



## REVIEW ARTICLE

# Epidemiology, risk factors, and prevention strategies of multiple myeloma cancer: a systematic review

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OPEN ACCESS

## PUBLISHED

31 December 2025

## CITATION

Lawanson, MO., Berleant, D., et al.,  
2025. Epidemiology, risk factors,  
and prevention strategies of multiple  
myeloma cancer: a systematic  
review. Medical Research Archives,  
[online] 13(12).

<https://doi.org/10.18103/mra.v13i12.7088>

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## DOI

<https://doi.org/10.18103/mra.v13i12.7088>

## ISSN

2375-1924

## ABSTRACT

Multiple myeloma is a disease arising from the proliferation of plasma cells, accounting for 1-2% of malignant neoplasms in the United States. Multiple myeloma is considered to be an incurable disease. With advancements in treatment, patients' survival rates have improved over time. The objective of this study was to carry out a review of epidemiology, risk factors, and prevention strategies for multiple myeloma. The review shows for example that multiple myeloma is more common in men than in women and more frequent among individuals of African descent compared to other racial groups. The disease mostly affects people aged 60 years and above. The risk factors include age, gender, genetic makeup, and occupation that exposes workers to certain chemicals such as benzene and pesticides. People who are overweight or obese and those with a history of other plasma cell disorders also have a higher chance of developing the disease. Family history of multiple myeloma or other blood cancers is another major risk factor. Prevention of multiple myeloma remains a challenge because many of the risk factors, such as age and genetics, cannot be changed. However, there are still important steps that can be taken to reduce the overall risk. These include avoiding exposure to harmful chemicals in work environment or workplace, eating a balanced diet, engaging in regular physical activity, and avoiding smoking. Early screening among high-risk populations may also help in detecting the disease in its early stages when treatment is more likely to be successful. In conclusion, multiple myeloma remains a growing public health concern due to its increasing prevalence and the difficulty in preventing it completely. More research is still needed to fully understand the causes of the disease and to develop better prevention and early detection strategies. Public health education and awareness campaigns can also play a key role in reducing the burden of this disease in communities around the world.

**Keywords:** Multiple myeloma, cancer, epidemiology, risk factors, prevention strategies.

## 1. Introduction

Multiple myeloma (MM) is a hematologic malignancy characterized by the uncontrolled proliferation of plasma cells in the bone marrow, resulting in bone destruction, immune suppression, anemia, renal impairment, and increased susceptibility to infections<sup>1</sup>. The most common symptoms associated with Multiple Myeloma (MM) include lytic bone lesions, renal failure, calcium dysregulation, anemia, and susceptibility to infections<sup>2</sup>. Multiple myeloma is the second most common hematologic malignancy, accounting for 10% of all cases<sup>3</sup>. The development of myeloma is a complex multistep process characterized by early and late genetic changes in the tumor cell, as well as unique supportive conditions within the bone marrow microenvironment<sup>4,5,6</sup>.

Although MM was likely around but undetected for many years before its official discovery, the first clinical presentation and documented diagnosis of MM was in 1844<sup>7</sup>. In this initial case, the individual reported extreme fatigue, multiple bone fractures, and severe bone pain and was treated with rhubarb and orange peel<sup>8</sup>, dying four years after the onset of symptoms<sup>7</sup>.

The global incidence of multiple myeloma has been on the rise, with over 176,000 new cases and more than 117,000 deaths reported worldwide in 2020<sup>9</sup>. With life expectancy increasing yearly, it is important to recognize that the prevalence of MM will likely continue to increase<sup>10</sup>. In the United States alone, an estimated 35,780 new cases and 12,540 deaths are expected in 2024<sup>11</sup>. The increasing incidence is partly attributed to an aging population, genetic susceptibility, environmental exposures, and disparities in healthcare access, especially among African Americans, who are twice as likely to be diagnosed with MM compared to Whites<sup>12</sup>.

Importantly, age has also emerged as a significant prognostic factor in MM. Younger patients tend to experience better survival outcomes, while older adults who comprise the majority of MM cases face higher mortality due to reduced treatment tolerance, comorbidities, and later-stage diagnosis. Recognizing the role of age in this review helps frame sections on epidemiology and risk factors, where demographic trends are explored in greater depth.

Although advances in diagnosis and therapy have improved outcomes, MM remains incurable, and the five-year survival rate varies significantly depending

on age, stage at diagnosis, and access to treatment<sup>13</sup>. Given these challenges, there is a critical need to focus on prevention strategies both primary and secondary to reduce the burden of the disease.

