

A CASE FOR CHANGE IN PATIENT CARE

THE MULTIPLE MYELOMA CALL-TO-ACTION

A Johnson & Johnson Initiative,
Developed with a Global Expert
Collaboration Council



PHARMACEUTICAL COMPANIES OF
Johnson & Johnson

FOREWORD

Over the past few years we have seen tremendous advances in the diagnosis and treatment of multiple myeloma. Our increased scientific understanding of how myeloma develops, the introduction of new diagnostic tools and an array of treatments with novel mechanisms of action, have led to an increase in survival and quality of life for patients.

This rapidly changing landscape also brings new challenges and opportunities for the global multiple myeloma community: patients, their caregivers, healthcare providers, researchers, the pharmaceutical industry, regulatory authorities and patient advocacy organizations.

Each challenge and opportunity requires careful consideration, collaboration and action to effectively enable change. To this end, I have had the privilege of chairing the Global MM Collaboration Council, a group of experts from across geographies and disciplines, each bringing unique perspectives from across the patient pathway. We collaborated to identify critical challenges and areas of focus to shape future solutions, united in our desire to provide equitable care for all patients living with myeloma and ultimately aim for cure.

We are incredibly excited to launch this first-of-its kind global Call-to-Action and hope this will inspire action for all. Within this document you will find our conclusions, priorities and suggested recommendations for care improvement.

We look forward to working with the global community through this Call-to-Action, guiding the multiple myeloma landscape towards cure - for every person whose life is touched by this disease.

Faith Davies,



Global MM Collaboration Council Chairperson
Director, Center for Blood Cancers, New York University

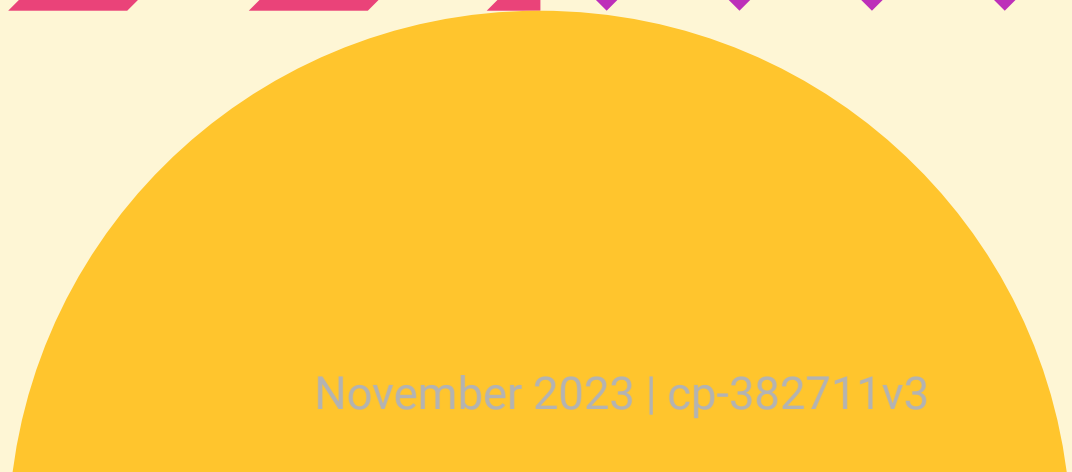
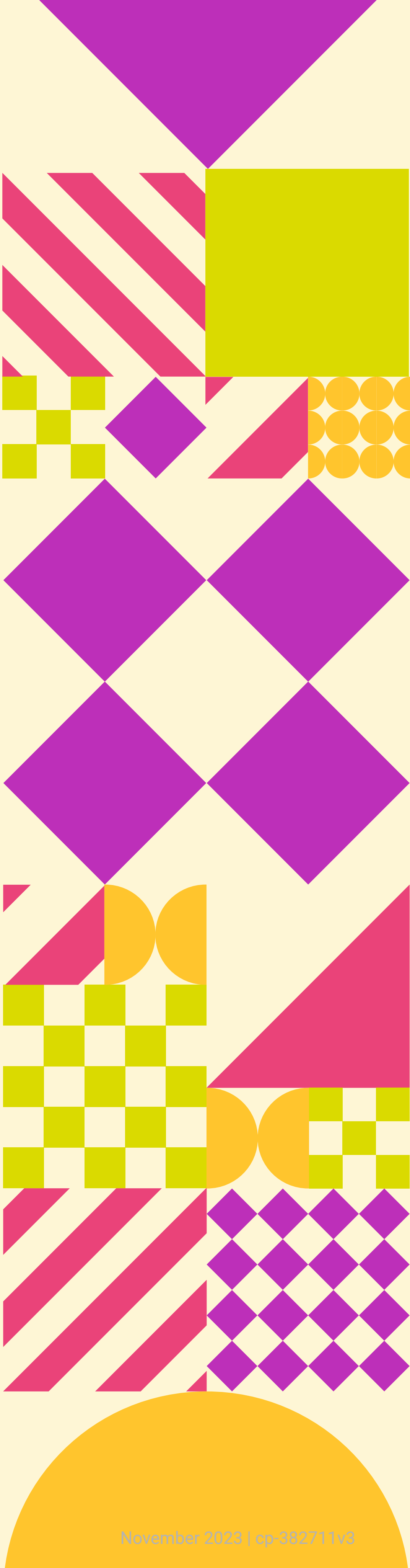


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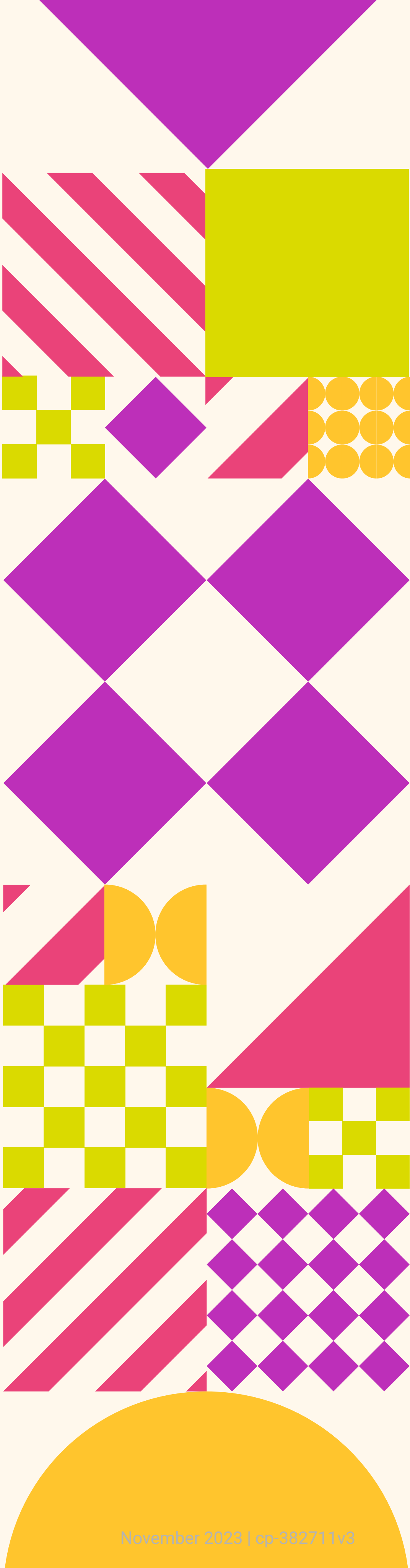
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Johnson & Johnson is committed to changing the course of multiple myeloma. This initiative strives to identify and address global unmet needs in multiple myeloma care, with a focus on supporting patients and healthcare systems beyond treatment alone.



INTRODUCTION

Our ultimate goal is not to treat multiple myeloma. It is to cure it.^{1*}

Globally, many stakeholders commit considerable effort towards improving patient outcomes and experience in multiple myeloma. Multiple initiatives have been launched by patient advocacy organizations, academic institutions, and the healthcare industry, many of which have added substantial value to the myeloma landscape. However, for stakeholders across the globe, no single collaborative approach that targets the most critical unmet needs in multiple myeloma care exists today.

This Call-to-Action outlines high-priority unmet needs and recommended areas of focus for the global multiple myeloma community, as identified by the Collaboration Council.[†] Through addressing the most prominent unmet needs to advance patient care, outcomes, and experience, the goal is to accelerate progress towards cure for people living with multiple myeloma.

* "Cure" in this document is defined as minimum of 5 years disease-free from date of documented minimal residual disease (MRD) negativity at a sensitivity level of 10^{-6} .¹

† Throughout this document, the Global MM Collaboration Council will be referred to as the Collaboration Council.



Development Approach

This document was developed through a combination of primary insights and expert opinions in the field of multiple myeloma with secondary research from targeted literature reviews and supplementary desk research **(see Appendix I)**.

