveillance, Epidemiology, and End Results; GBD = Global Burden of Disease; ARIMA = AutoRegressive Integrated Moving Average; OS = overall survival; ns = not significant.

Second primary malignancies contribute a measurable survivorship burden. In a Surveillance, Epidemiology, and End Results cohort of more than sixty thousand patients with myeloma, about six percent developed a second primary malignancy, most commonly solid tumors such as prostate cancer, while hematologic second primaries were enriched relative to the general population, including acute leukemias and non Hodgkin lymphoma. Standardized incidence ratios were highest for malignancies of bone and joints and for several leukemic entities, while several common solid tumors had lower than expected incidence. Older age and higher sequence number of cancers were associated with worse survival in patients with second primaries, whereas longer latency from myeloma diagnosis was protective (Dong et al., 2025).

Importantly treatment era changes are now discernible in real world treated epidemiology. In France between 2017 and 2022, use of carfilzomib based triplets increased in later lines and adoption of once weekly dosing expanded across regimens without clear detriment to overall response or overall survival at the population level, including in older adults. These shifts mirror broader uptake of anti CD38 monoclonal antibodies and immunomodulatory drug proteasome inhibitor triplets and help explain increasing survival in many high resource settings (Hulin et al., 2025). In Italy, modeled increases in first line use and the resultant rise in double refractoriness among relapsed patients anticipate evolving needs for next generation therapies and offer a framework for planning care delivery and resource allocation (Mina et al., 2025).

Importantly in Asia, the continent accounts for more than one third of global incident cases and is projected to see about two thirds growth in cases and nearly three quarters growth in deaths by 2040 if rates do not change, with clear correlations between national development indicators and incidence and mortality and an inverse correlation between development and the mortality to incidence ratio (Mousavi et al., 2025). In Brazil, increasing incidence, prevalence and mortality have occurred in every state since 1990, with steeper increases in lower development quintiles and higher absolute rates in higher development quintiles, underscoring both demographic and health system influences (Oliveira et al., 2024). In Puerto Rico, rising incidence coupled with less favorable survival in men compared with continental comparators points to the importance of context specific access and care pathways (Castañeda-Avila et al., 2024). In the Middle East and Africa, GLOBOCAN based summaries and institutional series point to rising burden with substantial between country variation in incidence, prevalence and mortality, a male predominance in many cohorts, frequent late stage diagnosis and cytogenetic profiles that include common high risk lesions, together with documented access limitations that likely worsen outcomes (Mattar et al., 2024).

Discussion & Conclusions:

The historical record from classic population cohorts already foreshadowed the epidemiology we see today. Scandinavian and United States registries in the late twentieth century showed a stable to slowly rising incidence in high income settings with a clear male excess and a twofold higher burden among people of African ancestry, while virtually all cases occurred after midlife (Alexander et al., 2007; Kristinsson et al., 2007; Kyle & Rajkumar, 2009; Nau & Lewis, 2008; Rajkumar et al., 2002). Sweden's national series, nearly fifteen thousand patients diagnosed from the early nineteen seventies through the early two thousands, documented small but steady gains in one year and five year relative survival, driven largely by younger patients, and revealed that where patients were diagnosed mattered, with non university hospitals associated with higher excess mortality. That single system signal reminds us that survival is not only biology but also organization of care (Kristinsson et al., 2007).

Two additional threads from the historical literature deserve emphasis because they still shape the present. First, structured therapy improves outcomes at a population level. The Finnish experiment comparing a trial region with protocol driven care to a reference region with usual practice demonstrated better five year survival in the protocol region, an effect that emerged after the early high risk period. This is an early proof that standardization and access can bend survival curves for an entire catchment area (Karjalainen & Palva, 1989). Second, the first wave of novel agents changed the life course of myeloma. Across reviews and national

cohorts, the introduction of high dose therapy with autologous transplant followed by thalidomide, bortezomib, and lenalidomide extended median survival by about one to one and a half years in unselected practice, with the largest absolute benefit in patients sixty to seventy years of age, and more modest gains in the oldest groups where early death remained common (Kastritis et al., 2009; Kyle & Rajkumar, 2009; Pulte et al., 2011). The Greek Myeloma Study Group quantified this shift with longer overall survival, higher response rates, and preserved prognostic separation by the International Staging System even after novel agents entered first line care (Kastritis et al., 2009). Period analyses from SEER confirmed that the survival improvement after the turn of the century reached every age group, including patients seventy five years and older, and that women accrued slightly larger gains than men (Pulte et al., 2011).