MM accounts for 1-2% of all cancers and ~10% of hematological malignancies in the USA<sup>14,15</sup>. There is a slight male predominance, with double the number of African Americans affected than whites<sup>16</sup>. Multiple myeloma is most common in older adults ages 65–74, with a median age of diagnosis of 69 years<sup>17</sup>, with ~18% diagnosed when <50 years of age<sup>18</sup>. Multiple myeloma is a relatively uncommon cancer, with an estimated 32,270 new cases diagnosed and 12,830 deaths in the United States in 2020, accounting for less than 2% of all new cancer cases diagnosed per year<sup>17,19</sup>. It is estimated that MM will have constituted approximately 1.8% of all new cancer diagnoses in 2023<sup>20</sup>. In another study, noted for the year 2020, MM accounted for approximately 1.8% of all cancer diagnoses in the US<sup>21</sup>. As of 2017, 140,779 people were living with MM in the United States<sup>17</sup>. With the advent of modern therapies, the 5-year relative survival rate increased from 32.1% in 2000 to 55.6% in 2017<sup>17</sup>. The cause of MM is largely unknown, with no established lifestyle, occupational, or environmental risk factors, though some studies have shown a direct relationship between MM and obesity<sup>22</sup>.

Multiple myeloma is a public health issue that deserves more research, and there are various factors to consider when addressing health disparities among multiple myeloma patients<sup>23</sup>. Although myeloma remains incurable, overall survival has improved over time because of advancements in the understanding of myeloma biology, ongoing development of novel therapies, and technological improvements in genetic sequencing affecting the therapeutic options and clinical outcomes<sup>24</sup>.

Given the serious public health burden posed by this disease, this paper intends to provide a comprehensive overview of multiple myeloma, integrating clinical presentation, epidemiologic patterns, biological mechanisms, and historical insights. We aim to contextualize the evolution of MM understanding from its earliest documentation to modern diagnostic and therapeutic advances, while highlighting persistent disparities and the pressing need for both primary and secondary prevention

strategies. By synthesizing current evidence, the research seeks to inform public health approaches, support equitable access to care, and guide future research efforts aimed at reducing the impact of MM on diverse and aging populations.

While current research continues to improve outcomes for patients with MM, it is important to recognize the historical roots of this disease. Understanding how MM was first identified provides valuable context for the evolution of diagnostic and therapeutic approaches.

## 2. Materials and Methods

### STUDY DESIGN

This review adopted a systematic review approach to literature review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses<sup>25</sup> structure. The study made sure that a transparent and rigorous approach to literature was utilized in its study. This approach ensured identification, selection, data extraction, and synthesis of information with adherence to the epidemiology, risk factors, and prevention strategies of multiple myeloma.

### RESEARCH QUESTION

What are the reported epidemiology, risk factors, and prevention strategies of multiple myeloma?

The PICO model guided the formulation of the research question.

**Population (P):** The study population comprised patients diagnosed with multiple myeloma.

**Intervention/Exposure (I):** Multiple myeloma.

**Comparison (C):** The study in its approach does not compare any effect from intervention or exposure. Hence, comparison is not applicable for this review, as the study centered more on the description of epidemiology, risk factors, and prevention strategies of multiple myeloma cases rather than a direct comparison of disease treatments.

**Outcome (O):** The survival or progression-free life of individuals remained the outcome of the study.

### ELIGIBILITY CRITERIA

#### Inclusion Criteria:

- i. Peer-reviewed studies published in English.
- ii. Studies reporting on epidemiology, risk factors, and prevention strategies for multiple myeloma remained the focus.
- iii. The researchers searched for literature between 1998 and 2025.

#### Exclusion Criteria:

- i. Case reports, editorials, opinion pieces, conference abstracts, and review articles (unless they provide primary data not found elsewhere).
- ii. Studies without clear data or information on multiple myeloma epidemiology or clarity on risk factors in MM patients.
- iii. Studies where MM patients cannot be disaggregated from other hematologic malignancies.

### INFORMATION SOURCES AND SEARCH STRATEGY

The primary academic database used for this review was Google scholar. Google Scholar was selected because it is a wide and general academic database for studies including medical publications. Duplicate studies identified during the search were removed manually by comparing titles, authors, publication years, and journal sources to ensure only unique records were retained. The search strategy used Boolean operators ("AND," "OR") and phrase searching to improve precision and coverage. Specifically, the following Boolean combinations were applied:

- "multiple myeloma" AND "epidemiology"
- "multiple myeloma" AND "risk factors"
- "multiple myeloma" AND "prevention strategies"
- ("multiple myeloma" OR "plasma cell myeloma") AND ("etiology" OR "causes")
- ("multiple myeloma" AND "public health") OR ("multiple myeloma" AND "incidence")

Quotation marks (" ") were used to ensure exact phrase matching, and filters were applied for English-language, peer-reviewed studies published between 1998 and 2025.

### FILTERS WERE APPLIED FOR:

Language: English

Publication Year: 1998-2025 (March 30<sup>th</sup>)

Study types: population-based research

### STUDY SELECTION

The literature from the initial search were gathered together, with duplications deleted. Later on, the literature was screened first by the document titles and abstracts to determine the usability for the study. Thereafter, the papers considered useable were subjected to full-text review. A PRISMA flow diagram is presented below to illustrate the selection process.