The Collaboration Council reviewed the primary and secondary research and shared their expert opinions to shape this Call-to-Action. Collaboration points included:

- **Collaboration Council initial meeting** – Reviewed and reflected on the challenges and unmet needs identified from the research
- **Live working session** – Identified priority unmet needs in multiple myeloma, their potential drivers, and how these can lead to disparities observed today
- **Asynchronous review and virtual engagement** – Discussed goals to improve multiple myeloma care and established Call-to-Action areas of focus to drive collective improvements globally

Johnson & Johnson would like to thank all Collaboration Council members for their feedback and commitment to the creation of this Call-to-Action.

This Call-to-Action is intended to serve as a baseline from which to measure progress in advancing multiple myeloma care over the next decade.



Introducing the Global MM Collaboration Council

Johnson & Johnson established the Global MM Collaboration Council, which combined experts from a wide range of geographies and disciplines, to gather perspectives and insights on multiple myeloma.

Chaired by Faith Davies, Professor of Medicine at New York University (NYU), the Collaboration Council brings together patient advocates, clinical leaders, researchers, and policy experts from 10 countries across 5 continents, and provides the driving force behind this Call-to-Action.

The Collaboration Council worked together to identify the most critical unmet needs, from their perspective, and recommended areas of focus for the global multiple myeloma community, to advance patient care and outcomes. Opinions of Collaboration Council members are included throughout this document to provide additional context and perspective on referenced data. Call-to-Action areas of focus should be considered broadly across multiple stakeholder groups.



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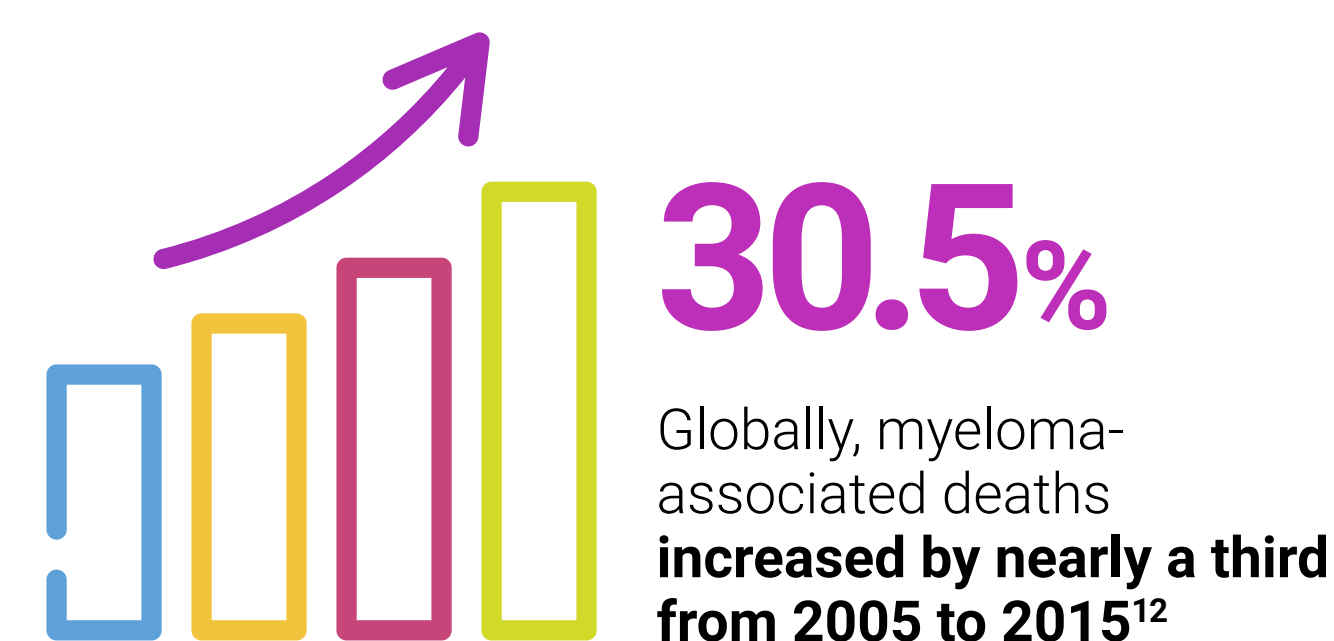


DISEASE BACKGROUND: THE MULTIPLE MYELOMA DIFFERENCE

Globally, 10% of patients with blood cancers are diagnosed with multiple myeloma,² representing 1% of patients with cancer overall.^{2,3} Multiple myeloma is often diagnosed late,⁴ possibly due to the number of non-specific symptoms that cause physicians to suspect more common diseases and illnesses. Although responses to treatments are improving and remission periods are lengthening,⁵ most patients will eventually relapse.⁶ Currently, multiple myeloma remains an incurable disease.⁶

The burden of disease increases over time. As multiple myeloma progresses, its symptoms and their impact become more severe.⁷

Incidence of multiple myeloma varies considerably between individuals of different ages and populations,⁸ with Black populations having twice the risk of multiple myeloma than white populations in a US population-based study.^{9,10} Multiple myeloma incidence is on the rise due to aging populations.^{8,11} Globally, from 2005-2015, an increase in myeloma-associated deaths was reported.¹² In the US, rates of mortality are higher for people from minority ethnic backgrounds,¹³ representing a clear example of disparity in multiple myeloma care.



The heterogeneity of this disease and its variation among those it affects greatly influence prognoses.¹⁴

Treatment guidelines for newly diagnosed patients currently focus on transplant eligibility and regimens containing proteasome inhibitors (PIs), immunomodulatory drugs (IMiDs), and anti-CD38 monoclonal antibodies.¹⁵ However, following multiple courses and combinations of treatment, there is no clear standard of care for patients with relapsed or refractory multiple myeloma (RRMM).^{15,16} Real-world evidence corroborates this; in one study of patients with triple-class exposed RRMM, 92 unique combinations of standard of care treatments were prescribed.¹⁶



In one real-world study of patients with triple-class exposed RRMM, **92 combinations** of standard of care treatments were prescribed.¹⁶

With such a large number of combinations, practitioners can struggle to optimize treatment strategies.

Disparities in wealth, racial background, access to treatment, HCP training, insurance coverage, and geographic location all influence the ability of practitioners to optimize care.¹⁷ For these reasons and more, patients with multiple myeloma in low- and middle-income countries have the least optimistic prognoses.

Multiple myeloma has historically been associated with the lowest patient health-related quality of life of all blood cancers.¹⁸ As the disease progresses over time, symptoms (such as bone pain and fatigue) and complications (such as infections) can worsen, increasingly affecting physical and emotional well-being.^{7,19} The burden of this incurable disease on patients, their loved ones, healthcare systems, and wider society are significant from the moment of diagnosis and worsen with each line of therapy.

There are many challenges in the future care of myeloma. Yet, each represents an opportunity to improve diagnosis, treatment, and management of patients with multiple myeloma. Through global collaboration and communication, one day every myeloma patient may have an opportunity to reach cure. This Call-to-Action represents the opening remarks in this interdisciplinary conversation.

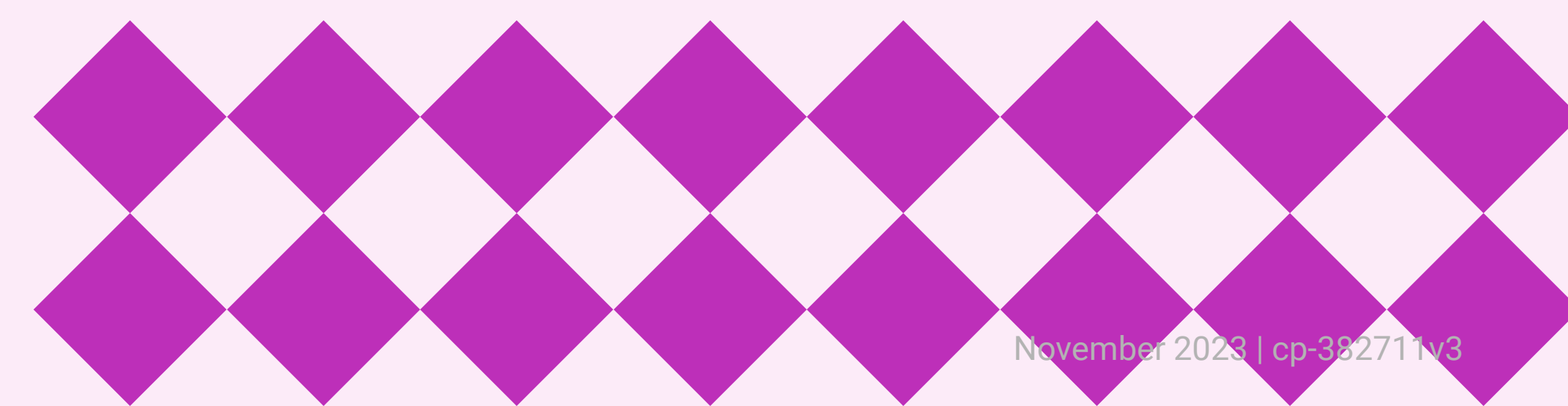


UNMET NEED 1: DELAYS IN TIMELY DIAGNOSIS OF MULTIPLE MYELOMA

Delays in diagnosis of patients with multiple myeloma impact both complications and outcomes²⁰

Delays in diagnosis of multiple myeloma can negatively affect outcomes.^{10,20,21} Multiple myeloma can be a challenging disease to diagnose due to non-specific symptoms and comorbidities that may mask its presence. In a real-world study of 2,626 patients with newly diagnosed multiple myeloma (NDMM) in the UK, nearly half of patients presenting with bone pain waited approximately 7 months for a diagnosis.²² Primary care physician (PCP) awareness of multiple myeloma may be low, potentially limiting appropriate referrals to hematologists.²³

Technology will play an integral part in advancing myeloma diagnosis.^{10,24} From enhancing the impact and reach of education, to providing new predictive techniques, the application of novel technology could contribute significantly to progressing the multiple myeloma treatment landscape.



