



Reporter's Guide to **Multiple Myeloma**

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What is **multiple myeloma**?

Multiple myeloma is a relatively rare form of blood cancer that accounts for roughly 1% of all cancers, or about 10% of all haematological malignancies, and roughly 2% of all deaths from cancer.^{1,2}

Multiple myeloma starts in the plasma cells of the bone marrow, the soft tissue part of the bones.^{3,4} It is characterised by an uncontrolled growth of cancerous plasma cells.^{3,4}

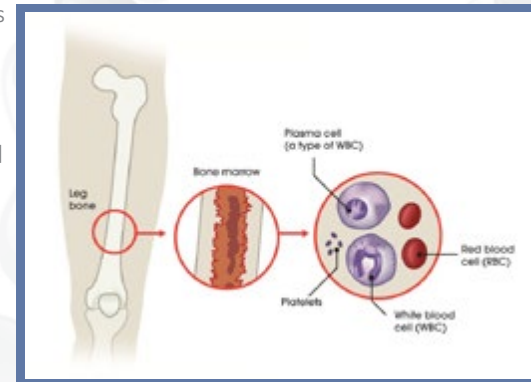
Normal plasma cells produce antibodies that help fight infection and disease. In myeloma, these plasma cells become abnormal, multiply uncontrollably and release only one type of antibody – known as 'M' proteins or paraproteins – which has no useful function. It is often through the measurement of 'M' proteins that myeloma is diagnosed and monitored.⁴

While some patients with MM have no symptoms at all, most patients are diagnosed due to symptoms which can include bone problems, low blood counts, calcium elevation, kidney problems or infections,³ and almost 29 percent of patients with MM will die within one year of diagnosis.⁵ Most of the medical complications related to myeloma are caused by the build-up of the abnormal plasma cells in the bone marrow and the presence of the paraprotein in the blood or in the urine.⁴

Myeloma can develop wherever there are plasma cells and often affects multiple places in the body, hence the name 'multiple myeloma'.³

Nearly 230,000 people worldwide are living with multiple myeloma.⁶ In Europe, approximately 77,000 people are estimated to be living with the disease and there are over 33,000 new cases and 20,000 deaths each year.⁴ In 2016 in the U.S., approximately 30,000 new patients are expected to be diagnosed with multiple myeloma and approximately 12,500 people are estimated to die from the disease.³

The incidence of multiple myeloma is expected to rise globally.⁷



Nearly **230,000** people worldwide and around 77,000 people in Europe are living with **multiple myeloma**⁶



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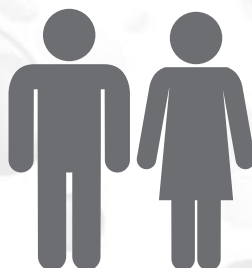
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What causes **multiple myeloma**?

It is not known exactly what causes multiple myeloma. However, exposure to certain chemicals, radiation, viruses, a weakened immune system and DNA mutations are thought to be potential causes or 'triggers'.^{3,8}

Researchers have also identified certain factors that may increase the risk of developing multiple myeloma, including:

Mainly affects people over the age of 60.⁷



- **Age:** This is the most significant risk factor for multiple myeloma. Multiple myeloma mainly occurs in people over 60 years old, although people under 60 years old can be affected.⁹
- **Gender:** Men have a slightly higher risk in developing multiple myeloma than women.⁹
- **Race:** The incidence of multiple myeloma in Afro-Caribbean men and women has been shown to be around twice that in Caucasian races.⁹
- **Other plasma cell diseases:** Monoclonal gammopathy of undetermined significance (MGUS) or single plasmacytoma tumours can be precursors to developing multiple myeloma.³

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What are the symptoms of multiple myeloma?

There are often no symptoms in the early stages of myeloma, and in some cases, it may be discovered during a routine blood test.³

Symptoms, if present, may be vague and confused with those of other conditions.^{3,10}

Most people will visit their doctor complaining of pain, often in the lower back or in the ribs. Pain is the most prominent symptom of myeloma.¹⁰

Other symptoms include:

- Bone pain or fractures¹⁰
- Fatigue, shortness of breath or weakness¹⁰
- Unusual bleeding or bruising more easily than normal¹⁰
- Excess urination¹⁰
- Swollen ankles¹⁰
- Thirst¹⁰
- Nausea¹⁰

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How is **multiple myeloma** diagnosed and staged?