## PRISMA Flow Diagram for Study Selection

Phase	Number of Records
Papers accessed through Google Scholar	150
Papers screened (titles/abstracts)	150
Papers excluded at title/abstract stage	68
Full-text articles assessed for eligibility	82

## DATA EXTRACTION

Data extraction was conducted independently by one reviewer and cross-checked by others to ensure accuracy.

## DATA SYNTHESIS

Due to anticipated heterogeneity in the papers accessed for the study, a narrative synthesis approach was primarily utilized. The narrative synthesis categorized findings based on:

- i. Epidemiology of multiple myeloma across different age groups.
- ii. The risk factors and their reported rates: factors influencing outcomes and complications (e.g., patient age, gender, race among others)
- iii. Specific complications, their incidence, and severity.
- iv. Prevention strategies for multiple myeloma.

## ETHICAL CONSIDERATION

As this systematic review involved the secondary synthesis of previously published data, no direct ethical approval was required. All original studies included in the review were assumed to have obtained appropriate ethical clearance from their respective institutional review boards.

### 3. Multiple Myeloma Epidemiology

As noted earlier, multiple myeloma (MM) is becoming more common, with an estimated 143% increase in diagnosed cases since 1975<sup>21</sup>. The understanding of MM, which is the second most common hematologic malignancy after non-Hodgkin lymphoma and represents about 1% of all cancers, is considered very necessary for early detection and effective treatment<sup>26</sup>. According to the American Cancer Society (ACS), the lifetime risk of MM in the United States is 1 in 132 (0.8%). In 2018, there were 30,770 new cases of MM (16,400 men and 14,370 women) and 12,770 deaths (6,830 men and 5,940 women) in the U.S.<sup>27</sup>. The condition most often affects older people, with over 60% of cases diagnosed in adults over 65. African Americans are more likely than the general population to be diagnosed with MM, and men are

about 1.5 times more likely to be diagnosed than women. Evidence also shows that people with a first-degree relative with MM are roughly 3.7 times more likely to develop the disease, suggesting there may be a hereditary component. Recent evidence demonstrates that age at diagnosis is a critical predictor of survival in MM, with younger patients (<40 years) showing higher survival probabilities and older patients (>70 years) experiencing significantly reduced survival<sup>28</sup>. This pattern aligns with broader cancer survival trends, highlighting the prognostic importance of age in clinical decision-making.

In summary, multiple myeloma is a disease that disproportionately affects older adults, men, and individuals of African descent. The elevated risk among first-degree relatives suggests a potential hereditary component, further emphasizing the need for targeted screening and early detection strategies. As the population ages and diagnostic capabilities improve, understanding these demographic patterns becomes increasingly important for guiding public health interventions and clinical decision-making.

The incidence of multiple myeloma has been rising over the past 25 years. Despite this increase, the survival rate for MM patients has dramatically improved with the development of new treatment options. Currently, the mortality rate from MM is estimated at 3.3 per 100,000, which represents a significant decline from 4.0 per 100,000 just 29 years ago<sup>21</sup>. In 2021, approximately 34,920 new cases were expected to be diagnosed in the United States, with around 12,410 deaths<sup>29</sup>. Men are more frequently affected than women, with 19,320 cases in men compared with 15,600 in women, and a similar pattern is seen in deaths, estimated at 6,840 for men and 5,570 for women<sup>29</sup>. The disease is most commonly diagnosed in adults aged 65–74, with a median age of 69 years at diagnosis<sup>30</sup>.

### 4. Diagnosis of Multiple Myeloma

The most common presenting symptoms of multiple myeloma are fatigue, bone pain, and



anemia<sup>31</sup>. Renal failure can also be a presenting feature, with about half of newly diagnosed patients showing elevated creatinine levels<sup>31</sup>. The clinical presentation of MM can be nonspecific, but the symptoms usually arise from bone infiltration by plasma cells or renal tubular damage caused by excess light chains<sup>32</sup>. Initial diagnostic procedures should begin with basic blood work, including a comprehensive metabolic panel—electrolytes, renal studies, liver function tests, calcium, phosphorus, uric acid, albumin, and globulin—along with a complete blood count with differential. Lactate dehydrogenase should also be measured, as it is frequently elevated in aggressive disease<sup>32</sup>. When MM is suspected from these initial tests, further specialized laboratory studies and diagnostics are warranted. Hypercalcemia is found at diagnosis in about one-third of patients and may require immediate intervention. While bone pain occurs in up to 60% of patients at diagnosis, approximately one-third also present with pathological fractures, most often affecting the axial skeleton but sometimes involving the long bones<sup>33</sup>.