UNMET NEED 1: DELAYS IN TIMELY DIAGNOSIS OF MULTIPLE MYELOMA

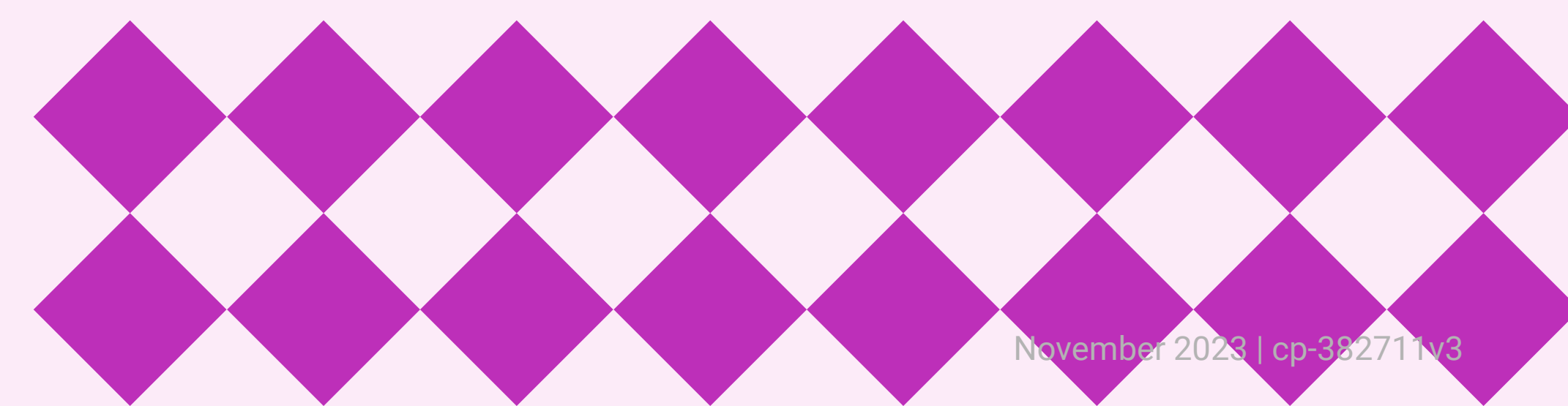
CALL-TO-ACTION AREAS OF FOCUS:

Increase education and awareness to drive earlier diagnosis

- Utilize existing and develop new educational resources for non-myeloma specialists, to increase index of suspicion for multiple myeloma and awareness of risk-stratified tools, that can help physicians to flag high-risk patients.
- Improve awareness of how comorbidities and confounding symptoms of other conditions can mask multiple myeloma.
- Foster collaboration among medical associations and patient advocacy organizations in developing CME-accredited courses, to educate on the importance of timely diagnosis.

Improve access to testing and expedite referral to specialists

- Increase non-myeloma specialist access to the most sensitive multiple myeloma diagnostic testing combinations.
- Enhance access to specialist multiple myeloma intervention by establishing a standardized process at referring centers, in collaboration with medical societies and regulatory bodies.
- Create localized academic support and outreach programs to community networks to improve multiple myeloma diagnoses and patient outcomes.
- Identify actionable solutions that reduce ethnic and socioeconomic disparities to provide equitable care for all patients with multiple myeloma.



UNMET NEED 2: COMPLEX TREATMENT DECISION-MAKING IN MULTIPLE MYELOMA

The complex myeloma treatment paradigm can impact optimal treatment decision-making^{25,26}

Optimization of multiple myeloma treatment strategies can be challenging due to the increasing number of novel agents and possible treatment combinations in conjunction with the inherent complexity of the disease itself and the highly heterogeneous patient population.²⁵⁻²⁸ Treatment choice becomes more complex with disease progression and patient comorbidity and frailty, alongside drug refractoriness.^{29,30} Access to therapy can be hindered by local reimbursement policies and lack of access to clinical trials, causing disparity in care.³¹⁻³⁴ A lack of clear consensus on treatment algorithm and disease markers limits the ability for treatments to be optimized for each individual.³⁵

The multiple myeloma treatment landscape is further complicated by the lack of universally determined surrogate measures and consensus on therapy goals.^{36,37} Immunodeficiency caused by the disease itself and the cumulative result of treatment regimens pose a significant infection risk for patients with multiple myeloma,³⁸ significantly impacting clinical outcomes.³⁹



UNMET NEED 2: COMPLEX TREATMENT DECISION-MAKING IN MULTIPLE MYELOMA

CALL-TO-ACTION AREAS OF FOCUS:

Enhance understanding of treatment response for an individualized approach

- Power clinical studies to enable effective subgroup analysis that explores the impact of treatment sequencing on outcomes and supports personalized treatment strategies, e.g., for patients with high-risk cytogenetics, extramedullary disease, etc.
- Redefine the treatment algorithm, incorporating novel therapies to drive the treatment landscape towards cure, creating a clear consensus from the multiple myeloma community on risk stratification measures.
- Develop strategies that improve access to the best available therapies globally, seeking equitable outcomes for every myeloma patient, by encouraging greater investments in research and development, and clinical trial infrastructure, as well as the coverage of standard of care treatments and specialized procedures.
- Ensure enhanced understanding and adoption of guidelines by all healthcare professionals to reduce the risk of infection in patients with multiple myeloma.
- Continue investment into the research of innovative therapies that limit the impact of infection on patients with multiple myeloma.

Drive consensus on utilization of minimal residual disease and other surrogate measures

- Drive consensus on the integration of minimal residual disease (MRD) into clinical trial design, by exploring optimal timing and testing techniques for MRD as a finite endpoint, to predict treatment-free intervals and inform consensus on duration of treatments.
- As key MRD decision-making studies are completed, create guidance for the use of MRD and encourage regulatory bodies, medical societies, and healthcare systems to adapt lab capabilities so MRD testing can be accessed globally.
- Educate on the role of MRD as it evolves from use in clinical trials to clinical practice and develop patient-focused educational materials, so myeloma specialists can understand and communicate about MRD with patients.
- Continue exploration of existing and novel biomarkers to further prognostic capability and inform treatment decision-making.



UNMET NEED 3: LIMITED APPLICABILITY AND DIVERSITY OF CLINICAL TRIALS

Multiple myeloma trials often do not reflect real-world populations, limiting application of results in clinical practice⁴⁰

Patients often fail to meet inclusion criteria due to comorbidity and/or frailty, and inclusion criteria are often too narrow to incorporate a significant proportion of patients with multiple myeloma into test populations.^{40,41}

Local availability of appropriate trial resources in middle- and low-income countries, as well as suboptimal infrastructure and staffing in smaller and rural institutions, can further limit trial inclusion and representation of patients from economically disadvantaged countries and geographies in multiple myeloma trials.^{42,43}



UNMET NEED 3: LIMITED APPLICABILITY AND DIVERSITY OF CLINICAL TRIALS

CALL-TO-ACTION AREAS OF FOCUS:

Reinforce access, diversity, and equality across clinical trial populations

- Create a clinical trial network that offers clear regulatory standards and guidance, combined with the necessary infrastructure and staff education to support the expansion of clinical trials into underserved communities.
- Strongly encourage collaboration between medical societies and research institutions to help countries prioritize available resources and improve access to treatments.
- Communicate and educate on trial availability, objectives, and execution to broad audiences, enabling discussion between healthcare professionals (HCPs) and patients to ensure more diverse participation in clinical trials.
- Increase awareness of sub-population and minority under-represented groups in myeloma trials to drive broader representation of these groups.
- Highlight the impact in global care disparity by using clear metrics, targeting policymakers, regulators, payors, and wider non-specialist audiences.

Increase prioritization of outcomes related to patient experience

- Drive collection of quality-of-life assessments as key clinical trial endpoints, to better understand patient experience and build a more complete and balanced picture of how efficacy and treatment response align with patient needs.
- Publicize and communicate the patient experience in clinical trials, to broaden understanding of the impact on multiple myeloma trials on quality of life.
- Establish routine integration of patient opinions to improve better representation of patient needs and insights into study design, selecting more meaningful endpoints in clinical trials.
- Elevate the patient voice and quality of life as an essential goal of therapy, i.e., by developing simple, standardized tools to regularly assess quality of life in clinical practice, for example, through enhanced utilization of simplified patient-reported outcomes (PROs).
- Generate real-world data on quality-of-life measures (e.g., health-related quality of life and PROs) to complement clinical trial data for a holistic picture.

