# Diagnostic challenges across the multiple myeloma pathway: perspectives of primary care physicians and orthopedic specialists

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### Key Takeaways



This research reveals that MM is not a primary diagnostic consideration for primary care physicians and orthopedic specialists in routine practice. Additionally, >85% of these practitioners do not typically perform the recommended tests for diagnosing MM, which may lead to delays in diagnosis. Providing targeted education on MM symptoms and testing protocols to non-specialists could enhance the timely and accurate diagnosis of MM.

### Conclusions



Disease rarity and a lack of local and national MM diagnostic criteria makes the diagnosis of MM complex, and therefore suboptimal in early identification.



Less than 15% of primary care physicians and orthopedic specialists order the recommended diagnostic tests for MM and additionally face challenges in interpreting the results, which is possibly due to a lack of disease awareness. Orthos rely on hematologist-oncologist colleagues conducting these tests, which could lead to delays in diagnosis and referrals.

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#### Introduction

Multiple myeloma (MM) is challenging to diagnose due to its nonspecific symptoms.<sup>1</sup> Patients often see multiple healthcare professionals prior to diagnosis, including primary care physicians (PCPs), orthopedic specialists (Orthos), nephrologists, rheumatologists, and internal medicine physicians.<sup>2</sup>

Delays in the diagnosis of MM have been associated with an increased risk of complications, which can significantly shorten the window for initiating effective treatment. <sup>3,4</sup> A delayed diagnosis can also lead to higher cancer stage at diagnosis, which is in turn associated with poorer survival.<sup>5</sup> Additionally, patients who face longer diagnostic intervals can have lower disease-free survival, encounter more treatment-related complications and experience a poorer quality of life.<sup>6,7</sup> One UK study reported that MM has the highest number of patients seeing >3 PCPs before specialist referral than any other reported cancer.8

The aim of this research is to better understand the barriers to timely and accurate diagnosis of MM for PCPs and Orthos, to inform solutions that could optimize the early diagnostic pathway.

#### **Methods**

Double-blind, virtual, 1-hour interviews were conducted between 05/02/24 and 05/29/24. Interviewees were required to have knowledge of MM and included 8 PCPs and 7 Orthos from 3 countries [Table 1]

#### Table 1: Country representation for PCPs and Orthos.

Country	PCPs	Orthos
The United States	5	4 5
Australia	3	1
France	0	2

Interviews evaluated three key focus areas, including MM suspicion, diagnostic testing and referral patterns, and educational needs of clinicians

Key words and phrases were identified to capture common themes discussed and quantify the findings. This methodology was used for all collated responses to identify the most common barriers to timely MM diagnosis

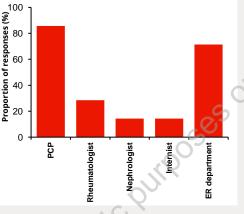
### Results

#### **MM** suspicion

All PCPs reported being an initial point of contact for patients who are later diagnosed with MM. In contrast, Orthos more frequently encounter MM via:

- Referrals of undiagnosed MM patients from other specialists, with 86% of patients reported as referrals from PCPs and 71% by emergency room (ER) departments [Figure 1]
- Referrals of diagnosed MM patients typically from hematologist-oncologists, for the treatment of MM-related skeletal complications

#### Figure 1: Referral sources to Orthos for undiagnosed patients with MM.

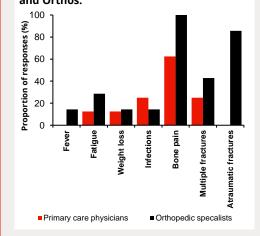


100% of interviewees noted that MM is rare and often not considered in differential diagnoses, especially among PCPs.

Lower back pain, weight loss, and fatigue were universally identified as symptoms of MM. Additionally, 63% of PCPs and all Orthos recognized bone pain, particularly weightbearing pain in the spine or femur, as a key symptom that increases suspicion of MM [Figure 2].

Orthos also identified complex skeletal issues like atraumatic fractures (86%) and multiple fractures (43%), as significant indicators for a possible MM diagnosis [Figure 2].

Figure 2: Symptoms that would increase the suspicion of MM among PCPs and Orthos.