The premalignant phase, termed monoclonal gammopathy of unknown significance (MGUS), occurs prior to the diagnosis of multiple myeloma. The presence of monoclonal immunoglobulins in blood or urine is linked to MGUS. MGUS is diagnosed in a clinical context when bone marrow plasma cells (BMPCs) are less than 10% and there are no end-organ abnormalities associated with myeloma, notably no hypercalcemia, renal impairment, anemia, or osteolytic bone lesions (CRAB symptoms). MGUS is detected in 3% of the population over the age of 50 years and progresses to active multiple myeloma in about 1% of these patients per year<sup>34, 35</sup>. People who have bone pain and subsequent osteolytic lesions on imaging, symptomatic or silent hypercalcemia, acute renal failure, unexplained anemia, or an increase in infections are at high risk of developing multiple myeloma. Anemia and bone pain are thought to be present in about 70% of patients at diagnosis, and approximately 98% of individuals with active multiple myeloma experience fatigue. Renal failure affects around 20% of individuals, while about 15% of people with newly diagnosed myeloma have hypercalcemia and an increase in infections. Other presenting symptoms include peripheral neuropathy, headaches suggestive of hyperviscosity, visual disturbances, and mucosal bleeding<sup>36</sup>.

#### 4.1 DIAGNOSTIC APPROACH

The diagnosis of multiple myeloma (MM) requires a high index of suspicion because the presenting symptoms are frequently nonspecific. MM should be considered in older patients who present with bone pain, unexplained anemia, hypercalcemia, or renal failure, for which there is no clear cause<sup>37</sup>. The most common features seen in patients with MM are immunoglobulin deposition within an organ or plasma cell infiltration into the bone marrow. Finding aberrant monoclonal plasma cells in the bone marrow, M protein in the urine or serum, osteolytic lesions, and end-organ destruction are all necessary for the diagnosis of MM. The term “CRAB” refers to the end-organ events that lead to a diagnosis of MM. In a review of over 1,000 patients with newly diagnosed MM, the following signs and symptoms were observed: hypercalcemia (28%), elevated creatinine (48%), anemia (73%), bone pain (58%), fatigue or weakness (32%), and weight loss (24%) (Kyle, 2003).

Multiple myeloma can present with a variety of other symptoms caused by the large proteins secreted by malignant plasma cells, including extramedullary plasmacytomas, cord compression, amyloidosis, recurrent infections, peripheral neuropathy, and symptomatic hyperviscosity syndrome (headache, blurred vision, altered mental status, and oral bleeding). Patients with smoldering myeloma or MGUS differ from those with symptomatic MM because they do not meet any of the previously mentioned CRAB criteria. However, individuals with MGUS or smoldering myeloma should be monitored closely for transformation to active symptomatic disease and the potential need for prompt treatment initiation<sup>38</sup>.

#### 4.2 CLINICAL EVALUATION PROCESS

The International Myeloma Working Group (IMWG) revised the criteria for the diagnosis of MM and related disorders in 2014<sup>14</sup>. When taking a patient history, special attention should be paid to bone pain, neurological complaints, infections, and constitutional symptoms if MM is suspected. During a clinical examination, pallor, bone soreness, spinal abnormalities, and infections should all be evaluated. A neurological examination is particularly important, especially to assess signs of neuropathy and spinal cord compression<sup>39</sup>.

As noted earlier, the investigations used in the diagnostic evaluation of multiple myeloma (MM)

are aimed at demonstrating the M-protein and clonal plasma cells in the bone marrow, as well as evaluating for end-organ damage<sup>37</sup>. Consequently, baseline investigations for MM include a full blood count (FBC) with differential and smear, along with measurement of the erythrocyte sedimentation rate (ESR)<sup>37</sup>. Advanced imaging modalities are more sensitive for the diagnosis of MM and have largely replaced the skeletal survey in the developed world. These imaging techniques include whole-body, low dose computed tomography (CT) scanning, among others<sup>37</sup>.

5. Risk Factors

As noted previously, MGUS is one of the most significant risk factors for multiple myeloma identified in literature. Additional risk factors include older age, male sex, Black race, and genetic characteristics. Age at diagnosis remains a strong prognostic factor, with studies showing that older MM patients, particularly those over 70, have a 3.3-fold increased risk of mortality compared to younger patients<sup>28</sup>. Younger patients tend to tolerate aggressive therapies better, have fewer comorbidities, and respond more effectively to treatment, which collectively explains higher survival outcomes.

Environmental exposures have also been reported, including contact with petroleum products, Agent Orange, and benzene. Certain agricultural or industrial occupations have been acknowledged, while obesity and dietary characteristics, though less frequently described, are associated with an increased risk of myeloma<sup>26</sup>. According to Singh and Jemal<sup>40</sup>, individuals living in more deprived areas or with lower education and income levels have higher mortality and incidence rates of various cancers. Lung, colorectal, cervical, stomach, and liver cancers

are the most common contributors to excess risk, with lower socioeconomic groups experiencing greater disparities, and African Americans showing higher cancer mortality rates. A number of factors, particularly those related to care costs, influence the outcomes associated with cancer diagnoses in general and, in particular, multiple myeloma diagnoses.