Improve applicability and relevance of clinical trial data in clinical practice

- Improve the generalizability of trial data, by working to modify standard inclusion and exclusion criteria.
- Design smaller studies for specific patient sub-populations (e.g., frail patients), furthering the ability to individualize treatment strategies.
- Consider differences in treatment discontinuation and toxicity between the real world and in clinical trials to support careful development of treatment strategies, accounting for the risk of adverse events and toxicity in each individual patient.
- Collect real-world evidence in parallel to clinical trials across a diverse range of geographies and socioeconomic populations, so that myeloma specialists can create optimal, individualized treatment strategies based on comprehensive and representative data.



UNMET NEED 4: INCONSISTENT HOLISTIC MANAGEMENT OF MULTIPLE MYELOMA

Current care models may not effectively address the broader needs of patients consistently, including psychosocial support and shared decision-making⁴⁴

With improved survival outcomes in multiple myeloma, survivorship starts at diagnosis due to the life-long burden associated with the disease.²⁶ Focus on quality of life is increasing through the use of patient-reported outcomes (PROs).^{45,46}

A holistic care model may provide an opportunity to shift burden away from patients and non-professional caregivers, offering support psychologically, socially, physically, spiritually, and financially.⁴⁷⁻⁴⁹ However, access to multidisciplinary team (MDT) care can be limited by socioeconomic status and geographical location, demonstrating inconsistent adoption of MDT care.⁵⁰ MDTs combine the unique abilities of a variety of specialists, are tailored to patients' needs, and offer an opportunity to improve patient experience and associated outcomes.⁵¹ MDT members include a variety of professionals adapted to patient requirements, i.e., MDTs for patients with NDMM may include transplant and intensive care specialists compared with RRMM MDTs, which may include social workers, palliative care, and spiritual support in addition to the core team of doctors, nurses, and pharmacists.

Improving HCP-patient communication can strengthen the practice of shared decision-making (SDM), which is essential to ensure both patient and doctor are aware and conscious of the myriad factors to be considered when creating an individual treatment strategy.⁵²



UNMET NEED 4: INCONSISTENT HOLISTIC MANAGEMENT OF MULTIPLE MYELOMA

CALL-TO-ACTION AREAS OF FOCUS:

Ensure awareness of patient needs along the multiple myeloma journey

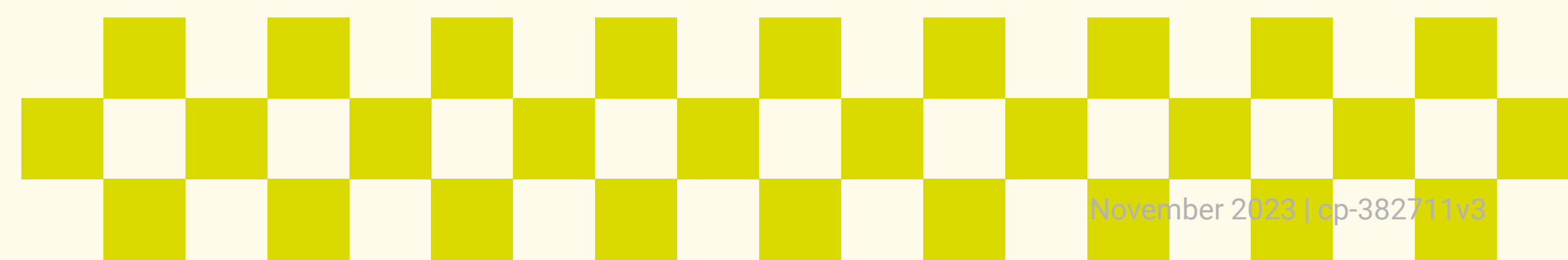
- Develop simple and standardized tools (such as simplified PROs) to be appropriately integrated into electronic medical records to consistently assess patient experience to meet their individual needs as they evolve over time.
- Guide patients to the correct HCP specialty by improving the integration of signposting throughout the multiple myeloma care pathway, e.g., via:
 - “Nurse navigators” to better guide patients to existing services within regions.
 - A centralized, global multiple myeloma portal to explore relevant and reputable services in each region.
 - A country-specific helpline to provide information and support to patients who would struggle to access online resources, with integrated interpretation services.
 - Creation of a network of patient group organizations for each country with support from established global multiple myeloma organizations such as the International Myeloma Foundation (IMF) and Myeloma Patients Europe (MPE).

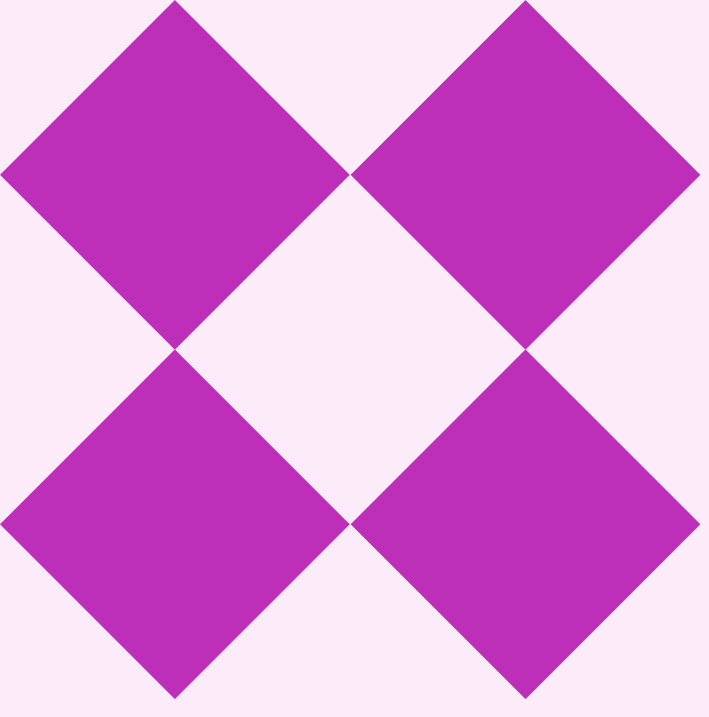
Drive consistent integration and access to MDTs at multiple myeloma care centers

- Develop guidance for the implementation and integration of holistic care models involving MDTs in multiple myeloma care centers to better support patients and reduce burden for patients and caregivers, utilizing technology where possible (e.g., telehealth communications) to support access to established MDTs for remote or rural communities.
- Encourage initiatives that work to integrate MDT approaches to care to improve patient experience and improve patient outcomes. Emphasize the importance of continuity of care within the MDT to further improve patient experience.
- Foster collaboration within the multiple myeloma community, defining standards of care to provide benefit to patients and their caregivers, improving their outcomes and their quality of life.

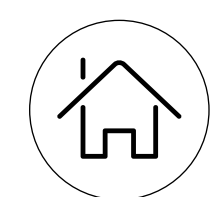
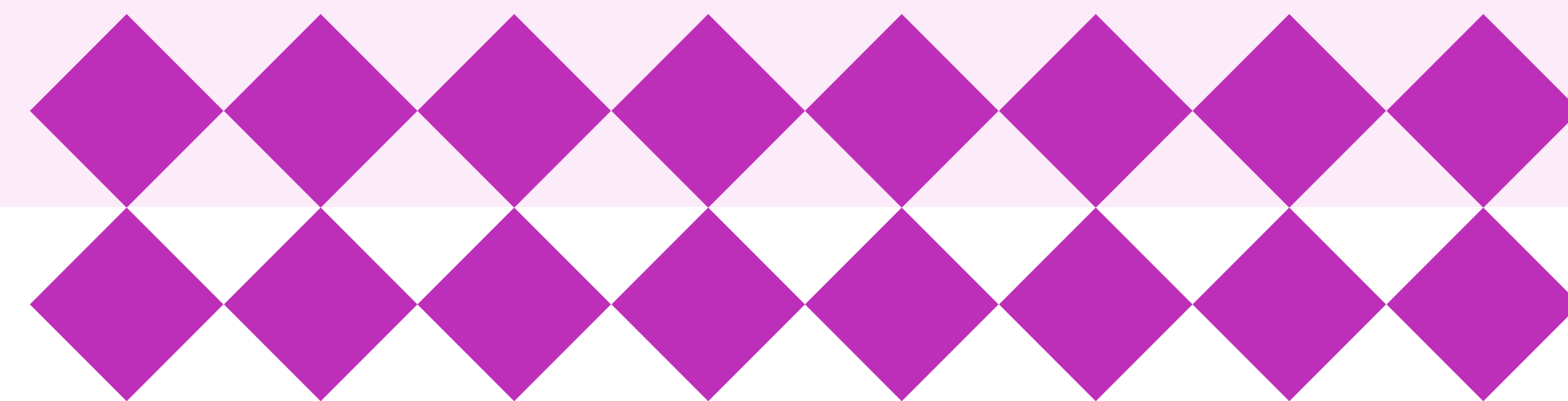
Establish the value of SDM in clinical practice

- Patient advocacy organizations can partner with healthcare institutions and medical societies to help raise awareness of SDM among the multiple myeloma community and more specifically, myeloma treatment teams.
- Conduct a real-world study in SDM, specific to multiple myeloma, to further validate its use within clinical practice.
- Develop SDM tools for both HCPs and patients, aid communication, and improve HCP-patient relationships, such as through the use of key question guides.
- Incorporate SDM into multiple myeloma HCP training programs, helping to raise awareness of the importance of SDM and improve understanding among HCPs.