Risk architecture described in the same era also anticipated present trends. The epidemiologic review by Adami and colleagues summarized the higher prevalence of monoclonal gammopathy in older adults and in African American populations with a steady one percent annual transition risk, and it highlighted adiposity as a credible modifiable determinant with relative risks around one and a half to two. In contrast, most occupational and environmental candidates lacked consistent dose response signals. These observations align with today's patterns of rising burden in aging and metabolically unhealthy populations and the persistence of striking racial and sex differences in incidence and mortality (Alexander et al., 2007). Contemporary reviews from that period also remind us that a sizable minority of patients present without symptoms, which has practical implications for timely detection through routine laboratory testing in primary care (Nau & Lewis, 2008).

Set against current evidence summarized in this review, the older studies provide the baseline from which modern gains should be judged. Incidence in high income countries has climbed gently, survival has improved markedly and more evenly across ages, and the early lead of younger and trial treated patients has gradually propagated to the general population. Yet the Swedish finding on hospital type and the United States pattern of sex and race differences already warned that delivery of care and social location would moderate progress. Those signals remain visible today. The task ahead is therefore twofold. Sustain biologic momentum with deeper first responses and effective salvage while closing the implementation gap that historical cohorts first exposed.

Conclusions

Multiple Myeloma concentrates in older adults with a male excess and marked ancestry related differences including the highest incidence and mortality in non Hispanic Black populations and the lowest in Asian American and Pacific Islander populations with additional modulation by geography and urbanicity. Clinical presentation remains dominated by symptomatic organ damage and in several Middle Eastern and African cohorts advanced International Staging System stage and high risk cytogenetics are frequent at diagnosis. Survival has improved across eras and age groups in registry and national datasets coincident with wider use of autologous transplantation proteasome inhibitors immunomodulatory agents and anti CD38 antibodies although early mortality in the oldest patients persists and health system factors such as site of care influence outcomes. High body mass index is the only quantified modifiable risk factor in global attribution analyses and its contribution has risen since 1990. Second primary malignancies occur in roughly six percent of patients with enrichment for hematologic cancers and worse survival associated with older age and multiple primaries. Regional summaries show rising incidence and heterogeneous outcomes in the Middle East and Africa increasing incidence prevalence and mortality across all Brazilian states with steeper relative growth in lower development areas and rising incidence in Puerto Rico where male survival lags several United States comparators. Forecasting studies attribute most future growth to ageing and population expansion and project continued increases in cases and deaths through 2040 to 2050 while some high income settings may see stable or declining age standardized rates.