Background literature consistently shows that socioeconomic status, access to care, and structural inequities play a substantial role in determining both incidence and survival outcomes among MM patients. Individuals with limited financial resources often experience delays in diagnosis due to inadequate access to primary care, limited health insurance coverage, or lack of awareness about early symptoms. These delays contribute to a higher likelihood of presenting with advanced disease, which is associated with poorer prognosis. Additionally, the high cost of diagnostic imaging, novel therapeutic agents, stem cell transplantation, and long-term maintenance therapies creates significant financial barriers that disproportionately affect underserved communities.

The literature highlights that socioeconomic disparities not only influence disease outcomes but also appear to indirectly shape risk through environmental exposures, occupational patterns, and chronic stress pathways, factors that are more prevalent in disadvantaged populations. When combined with known demographic risk factors such as age, race, and the presence of precursor conditions like MGUS, these structural barriers amplify the burden of MM in vulnerable groups. Understanding these interconnected factors is crucial for developing targeted prevention strategies, improving early detection efforts, and addressing inequities in access to treatment.

Summary of Key Risk Factors for Multiple Myeloma

Risk Factor	Description / Evidence	Approximate Risk or Association
Age	Incidence increases sharply with age; median age at diagnosis ~69 years.	>60% of cases occur in individuals >65 years old.
Sex	Slight male predominance.	Men have ~1.5× higher risk than women.
Race / Ethnicity	Higher incidence among African Americans.	2–3× higher risk compared to Whites.
Family History / Genetics	Familial clustering observed in first-degree relatives.	2× increased risk of MM or MGUS.
Environmental / Occupational Exposure	Exposure to pesticides, benzene, solvents, and petroleum products.	1.5–3× increased risk depending on duration and type of exposure.
Obesity	Chronic inflammation and altered cytokine profiles contribute to plasma-cell proliferation.	1.5× increased risk among obese individuals.
Socioeconomic Status (SES)	Lower SES linked to delayed diagnosis and reduced survival.	Up to 54% higher mortality in low-SES groups.

### 5.1 AGE

The frequency of multiple myeloma increases with age, and the disease is generally considered one of older adults. Age is a significant risk factor, with over 30% of newly diagnosed cases occurring in patients aged 65–74 years, while less than 3% of patients are diagnosed before age 44<sup>17</sup>. Although the development of innovative medicines has improved survival, these advances have not been as substantial in older populations. In addition, MM occurs about twice as frequently in the Black population compared with the White population<sup>41</sup>.

As noted previously, the risk of multiple myeloma increases with age<sup>42</sup>. In a survival study reported by Thorsteinsdottir et al.<sup>43</sup>, 21,502 patients were followed over a 40-year period from 1973 to 2013. The study found that 5-year and 10-year relative survival rates increased significantly for all age groups except the youngest (20–40 years at diagnosis) and the oldest (over 80 years at diagnosis), which showed no change in survival<sup>43</sup>. More recently, Costa et al.<sup>44</sup> analyzed improvements in outcomes among 34,505 multiple myeloma patients, including 13,229 patients (38.9%) under age 65, 9,834 patients (28.5%) aged 65–74, and 11,442 patients (33.2%) aged 75 or older.

### 5.2 DEMOGRAPHIC FACTORS PLAY A ROLE

Epidemiologic cohort studies have shown an increased risk of myeloma or MGUS in first-degree relatives of patients with myeloma or MGUS<sup>45</sup>. Familial clustering among first-degree relatives has been associated with a twofold increased risk of developing multiple myeloma and a twofold increased risk of MGUS<sup>46</sup>. Genetic differences may explain a fraction of variations in cancer mortality rates<sup>47</sup>. According to the American Cancer Society<sup>42</sup>, non-Hispanic Blacks are more likely than non-Hispanic Whites to develop multiple myeloma. The risk of dying from multiple myeloma is considerably higher for African Americans than for other racial groups.

The health inequalities among minority groups in the United States makes it necessary to investigate racial disparities in multiple myeloma care<sup>48</sup>. Hispanic and Asian patients with multiple myeloma are more likely to use Medicare than White and African American patients, raising the possibility that supplemental insurance may be used less frequently due to economic concerns<sup>48</sup>. African Americans living with multiple myeloma may not receive adequate care and can experience delays

in treatment initiation, which can result from financial and social disparities as well as a lack of cultural competency among healthcare teams<sup>49</sup>. Race and ethnicity play a significant role in cancer diagnosis, and a disproportionate number of cancer deaths occur within specific ethnic groups<sup>42</sup>. African Americans are the second-largest racial and ethnic minority group in the U.S., after Hispanics, and by 2060, they are projected to make up 15% of the total U.S. population. For most cancers, African Americans have the highest death rates and shortest survival rates of any racial or ethnic group in the U.S.<sup>42</sup> Disparities in overall survival and socioeconomic factors lead to reduced access to novel treatments and a shorter quality of life among African Americans<sup>50</sup>.