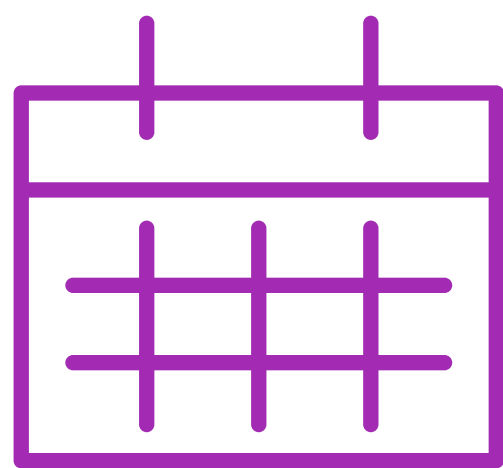
UNMET NEED 1: DELAYS IN TIMELY DIAGNOSIS OF MULTIPLE MYELOMA



UNMET NEED 1: DELAYS IN TIMELY DIAGNOSIS OF MULTIPLE MYELOMA

Delays in diagnosis of multiple myeloma are common and can negatively affect outcomes

Delays until diagnosis of multiple myeloma have been associated with an increased risk of complications, extramedullary disease, and lower disease-free survival.^{20,21} In a UK real-world cohort study of 2,626 patients with multiple myeloma, nearly half of all of patients presenting with bone pain waited approximately 7 months for a diagnosis.²² A recent survey by Myeloma Patients Europe (MPE) found that over a third of patients with multiple myeloma continue to report delays to their diagnosis, with nearly a quarter reporting that they waited 5 months or more.²³



In a UK real-world cohort study of 2,626 patients with multiple myeloma, nearly half of all of patients presenting with bone pain **waited approximately 7 months** for a diagnosis.²²

“I could say that I was lucky, I am an asymptomatic high-risk patient and I had gotten diagnosed in a short period of time, this is not the case for many other patients.”

- 47 year-old female patient with multiple myeloma, Serbia^{53‡}

As the first point of contact, non-myeloma specialists remain critical to achieving a timely multiple myeloma diagnosis

A patient survey from MPE found that 63% of patients initially presented to primary care physicians (PCPs).²³ Most PCPs, however, rarely encounter multiple myeloma in their clinical practice – a general practitioner in the United Kingdom will diagnose multiple myeloma on average once every 5 years.¹⁰

Low awareness of multiple myeloma in PCPs can cause significant delays to diagnosis.^{23,54} MPE found that 65% of hematologists believe there is a lack of awareness from PCPs regarding multiple myeloma.²³ In one UK study, the diagnostic interval was reported to be twice as long in patients who initially present to their PCP versus a hematologist.²⁰ Awareness of multiple myeloma and its precursor condition, monoclonal gammopathy of undetermined significance or MGUS, is low among PCPs. Furthermore, many PCPs have indicated that they would not feel comfortable solely monitoring MGUS patients of low/low-intermediate risk.⁵⁵

Multiple myeloma has the highest number of patients who receive more than 3 consultations prior to a specialist referral of any other reported cancer⁵⁶ and is associated with longer primary care interval time.⁵⁷

Awareness of multiple myeloma is also low among the public, with 84% of patients with multiple myeloma in an international prospective survey not knowing about the disease prior to diagnosis and relying on their doctors for multiple myeloma-related information.⁵⁸

Multiple myeloma is a difficult disease for non-myeloma specialists (such as PCPs and general community oncologists) to diagnose, as typical “red flag” symptoms are not present in multiple myeloma as they are in other cancers. The vague nature of how this disease presents is a considerable barrier to timely diagnosis. Moreover, the non-specific symptoms of multiple myeloma are also common in other comorbidities, which can lead to a confounding diagnosis.¹⁰



Multiple myeloma has the highest number of patients who receive **more than 3 consultations** prior to a specialist referral of any other reported cancer⁵⁶



CALL-TO-ACTION: IMPROVE ACCESS TO TESTING AND EXPEDITED REFERRAL TO SPECIALISTS

- Increase non-myeloma specialist access to the most sensitive multiple myeloma diagnostic testing combinations.
- Enhance access to specialist multiple myeloma intervention by establishing a standardized process at referring centers in collaboration with medical societies and regulatory bodies.
- Identify actionable solutions that reduce ethnic and socioeconomic disparities to provide equitable care for all patients with multiple myeloma.

[‡] Anonymous insights gathered through a survey questionnaire via Myeloma Patients Europe (MPE) with patients living with multiple myeloma (n=4), across 4 countries in Europe. Survey conducted in April 2023.

UNMET NEED 1: DELAYS IN TIMELY DIAGNOSIS OF MULTIPLE MYELOMA

As multiple myeloma is often diagnosed later in life, symptoms including back pain, bone pain, fatigue, and infections¹⁰ may not at first raise any suspicion in the patient or their physician.²³

Osteoporosis and degenerative vertebral disorders, which are common in the elderly, have effects and complications that resemble multiple myeloma, masking it when both are present.⁵⁴ Twenty percent of multiple myeloma cases present with a pathological fracture, and MGUS increases the risk of vertebral fracture by a factor of 2.5. For patients with newly diagnosed osteoporosis, 1 in 20 has underlying multiple myeloma or MGUS.⁵⁹ This subsequently leads to referral delays to a hematologist, potentially due to confounding diagnoses.⁶⁰

“The orthopedic doctor diagnosed me with degenerative hip disease, and I was treated with physical therapy and pain medication for 2 years.”

- 60+ year-old female patient with multiple myeloma, US ⁶¹

When symptoms and basic laboratory findings might be suggestive of multiple myeloma, the PCP should investigate further and order extended diagnostics, including a number of protein assays to eliminate other possibilities.²⁴ Laboratory workup should include serum protein electrophoresis, immunoglobulin-free light chain assay, and immunofixation. Combining these tests substantially increases diagnostic sensitivity of multiple myeloma and may reduce treatment delay.²⁴ According to a study from MPE, a third of hematologists reported that limited access to testing can slow diagnosis, highlighting another unmet need in myeloma testing.²³



CALL-TO-ACTION: INCREASE EDUCATION AND AWARENESS TO DRIVE EARLIER DIAGNOSIS

- Utilize existing and develop new educational resources for non-myeloma specialists, to increase index of suspicion for multiple myeloma.
- Improve awareness of how comorbidities and confounding symptoms of other conditions can mask multiple myeloma.

UNMET NEED 1: DELAYS IN TIMELY DIAGNOSIS OF MULTIPLE MYELOMA

Disparities in access to care disproportionately affect racial minorities, ethnic minorities, and people of lower socioeconomic status

In the US, Black patients account for 20% of multiple myeloma cases⁶² despite making up only 13% of the total population.⁶³ Black patients are more likely to experience diagnostic delays⁶⁴ and are less likely than white patients to undergo a complete diagnostic evaluation.²⁴ The probability of 3 or more consultations before a referral to a specialist is greater if the patient is of an ethnic minority.⁵⁶ Subsequently, this causes delays in referrals to specialist care.⁶⁵ However, based on a study in Veterans Affairs hospitals, when Black patients have equal access to care, they often have better survival outcomes than their white counterparts.⁶⁶ Taken together, these facts begin to outline the considerable disparities in care for patients with multiple myeloma of an ethnic minority.

According to a study from MPE, the accessibility of care remains a contributing factor to disparities experienced in multiple myeloma.²³

Accessibility is particularly challenging in countries with a mixed system of public and private health insurance, and patients often find difficulty in accessing public health care. This may create further disparity between patients of higher or lower socioeconomic status, as patients with fewer financial resources more often utilize public health care.²³

Advancing multiple myeloma diagnosis through education and technology

Multiple myeloma is rare, and vague in presentation.¹⁰ Education of PCPs may increase disease awareness and reduce diagnostic delay.