Multiple myeloma can be diagnosed through a number of tests, including:

- **Blood tests:** There are a number of different blood tests that can be done, each analysing various chemicals and identifying indicators of multiple myeloma.¹¹
- **Urine tests:** Various urine tests can be conducted as well, measuring abnormal immunoglobulins in the urine.¹¹
- **Biopsy/aspiration:** When bone marrow tissue or fluid is removed from the body for testing.¹²
- **Imaging tests:** Different types of imaging tests can reveal bone lesions and other abnormalities in the bone marrow.¹³

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Doctors will look at a number of factors holistically before diagnosing a patient with multiple myeloma, including:¹¹

- Observed symptoms
- Physical exam results
- Results of blood/urine tests
- Results of biopsy tests
- Imaging tests

Once diagnosed, doctors also use a series of tests to 'stage' the cancer so that prognostic estimates can be made. There are currently two staging systems used for multiple myeloma:

- The **Durie-Salmon Staging System** has historically been the most widely used system. Lately, its use has been limited due to newer diagnostic methods, however.³ It is based on a number of different criteria, including the level and type of monoclonal protein, haemoglobin levels, the amount of calcium in the blood and number of bone lesions.
- **The International Staging System**, a more cost effective, and sensitive system, looks at the results of blood tests - β 2-microglobulin (β 2-M), albumin, serum lactate dehydrogenase (LDH) and chromosomal abnormalities - as part of staging.^{3,14}

Both staging systems are useful for estimating prognosis but not for choosing therapy and both have limitations.

Relapsed and refractory myeloma is defined as disease that is nonresponsive while on salvage therapy, or progresses within 60 days of last therapy in patients who have achieved minimal response (MR) or better at some point previously before then progressing in their disease course.¹⁵

Primary refractory myeloma is defined as disease that is nonresponsive in patients who have never achieved a MR or better with any therapy.¹⁵

Relapsed myeloma is defined as previously treated myeloma that progresses and requires the initiation of salvage therapy but does not meet criteria for either "primary refractory myeloma" or "relapsed-and-refractory myeloma" categories.¹⁵

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Living with **multiple myeloma**

Multiple myeloma impacts patients both physically and emotionally. Physical symptoms can include fatigue, pain, fractures and breaks, mobility problems and risk of infection. However, physical symptoms are only part of its impact on the patient. Emotionally, there is often a risk of anxiety and depression, feelings of exclusion, loss of self-esteem or decreased libido.^{16,17}

Daily life can be a struggle, with normal tasks taking longer and patients needing significant day-to-day support. In fact, the emotional, financial and physical impact on people who care for multiple myeloma patients is sometimes just as great as on the patient themselves.¹⁸

“

“On a bad day you just don't feel like doing anything. I don't feel well, no energy. I don't feel like having food. Having multiple myeloma you just have to live with fatigue, you don't have the energy for anything.”

Patient, UK

“

“My house is not as it used to be, I used to enjoy looking at it and considered it to be very pretty. Now I don't care anymore, all these things are no longer important.”

Patient, Spain

“

“I heard someone say it is not the disease that matters, but the way you deal with it.”

Patient, Italy

“

“I remember the moment of diagnosis. When I got into the car, I just started crying with my wife and I couldn't stop.”

Patient, Italy

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What is the prognosis for multiple myeloma?

Although multiple myeloma is **incurable**, the prognosis will depend on the extent or stage of the disease at the time of diagnosis.¹⁹

The five-year **survival rate** of people with multiple myeloma ranges from 23-47% across Europe. However, a patient's age and overall health can impact these survival rates.^{20,21}

Treatment is usually aimed at **preventing** or **addressing** symptoms and complications, **destroying** myeloma cells and **slowing progression** of the disease.^{22,23}

5-year survival rate**23-47%**
survive²⁰

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How is **multiple myeloma** treated?

There is currently **no cure** for multiple myeloma so the primary goal of **treatment** is to **prolong survival** and **manage symptoms** such as bone fractures and lesions, kidney damage, infections and anaemia.^{23,24}

The choice of treatment is influenced by the **age** and **general health** of a patient, the number and types of **previous treatments** they've been given and the **complications** of their disease.²⁴ Treatment options include:

- Chemotherapy³
- Corticosteroids³
- Proteasome inhibitors (PIs)³
- Immunomodulating agents (IMiDs)³
- Radiation³
- Surgery³
- Biologic therapy³
- Stem cell transplant³
- Supportive therapy,³ including bisphosphonates
- HDAC inhibitors³

Often, these treatments are combined and are more effective than any single therapy.²⁵

The number of multiple myeloma treatment options have **increased significantly** over the **last 10 years** and has resulted in **improved survival rates**. In fact, in the last ten years, **survival rates** for multiple myeloma have nearly **doubled**.²⁶

Nevertheless, many patients relapse soon after the completion of initial therapy or do not respond to therapy, and 29% of patients die within one year of diagnosis.⁵

Emerging classes of investigational monoclonal antibodies (mAbs) – such as CD38-directed and anti-CS1 mAbs – may offer a new approach to treating multiple myeloma patients who are relapsed or refractory for whom there is a high unmet need.²⁷

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