### 5.3 ENVIRONMENTAL FACTORS

Multiple myeloma development has been linked to a variety of occupational exposures. Workers in agriculture who are exposed to hazardous chemicals, such as pesticides, may be more susceptible to myeloma. In Canada, Tsang et al.<sup>51</sup> analyzed the geographical distribution of myeloma cases from 1992 to 2015, during which over 32,000 people received a myeloma diagnosis. The study found that myeloma incidence rates are higher in rural and agricultural areas and lower in urban areas. Similarly, an epidemiologic study in France examined associations between multiple myeloma and crop- or animal-related activities resulting in pesticide exposure<sup>52</sup>. Information was collected from more than 155,000 participants between 2005 and 2007, among whom 269 were diagnosed with myeloma. The study found that myeloma risk was increased in farmers who used pesticides on crops in the 1960s, and in those who applied pesticides on corn, insecticides on animals, or disinfectants in animal barns<sup>52</sup>.

Gasoline contains hydrocarbons such as xylene, toluene, and benzene. While these substances are biodegradable in specific laboratory settings, they can persist in subsoils for extended periods if proper cleanup procedures are not followed. De Roos et al.<sup>53</sup> investigated the relationship between myeloma development and occupational exposures to aromatic hydrocarbon solvents, including benzene, toluene, and xylene. In a large epidemiologic study of more than 13,000 individuals, those exposed to any of these three solvents had a 42%–63% increased risk of developing myeloma<sup>53</sup>.

Environmental exposures are only one dimension of the complex risk landscape for multiple myeloma. Equally important are the social and demographic factors that shape disease incidence and outcomes. Among these, race and ethnicity play a critical role, with African American populations experiencing disproportionately higher rates of MM and worse clinical outcomes. The following section explores how systemic inequities, and racial disparities contribute to these patterns.

#### 5.4 ETHNICITY AND RACE

African Americans have a two- to threefold higher incidence of multiple myeloma than people of other ethnicities, according to numerous epidemiologic reports. Multiple myeloma is the leading hematologic malignancy in African Americans, Afro-Caribbeans, and Africans compared with individuals of European, Japanese, and Mexican descent<sup>54,55,56,49,57</sup>. Black American patients have higher mortality rates and longer delays to first therapy compared with White patients. The reasons for this racial disparity are multifactorial, involving access to health care including clinical trials, higher comorbidities, lower treatment utilization, and socioeconomic factors<sup>48,24,49, 57</sup>.

As we have described, the risk of multiple myeloma is higher in both male and African American patients<sup>17</sup>. Patients with a personal history of MGUS or a family history of MM are more likely to develop symptomatic MM, with an approximate 1% annual progression rate from MGUS to active myeloma. Most African American–White disparities in MM are due to variations in socioeconomic status and access to care resulting from decades of structural racism<sup>47</sup>. African Americans bear a disproportionate share of the cancer burden in the U.S., often experiencing lower socioeconomic status that leads to inequities such as inadequate insurance coverage<sup>58</sup>. Over the past few decades, significant strides have been made to lessen cancer disparities; still, more work is needed to achieve equitable outcomes. Cancer is the second leading cause of death among both men and women, with 34,510 non-Hispanic African American women and 35,215 non-Hispanic African American men in 2016<sup>58</sup>. Among non-Hispanic White participants, 21% of women and 23% of men were diagnosed with cancer in the same survey.

#### 5.5 SOCIOECONOMIC FACTORS

Socioeconomic status, including associated lifestyle risk factors such as diet and obesity, is linked to the

development of multiple myeloma. Socioeconomic characteristics, including high body mass index, income, and education, may also impact the overall survival of MM patients. Research examining various socioeconomic factors found that worse socioeconomic position was associated with lower survival rates, particularly among younger patients. Similarly, an institutional study by Fiala et al<sup>59</sup> compared socioeconomic status to SEER data and found that patients with low socioeconomic status had a 54% higher mortality rate compared with those with high socioeconomic status.

Socioeconomic status (SES) is the social standing or class of an individual or group, often measured by a combination of education, income, and occupation<sup>60</sup>. Examining socioeconomic and racial/ethnic patterns in cancer mortality and incidence is crucial because it allows us to measure health disparities between the most and least advantaged social groups. This analysis helps identify populations at the greatest risk of cancer diagnosis and mortality who may benefit from targeted social and medical interventions<sup>40</sup>. People with lower SES are more likely to experience higher cancer mortality rates compared with those of higher SES, and they have a higher probability of advanced-stage cancer at diagnosis and a lower chance of early detection<sup>40</sup>. Researchers have also found that social factors, including economic disadvantages, inequities in education, and lack of access to health care, impact a person's ability to lead a healthy and productive life<sup>61</sup>.