REFERENCES

1. Alexander, D. D., Mink, P. J., Adami, H. O., Cole, P., Mandel, J. S., Oken, M. M., & Trichopoulos, D. (2007). Multiple myeloma: A review of the epidemiologic literature. *International Journal of Cancer*, 120(SUPPL. 14), 40–61. <https://doi.org/10.1002/ijc.22718>
2. Castañeda-Avila, M. A., Suárez-Ramos, T., Torres-Cintrón, C. R., Epstein, M. M., Gierbolini-Bermúdez, A., Tortolero-Luna, G., & Ortiz-Ortiz, K. J. (2024). Multiple myeloma incidence, mortality, and survival differences at the intersection of sex, age, and race/ethnicity: A comparison between Puerto Rico and the United States SEER population. *Cancer Epidemiology*, 89(January). <https://doi.org/10.1016/j.canep.2024.102537>
3. Caulier, A., Roussel, M., Morel, P., Lombion, N., Branco, B., Galtier, J., Hulin, C., Perrot, A., Richez, V., Michaud, A. V., Touzeau, C., Doyen, C., Mariette, C., Caillot, D., Harel, S., Lenain, P., Ivanoff, S., Fontan, J., Stoppa, A. M., ... Royer, B. (2021). Epidemiological landscape of young patients with multiple myeloma diagnosed before 40 years of age: the French experience. *Blood*, 138(25), 2686–2695. <https://doi.org/10.1182/blood.2021011285>
4. Cowan, A. J., Green, D. J., Kwok, M., Lee, S., Coffey, D. G., Holmberg, L. A., Tuazon, S., Gopal, A. K., & Libby, E. N. (2022). Diagnosis and Management of Multiple Myeloma: A Review. *Jama*, 327(5), 464–477. <https://doi.org/10.1001/jama.2022.0003>
5. Dimopoulos, M. A., Merlini, G., Bridoux, F., Leung, N., Mikhael, J., Harrison, S. J., Kastiris, E., Garderet, L., Gozzetti, A., van de Donk, N. W. C. J., Weisel, K. C., Badros, A. Z., Beksac, M., Hillengass, J., Mohty, M., Ho, P. J., Ntanasis-Stathopoulos, I., Mateos, M. V., Richardson, P., ... Terpos, E. (2023). Management of multiple myeloma-related renal impairment: recommendations from the International Myeloma Working Group. *The Lancet Oncology*, 24(7), e293–e311. [https://doi.org/10.1016/S1470-2045\(23\)00223-1](https://doi.org/10.1016/S1470-2045(23)00223-1)
6. Dong, N., Ye, B., & Liu, S. (2025). Investigating additional malignancy rates and prognostic factors in multiple myeloma patients: a Surveillance, Epidemiology, and End Results (SEER) database retrospective cohort study. *Translational Cancer Research*, 14(4), 2192–2206. <https://doi.org/10.21037/tcr-24-1721>
7. Elsabab, H., El Omri, H., Habas, E., Taha, R. Y., ElKourashy, S. A., Ibrahim, F., Nashwan, A. J., Kassem, N., Ojha, L., Singh, R., Ghasoub, R., & El Omri, A. (2024). Real world evidence of epidemiological trends, clinical presentation, and prognostic outcomes of multiple myeloma (2007-2021). *Frontiers in Medicine*, 11(February). <https://doi.org/10.3389/fmed.2024.1338552>
8. Hou, Q., Li, X., Ma, H., Fu, D., & Liao, A. (2025). A systematic epidemiological trends analysis study in global burden of multiple myeloma and 29 years forecast. *Scientific Reports*, 15(1), 1–12. <https://doi.org/10.1038/s41598-024-83630-x>