Collaborative development of continuing medical education (CME)-accredited courses could improve awareness of the signs of multiple myeloma among PCPs. As in all systems, communication is critical to collaboration, and supporting the flow of knowledge between primary and specialty care is a clear priority. One such example of an initiative to bridge the gap between HCPs is from the UK Myeloma Academy, which provides educational content tailored to a number of different HCPs.⁶⁷

Unlike many other cancers, routine screening for multiple myeloma is not recommended,²⁴ despite the existence of a benign precursor condition (MGUS), for which populations could, in theory, be screened for.⁶⁸ The risk of progression from MGUS to multiple myeloma is only around 1% per year,⁶⁸ as a result, over-testing of MGUS could lead to an increased psychological burden on patients and financial burden on healthcare systems.²⁴ The iSTOP MM trial is a large Icelandic population-based study that is currently assessing whether MGUS screening provides clinical benefit or impacts psychological well-being.⁶⁹ Advancements in genetic investigation technologies may help screening occur more accurately, particularly for those who are deemed highest-risk for progression from MGUS to multiple myeloma (e.g., based on age and race).⁶⁸

Any genetic testing must be provided at minimal cost to individuals and healthcare systems. However, it is likely that increasing multiple myeloma awareness overall will support a more appropriate population-level disease mitigation strategy, alongside studies to identify disparities in precision medicine.⁷⁰

Many awareness initiatives and outreach programs have resulted in improvements to multiple myeloma referral times, facilitating earlier treatment initiation.^{59,71} As in other cancers, early treatment could reduce disease progression and related mortality.⁷²

“Better communication between departments in the hospital could have saved me nearly 6 months, if the orthopedic department had consulted experts on blood diseases.”

- 75 year-old male patient with multiple myeloma, Norway^{53‡}

[‡] Anonymous insights gathered through a survey questionnaire via Myeloma Patients Europe (MPE) with patients living with multiple myeloma (n=4), across 4 countries in Europe. Survey conducted in April 2023.

UNMET NEED 1: DELAYS IN TIMELY DIAGNOSIS OF MULTIPLE MYELOMA

In particular settings, such as fracture-liaison services, there is clear value in the implementation of multiple myeloma screening (**Case Study 1**).⁵⁹

From a large case control study using electronic records, multiple myeloma symptoms were found to individually have a positive predictive value of less than 1%.⁷³ When combined with abnormalities in blood tests, their predictive value increases.⁷³ This suggests that further development of tools to capture and stratify patients based on their risk level may help non-myeloma specialists to overcome some of the challenges in identifying and diagnosing multiple myeloma.¹⁰ Such tools could even work with electronic medical record systems, by automatically flagging potential myeloma cases for review.²⁴ Electronic trigger-based interventions have been shown to be effective in both colorectal and prostate cancer.⁷⁴

The Multiple Myeloma Research Foundation (MMRF) and Intermountain Healthcare conducted a study which found that a community health system can provide sufficient high-quality information to power a myeloma-specific clinical decision support tool.⁷⁵ The MMRF seeks to recruit additional integrated delivery networks to obtain the patients to power more generalized functionality.⁷⁵

CASE STUDY 1:

MYELOMA SCREENING AND REFERRALS IN FRACTURE LIAISON SERVICES (FLS)

There is an opportunity to share examples of best practices among various specialties to enhance the diagnosis and referral process of multiple myeloma, and potentially introduce minimum standards of care with appropriate audit and review.

For example, both multiple myeloma and MGUS drive bone fragility and there may be a potential value in screening for multiple myeloma in FLS. In a UK study, FLS-initiated multiple myeloma screening identified 1 per 195 new multiple myeloma cases for immediate referral and 1 per 13 new MGUS cases for annual surveillance, that may have otherwise been missed.⁵⁹

Further exploration into cross-specialty healthcare intervention is needed to understand the benefits of screening in real-world clinical practice.



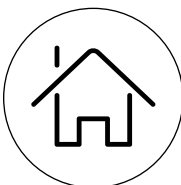
CALL-TO-ACTION: INCREASE EDUCATION AND AWARENESS TO DRIVE EARLIER DIAGNOSIS

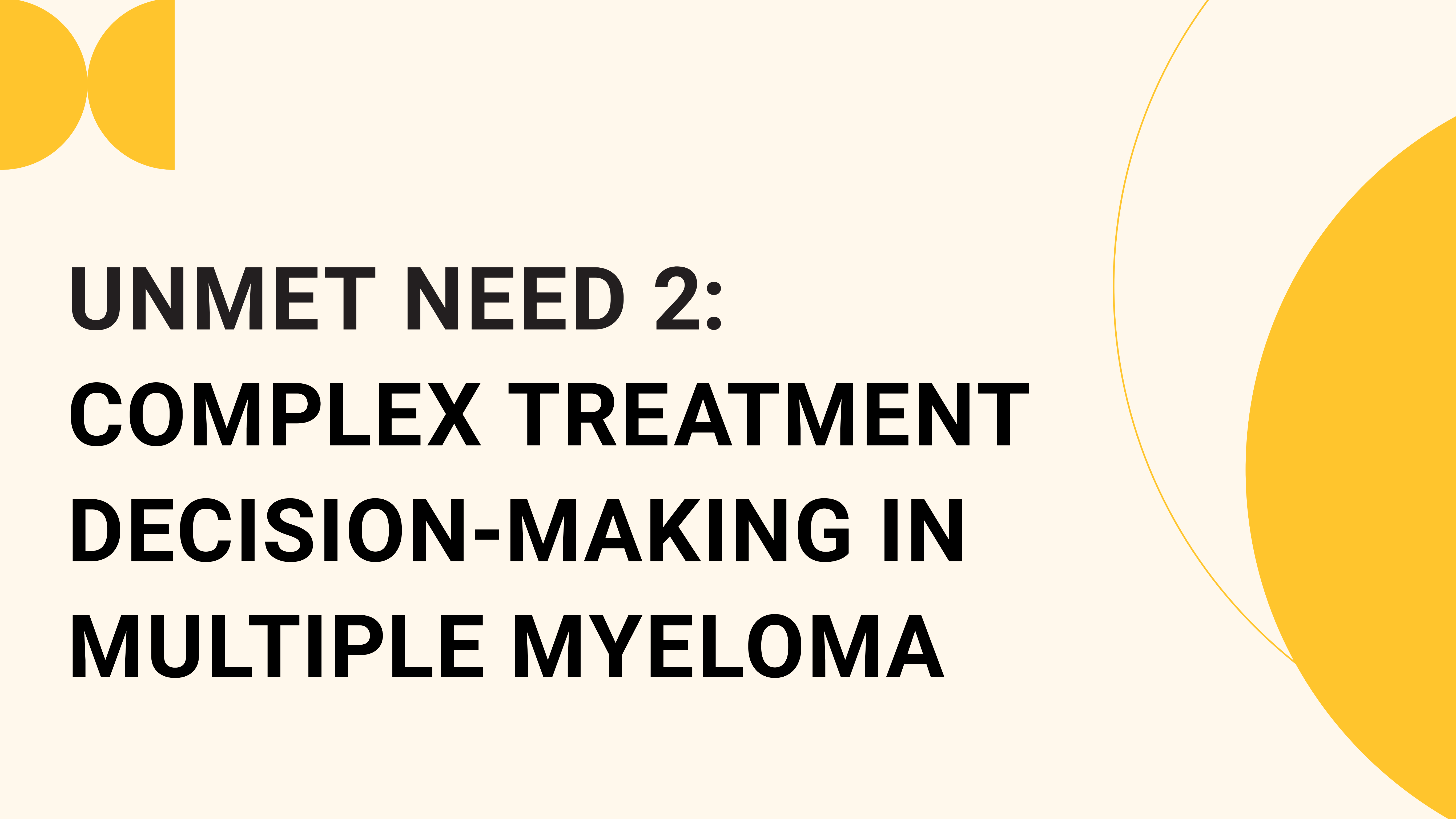
- Foster collaboration among medical associations and patient advocacy organizations in developing CME-accredited courses, to educate on the importance of timely diagnosis.
- Continue the development and awareness of risk-stratified tools that can help physicians flag high-risk patients, i.e., risk stratification based on their presenting symptoms and blood work.