## 6. Prevention Approaches to Multiple Myeloma Cancer

Multiple myeloma (MM) is a hematologic malignancy characterized by the uncontrolled proliferation of plasma cells in the bone marrow, resulting in bone destruction, immune suppression, anemia, renal impairment, and increased susceptibility to infections<sup>2</sup>. The disease remains incurable and follows a relapsing and remitting course. Although advances in diagnosis and therapy have improved outcomes, the five-year survival rate varies significantly depending on age, stage at diagnosis, and access to treatment<sup>13</sup>. The cost of treatments for MM is substantial, including the expenses required to achieve a deep and durable response. However, recent research has identified several modifiable risk factors capable of



reducing risk or delaying disease progression. Given these challenges, there is a critical need to focus on both primary and secondary prevention strategies to reduce the burden of MM.

Cancer treatment imposes a heavy burden on patients, their families, payers, and society at large. In the United States, the estimated total direct medical costs attributable to cancer treatment were around \$125 billion in 2010<sup>62</sup>. Although multiple myeloma (MM) accounts for a relatively small proportion of cancer patients, healthcare costs for MM treatment are higher than those for most other types of cancer<sup>63</sup>. Studies examining the incremental costs of MM have reported a significant increase over the past decade, with outpatient care, hospitalizations, and drug expenses identified as the main drivers of this rising cost<sup>64</sup>.

Healthcare expenditures vary across the different phases of multiple myeloma (MM) care. As the disease progresses, treatments change, and costs differ for each phase of care. This variation contributes to MM having one of the highest lifetime costs among all types of cancer<sup>65</sup>.

Multiple myeloma prevention strategies can be classified into three main types: primary, secondary, and tertiary prevention.

### 6.1 PRIMARY PREVENTION

Primary prevention strategies for multiple myeloma include avoiding known environmental and occupational carcinogens. Exposure to certain hazards has been linked to an increased risk of MM, including pesticides (OR = 3.29), asphalt (OR = 2.42), coal dust (OR = 2.27), organic vapors (OR = 2.11), metal dust (OR = 2.07), exhaust fumes (OR = 2.03), and other chemicals (OR = 1.80). Lifestyle modifications are another component of primary prevention, including regular physical activity, diet, and smoking cessation. Engaging in systematic sports for at least six months was associated with a significantly lower risk of developing MM in a multicenter case-control study conducted in Poland<sup>66</sup>. Dietary patterns also play a role; consuming plant-based diets rich in fruits, vegetables, whole grains, and legumes may provide protective effects. The EPIC study found reduced cancer risk among vegetarians, vegans, and fish eaters, particularly for MM. Additionally, a high-fiber, plant-based diet can improve metabolic profiles and gut microbiota diversity, potentially delaying progression from MGUS or smoldering myeloma to MM<sup>67</sup>.

Dietary habits are an important aspect of primary prevention for multiple myeloma. Moderate fish consumption, which provides omega-3 fatty acids, has been associated with a decreased risk of MM, as omega-3s exhibit anti-inflammatory properties and may inhibit MM cell growth. In contrast, high consumption of red meat and dairy products has been linked to increased levels of insulin-like growth factor 1 (IGF-1), which may promote MM cell proliferation, suggesting that limiting intake of these foods could be beneficial. Therapeutic strategies also contribute to prevention; for example, daratumumab, a monoclonal antibody, has shown promise in delaying progression from high-risk smoldering multiple myeloma to active MM. A recent international trial reported a 51% reduction in the risk of disease progression or death among patients treated with Darzalex. Public education and health promotion campaigns are another highly effective primary prevention strategy for multiple myeloma.

Although multiple myeloma is not entirely preventable, several modifiable risk factors have been identified. Obesity increases risk through chronic inflammation and altered cytokine profiles<sup>68</sup>. Occupational exposures, including contact with agricultural pesticides, petroleum products, and ionizing radiation, also increase MM risk<sup>69</sup>. Chronic immune stimulation from infections such as HIV or from autoimmune diseases is another risk factor. By targeting these modifiable risks, it is possible to reduce the incidence of MM through lifestyle modification, workplace safety measures, and vaccination programs.

### 6.2 SECONDARY PREVENTION (EARLY DETECTION & RISK STRATIFICATION)

Secondary prevention strategies for multiple myeloma focus on early detection in high-risk individuals, such as those with MGUS or a family history of MM, and include genetic testing, personalized surveillance, and the use of artificial intelligence and digital tools for cancer detection. Management of MGUS and smoldering multiple myeloma (SMM), including surveillance protocols and supportive therapies such as bisphosphonates and vaccination, is an important secondary prevention strategy.