9. Hulin, C., Belhadj Merzoug, K., Royer, B., Caillot, D., Bobin, A., Macro, M., Karlin, L., Mohty, M., Frenzel, L., Perrot, A., Vincent, L., Dib, M., Piocell, F. O., Benramdane, R., Calmettes, C., Chalopin, T., Garlantézec, R., Désaméricq, G., Mechiche, H., & Decaux, O. (2025). Real-World Utilization of Carfilzomib (Once or Twice Weekly) Initiated in Patients After a First Relapse Between 2017 and 2022 in France: An Analysis From a Large-Scale Epidemiology of Multiple MYeloma (EmmY) Cohort. *Clinical Lymphoma, Myeloma and Leukemia*. <https://doi.org/10.1016/j.clml.2025.08.002>
10. Hungria, V., Robak, P., Hus, M., Zherebtsova, V., Ward, C., Ho, P. J., Ribas de Almeida, A. C., Hajek, R., Kim, K., Grosicki, S., Sia, H., Bryant, A., Pitombeira de Lacerda, M., Aparecida Martinez, G., Sureda Balarí, A. M., Sandhu, I., Cerchione, C., Ganly, P., Dimopoulos, M., ... Mateos, M.-V. (2024). Belantamab Mafodotin, Bortezomib, and Dexamethasone for Multiple Myeloma. *New England Journal of Medicine*, 391(5), 393–407. <https://doi.org/10.1056/nejmoa2405090>
11. Karjalainen, S., & Palva, I. (1989). Do treatment protocols improve end results? A study of survival of patients with multiple myeloma in Finland. *British Medical Journal*, 299(6707), 1069–1072. <https://doi.org/10.1136/bmj.299.6707.1069>
12. Kastiris, E., Zervas, K., Symeonidis, A., Terpos, E., Delimbassi, S., Anagnostopoulos, N., Michali, E., Zomas, A., Katodritou, E., Gika, D., Pouli, A., Christoulas, D., Roussou, M., Kartasis, Z., Economopoulos, T., & Dimopoulos, M. A. (2009). Improved survival of patients with multiple myeloma after the introduction of novel agents and the applicability of the International Staging System (ISS): An analysis of the Greek Myeloma Study Group (GMSG). *Leukemia*, 23(6), 1152–1157. <https://doi.org/10.1038/leu.2008.402>
13. Kristinsson, S. Y., Landgren, O., Dickman, P. W., Derolf, Å. R., & Björkholm, M. (2007). Patterns of survival in multiple myeloma: A population-based study of patients diagnosed in Sweden from 1973 to 2003. *Journal of Clinical Oncology*, 25(15), 1993–1999. <https://doi.org/10.1200/JCO.2006.09.0100>
14. Kyle, R. A., & Rajkumar, S. V. (2009). Treatment of multiple myeloma: a comprehensive review. *Clinical Lymphoma & Myeloma*, 9(4), 278–288. <https://doi.org/10.3816/CLM.2009.n.056>
15. Landgren, O., Prior, T. J., Masterson, T., Heuck, C., Bueno, O. F., Dash, A. B., Einsele, H., Goldschmidt, H., Knop, S., Li, C., Mellqvist, U. H., McFadden, I., Oprea, C., Ross, J. A., Talpes, M., Hydren, J. R., Ahlstrom, J. M., Kazandjian, D., Weinhold, N., ... Devlin, S. M. (2024). EVIDENCE meta-analysis: evaluating minimal residual disease as an intermediate clinical end point for multiple myeloma. *Blood*, 144(4), 359–367. <https://doi.org/10.1182/blood.2024024371>