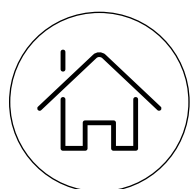
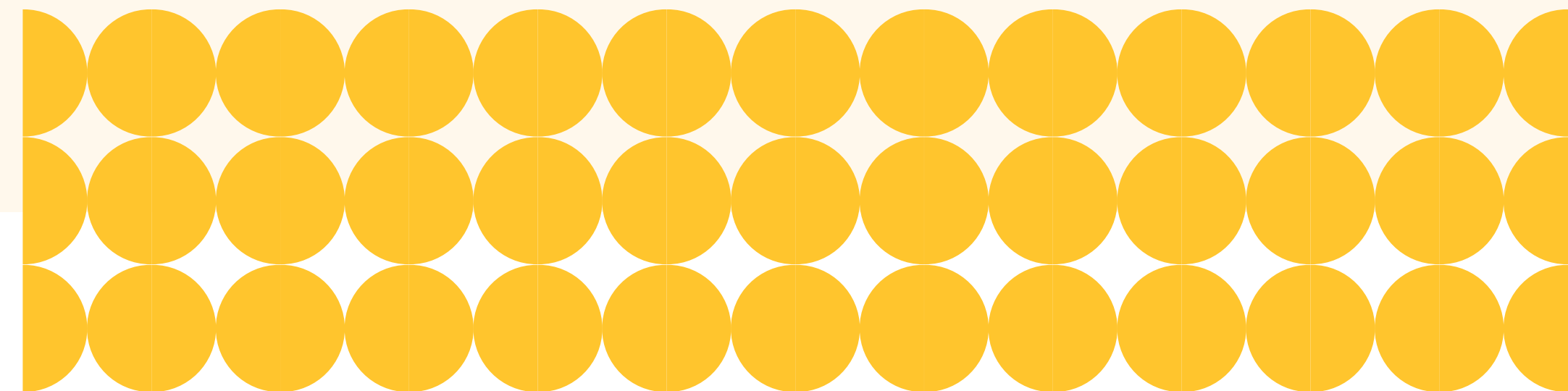
CALL-TO-ACTION: IMPROVE ACCESS TO TESTING AND EXPEDITED REFERRAL TO SPECIALISTS

- Create localized academic support and outreach programs to community networks to improve multiple myeloma diagnoses and patient outcomes.





UNMET NEED 2: COMPLEX TREATMENT DECISION-MAKING IN MULTIPLE MYELOMA



UNMET NEED 2: COMPLEX TREATMENT DECISION-MAKING IN MULTIPLE MYELOMA

The complexity of the multiple myeloma treatment paradigm will increase with the introduction of additional agents

The treatment landscape for patients with multiple myeloma is broadening, and outcomes are improving.^{25,26} However, the increase in available treatment options²⁷ has led to significant complexity, which is proving challenging for practitioners to navigate.^{25,27,28} Supporting highly heterogeneous groups of patients requires both accurate personalized treatment approaches and alert practitioners who keep pace with advances in multiple myeloma care.⁷⁶

Additional therapies (e.g., chimeric antigen receptor T cells (CAR-T) and other immunotherapies),⁷⁷ where available, are likely to be of increasing importance in treating multiple myeloma.²⁹ However, there is currently no consensus on strategies for optimizing treatment selection, combination, and sequencing in clinical practice for newly diagnosed or relapsed/refractory patients.

“To be honest it’s becoming a bit unclear as to what the best order of treatment is, because there are all kinds of drugs available.”

- Specialist Hematologist, Japan³⁵

Some therapies, such as lenalidomide, have enabled upfront treatment of multiple myeloma to achieve deeper and more prolonged responses to treatment.^{28,78} Multi-drug combination therapies have been shown to improve response rates and length of survival times.²⁹

However, individual patients require individualized care, so it is critical that practitioners consider all the factors that may influence treatment choices. Use and exposure to multiple drug classes may increase the risk of toxicity,²⁹ requiring careful clinical management and consideration of toxicities from earlier treatments when prescribing. Based on patient-identified treatment goals, practitioners must balance quality of life, toxicity, and survival to achieve the optimal result for their patients.³⁰

Treatment decision-making increases in complexity as the disease progresses and patients age

Treatment decisions in multiple myeloma are challenging for practitioners. In addition to the variety of factors for consideration, over time the aims of treatment may change.³⁰ Generally, for earlier lines of treatment, the aim is to achieve complete response (CR) or minimal residual disease (MRD) negativity.³⁰ For patients in later lines of treatment, it may be more appropriate to focus on disease control.³⁰ This may be due to patients aging and becoming more frail, exhausting treatment options, experiencing toxicity from previous treatment, and comorbidities.

Diagnostics including whole body imaging and bone marrow analysis should be undertaken at relapse, and, at the very least, cytogenetic testing should be done to confirm the presence of high-risk markers that accumulate over time.³⁰ Genetic and clonal heterogeneity can be used to investigate prognostic relevance, survival, outcomes, and treatment response.^{79,80} Unfortunately, many practitioners still express that selecting treatments for patients with several different mutations is challenging.

“High-risk cytogenetics patients are definitely a challenge because they have a poorer prognosis than other patients so they don’t have as much time.”

- Multiple Myeloma Specialist Hematologist, US³⁵

UNMET NEED 2: COMPLEX TREATMENT DECISION-MAKING IN MULTIPLE MYELOMA

“Not all myelomas are the same, so some patients are not served well by current treatment options.”

- Multiple Myeloma Specialist Hematologist, UK³⁵

Every patient deserves the best care available. Through appropriate analysis and utilization of data, optimal treatment strategies would be possible for every patient, regardless of prior treatments.

Refractoriness impacts treatment decisions and is influenced by a number of resistance mechanisms.⁸¹ Both second-generation therapies and resistance pathway targeting agents have overcome proteasome inhibitor (PI) and immunomodulatory drug (IMiD) resistance.^{26,81} The accumulating and ongoing complexity of genetic factors, combined with the bi-directional relationship between multiple myeloma and the bone marrow microenvironment, remain clear obstacles to cure.^{26,81}

Furthermore, the complexity, dynamism, and heterogeneity of multiple myeloma presents a significant challenge for researchers investigating specific mechanisms of resistance to treatment. Research has exposed many of these, yet there exists no single molecular marker, genotype, or mechanism that is understood to be universally responsible for conferring resistance to a specific therapy.⁸¹

Despite the wealth of information accumulated on treatment resistance, more is necessary to accurately integrate resistance considerations into decisions for treatment optimization.

The risk of infection further complicates multiple myeloma care

Infection is a major complication and a leading cause of death in patients with multiple myeloma,³⁹ due to the immunodeficiency caused by the disease itself and the cumulative result of treatment regimens given throughout the disease course.³⁸ In recent years, significant progress in the management of multiple myeloma has resulted in improvement in survival.⁸² Guidelines are in place to recommend appropriate antimicrobial prophylaxis depending on selected treatment regimens,⁸³ however, further treatment solutions are needed to help physicians reduce the risk of infection in patients with multiple myeloma.



CALL-TO-ACTION: ENHANCE UNDERSTANDING OF TREATMENT RESPONSE FOR AN INDIVIDUALIZED APPROACH

- Conduct effectively powered subgroup analysis in clinical trials to better understand the impact of treatment sequences on outcomes that help support personalization of treatment strategies, e.g., for patients with high-risk cytogenetics, extramedullary disease, etc.
- Ensure enhanced understanding and adoption of guidelines by all healthcare professionals to reduce the risk of infection in patients with multiple myeloma.
- Continue investment into the research of innovative therapies that limit the impact of infection on patients with multiple myeloma.



UNMET NEED 2: COMPLEX TREATMENT DECISION-MAKING IN MULTIPLE MYELOMA

The lack of universally determined surrogate measures and consensus on therapy goals further complicates the multiple myeloma treatment landscape

The advent of more effective therapies with high CR rates has led to the need for improved metrics to record and assess deeper levels of response.²⁶ The advancement of techniques to improve sensitivity of MRD detection has been instrumental in classifying MRD-negative patients, who have been shown to have superior outcomes compared with patients who fail to reach MRD negativity.⁸⁴ However, at present, the utilization of MRD negativity in clinical practice remains unclear, despite ongoing research.

MRD testing is used in other cancers, such as lymphoma and leukemia, to act as prognostic indicators, guide treatment decisions, and assess treatment response.⁸⁵ MRD testing is now becoming a consideration in multiple myeloma treatment strategy; as of 2021, there were at least 35 ongoing, Phase 3 trials incorporating MRD as a primary or secondary endpoint.⁸⁶

Although advancements have been made, a survey of 84 hematologists with access to MRD testing showed a large disparity between the proportion of physicians that assess MRD in clinical trials or standard of care settings (91%) versus those who use it to guide treatment decision-making (37%).³⁶ The most common reasons for low MRD utilization are outlined in **Figure 1**.^{37§}