Recent advances in precision medicine have introduced **biomarker monitoring** as a promising strategy for secondary prevention of multiple myeloma. Biomarkers such as circulating free light

chains, serum M-protein levels, genetic mutations (e.g., *TP53*, *KRAS*, *NRAS*), and microRNA signatures are being increasingly studied for their potential to predict disease progression from MGUS or smoldering multiple myeloma (SMM) to symptomatic MM<sup>12, 69</sup>. Continuous biomarker surveillance, combined with advanced imaging techniques like whole-body MRI and PET-CT, allows clinicians to identify early biological changes before clinical symptoms develop. Integrating biomarker-based risk stratification with artificial intelligence and digital monitoring tools may enable earlier intervention, personalized surveillance, and improved prognostic accuracy.

### 6.3 TERTIARY PREVENTION (AVOIDING COMPLICATIONS AND PROGRESSION)

Regular monitoring of individuals with MGUS or smoldering multiple myeloma (SMM) is crucial for early detection and timely intervention, while advancements in biomarker development and imaging techniques can help identify high-risk patients who may benefit from preventive strategies.

Multiple myeloma often develops silently and is preceded by asymptomatic conditions, which provide a window of opportunity for early intervention. However, the absence of routine screening programs and low awareness means many patients are diagnosed at advanced stages, when irreversible organ damage has already occurred<sup>71</sup>. Adherence to treatment protocols, management of comorbidities, and prevention of complications such as bone fractures, kidney failure, or infections can help limit severe damage. Psychosocial support and rehabilitation services further contribute to improving patient outcomes.

### 7. CHALLENGES AND GAPS IN PREVENTION

A major challenge in preventing multiple myeloma is the absence of standardized screening guidelines. Limited understanding of modifiable risk factors also hinders prevention efforts. Prevention research faces additional gaps due to underrepresentation of populations in MM studies, as well as ethical and cost-effectiveness considerations. MM treatment itself involves costly regimens, including immunomodulatory drugs, monoclonal antibodies, and stem cell transplantation, which often lead to financial toxicity for patients and their families<sup>72</sup>. By preventing disease onset or progression, it is possible to reduce the economic burden on healthcare systems and improve patients' quality of life.

## 8. Limitations

This review has several limitations that should be considered when interpreting the findings. Only one database (Google Scholar) was searched, which may have resulted in the omission of relevant studies from other sources. Additionally, the screening and data extraction were performed by a single author, which increases the potential for selection and interpretation bias. The inclusion of only English-language publications may also limit the generalizability of the results. Despite these limitations, this review provides valuable insights into the epidemiology, risk factors, and prevention strategies for multiple myeloma.

## 9. Conclusion

Multiple myeloma is a serious and growing health problem, primarily affecting older adults, with higher rates observed among men and people of African descent. The exact cause of MM is not fully known, as multiple factors contribute to its development, including age, gender, family history, obesity, certain environmental exposures, and pre-existing plasma cell disorders. Many of these risk factors are non-modifiable, which makes prevention challenging. While MM remains incurable, emerging evidence suggests that lifestyle modifications, dietary interventions, certain supplements, and pharmacological agents may help prevent or delay its onset. Further research is needed to establish definitive preventive measures and guidelines. Investments in epidemiological studies are essential to understand population-specific risk factors, particularly among underserved groups. National cancer control plans should integrate MM prevention strategies to improve early detection, reduce disparities, and promote equitable healthcare delivery. Cancer-related organizations, especially those focused on multiple myeloma, are already advocating for such initiatives, but additional support from governments and global health agencies is required.

Prevention of multiple myeloma is both a public health necessity and a medical imperative. Although a complete cure remains elusive, reducing incidence, delaying progression, and minimizing complications are achievable through comprehensive prevention strategies. These strategies not only lessen the burden on healthcare systems but also improve quality of life for individuals at risk or affected by

MM. A proactive and integrated approach involving education, research, policymaking, and community engagement is therefore essential to achieve these goals.

## 10. Recommendations

**1. Public Awareness:** Governments, health workers, and media should help educate the public about multiple myeloma, especially in high-risk populations. People should know the warning signs and when to seek medical help.

**2. Health Screening:** High-risk groups, such as older adults and those with a family history of blood cancers, should be regularly screened. Early diagnosis can improve treatment results and quality of life.

**3. Lifestyle Promotion:** Health promotion programs should encourage regular physical activity, healthy diets, and avoidance of smoking and exposure to toxic substances. These efforts may reduce the number of new cases.

**4. Workplace Safety:** Policies should be put in place to protect workers from harmful chemicals such as benzene and pesticides, especially in industries where exposure is high.

**5. Research Support:** More funding should be directed toward research into the causes, early detection, and better prevention strategies for multiple myeloma. This includes genetic studies and trials of new screening tools.

**Access to Care:** Efforts should be made to ensure that all people, including those in low-income or rural areas, have access to both early diagnosis and quality treatment.

## Conflict of Interest Statement:

None.

## Funding Statement:

This work and the APC were funded in part by the National Institutes of Health, grant NIH 5P20GM103429-23, Subaward 54077-CRG, and in part by the National Science Foundation, grant OIA-1946391.

## Acknowledgements:

None.

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