16. Lin, Y., Qiu, L., Usmani, S., Joo, C. W., Costa, L., Derman, B., Du, J., Einsele, H., Fernandez de Larrea, C., Hajek, R., Ho, P. J., Kastritis, E., Martinez-Lopez, J., Mateos, M. V., Mikhael, J., Moreau, P., Nagarajan, C., Nooka, A., O'Dwyer, M., ... Martin, T. (2024). Consensus guidelines and recommendations for the management and response assessment of chimeric antigen receptor T-cell therapy in clinical practice for relapsed and refractory multiple myeloma: a report from the International Myeloma Working Group Immuno. *The Lancet Oncology*, 25(8), e374–e387. [https://doi.org/10.1016/S1470-2045\(24\)00094-9](https://doi.org/10.1016/S1470-2045(24)00094-9)
17. Mattar, M., Bazarbachi, A., Abduljalil, O., Francis, B., Alam, A., & Blunk, V. (2024). Epidemiology, Treatment Trends, and Outcomes of Multiple Myeloma in the Middle East and Africa: A Systematic Review. *Clinical Hematology International*, 6(1), 67–83. <https://doi.org/10.46989/001c.92555>
18. Mina, R., Mangiacavalli, S., Rossini, B., Ghetti, G., Pellizzaro, S., Iannello, F., & Bellucci, S. (2025). Multiple Myeloma in Italy: An Epidemiological Model by Treatment Line and Refractoriness Status. *Clinical Lymphoma, Myeloma and Leukemia*, 25(5), e253–e261. <https://doi.org/10.1016/j.clml.2024.12.012>
19. Mousavi, S. E., Ilaghi, M., Aflatoonian, S., & Nejadghaderi, S. A. (2025). Epidemiology, socioeconomic correlates, and trend projections of multiple myeloma in Asia over 2020–2040. *Heliyon*, 11(9), e43325. <https://doi.org/10.1016/j.heliyon.2025.e43325>
20. Nau, K. C., & Lewis, W. D. (2008). Multiple myeloma: diagnosis and treatment. *American Family Physician*, 78(7), 853–859. <http://www.ncbi.nlm.nih.gov/pubmed/18841734>
21. Oliveira, M. M. de, Veloso, G. A., Malta, D. C., Curado, M. P., & Pádua, C. M. de. (2024). Multiple myeloma in Brazil: an assessment of Global Burden Disease study 2019. *Saúde Em Debate*, 48(142). <https://doi.org/10.1590/2358-289820241428855i>
22. Park, B., Yoon, J., Lee, Y. S., Park, Y. J., & Eom, H. S. (2024). Trends in multiple myeloma incidence, prevalence, mortality, and survival rate in South Korea: a nationwide population-based study. *Annals of Hematology*, 103(10), 4111–4119. <https://doi.org/10.1007/s00277-024-05701-3>
23. Pulte, D., Gondos, A., & Brenner, H. (2011). Improvement in Survival of Older Adults with Multiple Myeloma: Results of an Updated Period Analysis of SEER Data. *The Oncologist*, 16(11), 1600–1603. <https://doi.org/10.1634/theoncologist.2011-0229>
24. Raje, N. S., Anaissie, E., Kumar, S. K., Lonial, S., Martin, T., Gertz, M. A., Krishnan, A., Hari, P., Ludwig, H., O'Donnell, E., Yee, A., Kaufman, J. L., Cohen, A. D., Garderet, L., Wechalekar, A. F., Terpos, E., Khatry, N., Niesvizky, R., Yi, Q., ... Munshi, N. C. (2022). Consensus guidelines and recommendations for infection prevention in multiple myeloma: a report from the International Myeloma Working Group. *The Lancet Haematology*, 9(2), e143–e161. [https://doi.org/10.1016/S2352-3026\(21\)00283-0](https://doi.org/10.1016/S2352-3026(21)00283-0)
25. Rajkumar, S. V., Gertz, M. A., Kyle, R. A., & Greipp, P. R. (2002). Current therapy for multiple myeloma. *Mayo Clinic Proceedings*, 77(8), 813–822. <https://doi.org/10.4065/77.8.813>
26. Rajkumar, S. V., & Kumar, S. (2016). Multiple Myeloma: Diagnosis and Treatment. *Mayo Clinic Proceedings*, 91(1), 101–119. <https://doi.org/10.1016/j.mayocp.2015.11.007>
27. Rodriguez-Otero, P., van de Donk, N. W. C. J., Pillarisetti, K., Cornax, I., Vishwamitra, D., Gray, K., Hilder, B., Tolbert, J., Renaud, T., Masterson, T., Heuck, C., Kane, C., Verona, R., Moreau, P., Bahlis, N., & Chari, A. (2024). GPRC5D as a novel target for the treatment of multiple myeloma: a narrative review. *Blood Cancer Journal*, 14(1), 1–13. <https://doi.org/10.1038/s41408-023-00966-9>
28. Wang, C., Wang, W., Wang, M., Deng, J., Sun, C., Hu, Y., & Luo, S. (2024). Different evasion strategies in multiple myeloma. *Frontiers in Immunology*, 15(February), 1–15. <https://doi.org/10.3389/fimmu.2024.1346211>
29. Zhou, L., Yu, Q., Wei, G., Wang, L., Huang, Y., Hu, K., Hu, Y., & Huang, H. (2021). Measuring the global, regional, and national burden of multiple myeloma from 1990 to 2019. *BMC Cancer*, 21(1), 1–13. <https://doi.org/10.1186/s12885-021-08280-y>
30. Zhou, P., Chen, X., Wang, W., Wei, L., Chen, X., Peng, X., Lin, Z., Hua, Q., & Nie, X. (2025). *Global Epidemiology, Burden, and Risk Factor of Multiple Myeloma: Past, Present, and Future* (Vol. 6, Issue 6, pp. 1–4). <https://doi.org/10.2139/ssrn.5140918>
31. Zhu, D. T., Park, A., Lai, A., Zhang, L., Attar, H., & Rebbeck, T. R. (2024). Multiple myeloma incidence and mortality trends in the United States, 1999–2020. *Scientific Reports*, 14(1), 1–9. <https://doi.org/10.1038/s41598-024-65590-4>
32. Zhuge, L., Lin, X., Fan, Z., Jia, M., Lin, C., Zhu, M., Teng, H., & Chen, G. (2025). Global, regional and national epidemiological trends of multiple myeloma from 1990 to 2021: a systematic analysis of the Global Burden of Disease study 2021. *Frontiers in Public Health*, 13(January), 1–14. <https://doi.org/10.3389/fpubh.2025.1527198>