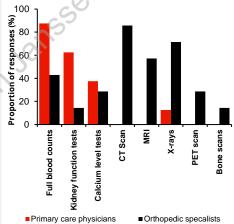
### **Diagnostic testing**

On suspicion of MM, 73% of interviewees reported conducting standard blood tests, including full blood counts (FBC), kidney function tests, and calcium levels.

Standard blood tests were ordered more frequently by PCPs than by Orthos, with FBCs being ordered by 88% of PCPs compared with 43% of Orthos, and kidney function tests being ordered by 63% of PCPs compared with 14% of Orthos.

The majority of Orthos ordered skeletal scans, such as CT scans (86%) or X-rays (71%) [Figure 3].

Figure 3: Tests ordered by PCPs and Orthos as part of initial investigations of MM.



While all PCPs acted on abnormal blood work with further testing or referrals to hematologistoncologists, 63% reported that distinguishing MM from other conditions, based on initial tests, was a challenging process. Clinical indicators identified by PCPs that would primarily raise suspicion of MM include anemia or elevated serum creatinine (62% and 38% respectively).

In contrast, 71% of Orthos stated that MM exhibits distinctive features and was a relatively straight forward to diagnosis based on skeletal scans.

The recommended approach to testing for MM includes both serum or urine protein electrophoresis (SPEP or UPEP, respectively) and serum-free light chain assay tests.9 However, only 13% PCPs and 14% Orthos order both the recommended tests on suspicion of MM [Figure 4].

### **Referral pattern**

The majority of PCPs reported that the scarcity of specialists in their geographical area can affect their ability to make timely referrals and secure specialist reviews for their patients (63%). In contrast, only 28% of Orthos encountered the same access barrier to specialist input.

Several Orthos noted that working within wellintegrated hospital systems naturally promotes suspicion of MM, suggesting that their connections with oncology and hematology departments alongside streamlined referral processes, better position them to manage and refer suspected cases compared with PCPs.

"If someone comes to the hospital, your access to all these services is much higher than if it's done through outpatient basis, So every hospital has a hematologist or oncologist available from just calling them. And they'll generally see them within a day.

"

- Ortho, US

Additionally, some Orthos identified that strong relationships with orthopedic oncologists could be leveraged to directly arrange patient consultations, bypassing electronic referral systems and ensuring timely care for their patients with suspected MM.



"It's important to make relationships with orthopedic oncologists to help expedite patient referrals. I sometimes call them, and they sometimes call me - it's a quicker way to get tests and examinations conducted.

- Ortho, US

#### **Educational needs**

All interviewees reported receiving no MMspecific training outside of medical school. 57% of Orthos gained familiarity of MM from fellowships and residency experience.

While both groups recognize the need for MM education, PCPs outlined multiple challenges in educating peers about suspecting and testing for MM; the most frequent challenge reported was PCPs having varying special interests or educational preferences (63%). PCPs believe that without personal interest in MM, their peers may not be receptive to educational efforts aimed at raising their suspicion of the disease.



Some primary care physicians believe that only those with a personal interest in MM will engage with educational materials. This presents an opportunity for the myeloma community, including pharmaceutical companies, to offer actionable support and guidance to non-specialists, to aid the timely diagnosis of MM.



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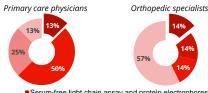
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" "The symptoms are very vague and nonspecific...it is a very difficult thing to diagnose. And it often takes time and is diagnosed sometimes pretty late in the course."

- PCP, US

#### Figure 4: MM-specific diagnostic tests ordered by PCPs and Orthos.



Serum-free light chain assa and protein electropho Serum-free light chain assay only SPEP only UPEP only None ordered

75% of PCPs and 72% of Orthos reported discomfort with interpreting recommended diagnostic MM tests. These tests are often completed by hematologists-oncologists due to expert knowledge, liability, and cost concerns, which may potentially hinder timely diagnosis.

"What would make me comfortable having someone who has much more experience than me...double checking to make sure I'm doing the right thing."

( "

- PCP, US

*"I think there should be more training to* suspect and test for hematologic diseases. I mean, that's why a lot of it I'm not comfortable with.

""

- PCP, Australia

In contrast, Orthos did not raise challenges related to educating peers about suspecting and testing for MM. In addition, most Orthos were aligned on their preference for interactive learning formats directly from hematologistsoncologists.

67% of interviewees identified referral criteria, guidance, or testing protocols as potential tools to support education.

Multiple Myeloma



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