Reasons for not using **MRD** among clinicians³⁷

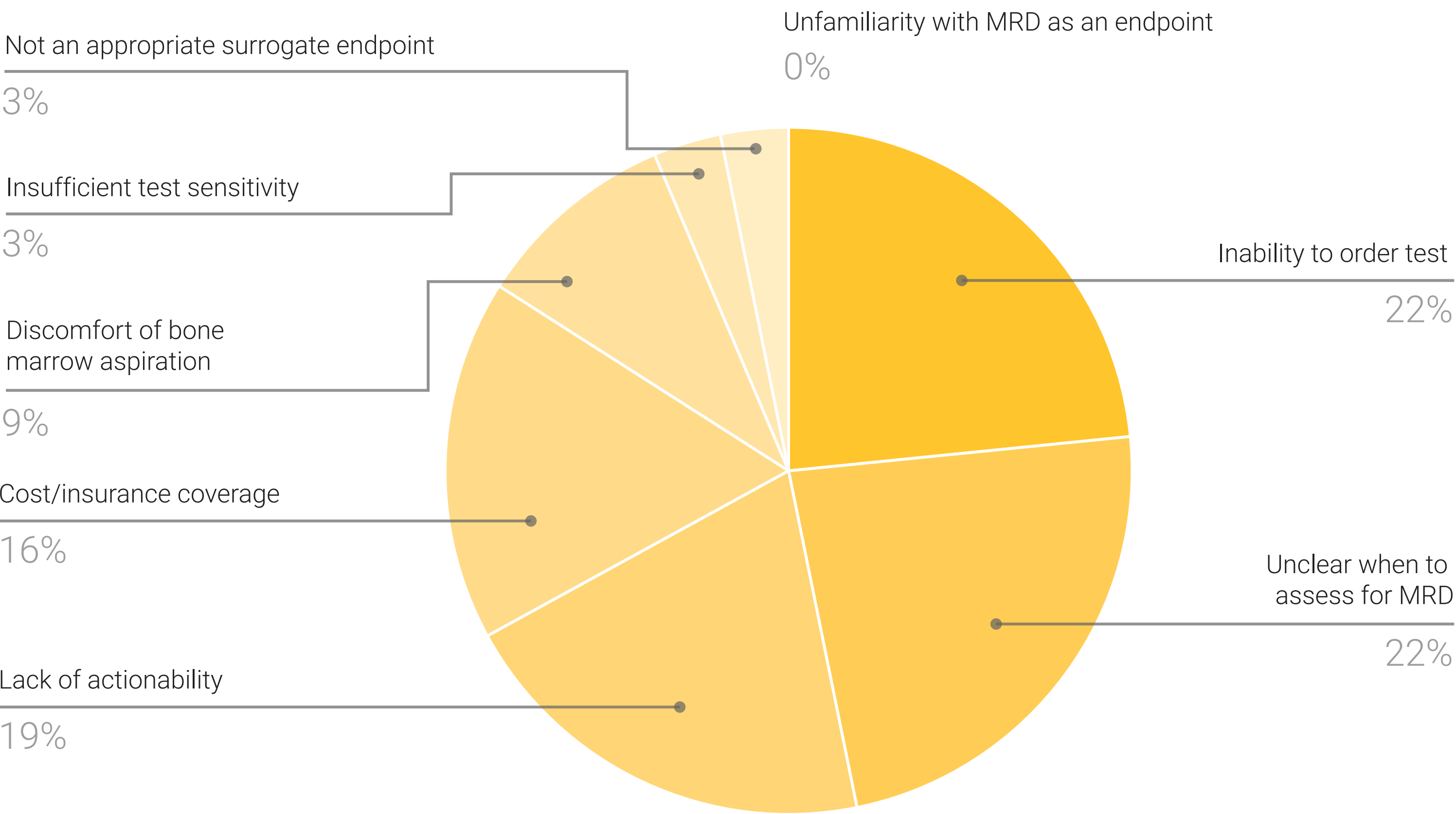


Figure 1: A total of 89 clinicians were surveyed across 5 continents. 32 clinicians were identified as non-MRD users, the most common reasons for not using MRD were selected from 8 choices.³⁷

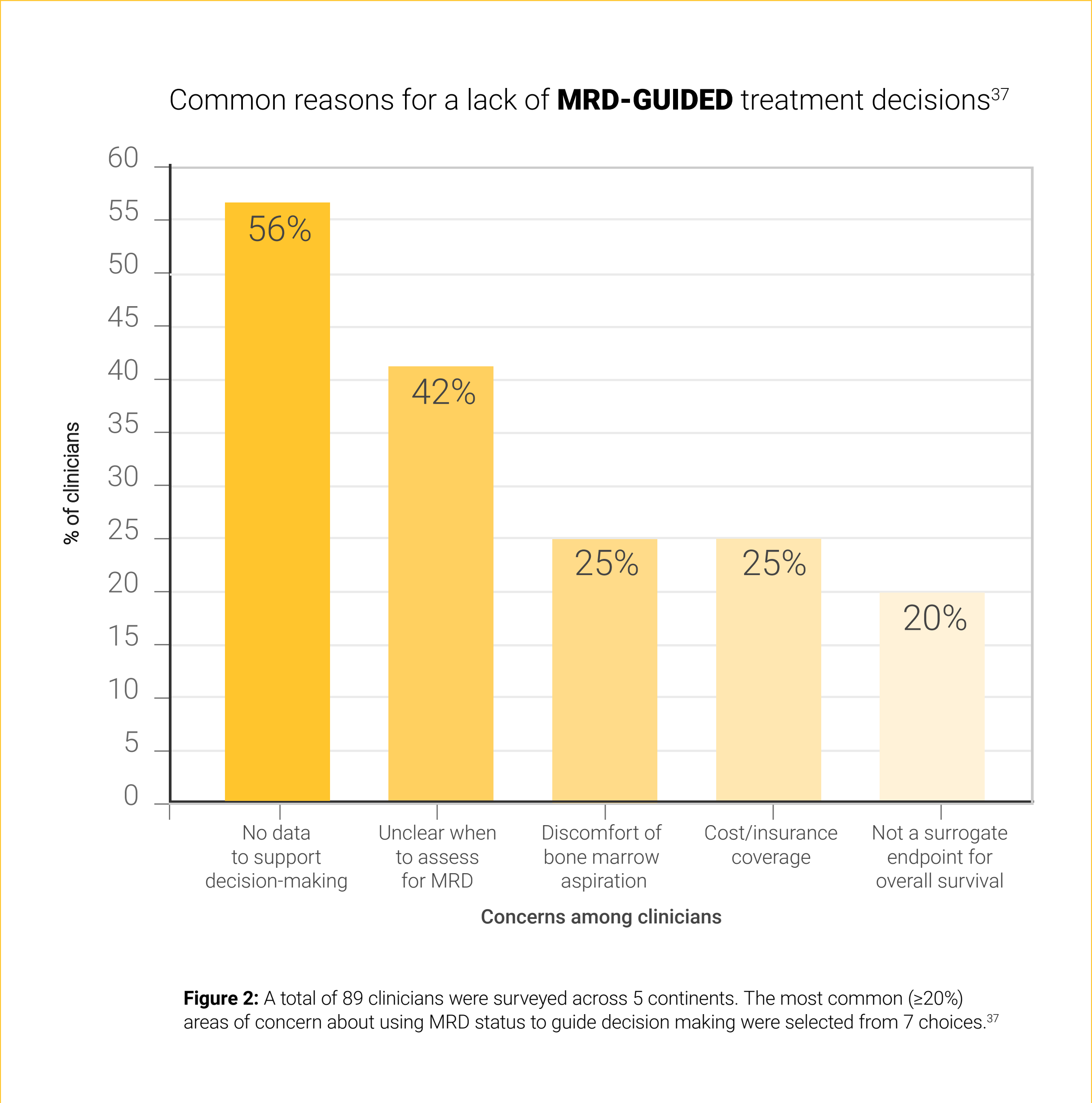
§ In this survey from the Multiple Myeloma Research Foundation, 89% of respondents were employed from academic centers as opposed to private practice or a hybrid setting.

UNMET NEED 2: COMPLEX TREATMENT DECISION-MAKING IN MULTIPLE MYELOMA

The most common reasons for a lack of MRD guided treatment decision-making by physicians are outlined in **Figure 2**.^{37§}

Research into genomic and cellular testing techniques, including next-generation sequencing and flow cytometry, circulating tumor cells, and mass spectrometry continues to improve the understanding of assessing MRD. Techniques are not yet standardized across trials.⁸⁷ An online survey of hematologists in academic centers found that over 90% measured MRD, but only half did so at a depth of 10⁻⁶.³⁶ Practitioners may be failing to benefit from the superior level of fidelity in prognosis that increased depth provides – although this may be influenced more by disparity in next-generation diagnostic access between practices.³⁶ Hematologists noted that for MRD testing to be implemented responsibly and equitably in all settings, laboratory capacity needs to be expanded to extend testing access.⁸⁸ Notably, insurance limitations also play a role in low uptake, with the burden of testing costs falling to the patient in some countries.⁸⁸

Both patients and their practitioners agree that MRD testing is a complicated topic, with hematologists not necessarily having the time and/or the tools to discuss it simply and clearly with their patients.⁸⁸ Hematologists also indicated that they would require additional training on when to recommend MRD testing, and how to effectively interpret findings to guide treatment decisions. Broader uptake and utilization of MRD as a marker in multiple myeloma care requires community consensus, guidance, and education.⁸⁸



CALL-TO-ACTION: DRIVE CONSENSUS ON UTILIZATION OF MRD AND OTHER SURROGATE MEASURES

- Drive consensus on the integration of MRD into clinical trial design, by exploring optimal timing and testing techniques for MRD as a finite endpoint, to predict treatment-free intervals and inform consensus on duration of treatments.
- As key MRD decision-making studies are completed, create guidance for the use of MRD and encourage regulatory bodies, medical societies, and healthcare systems to adapt lab capabilities so MRD testing can be accessed globally.
- Educate on the role of MRD as it evolves from use in clinical trials to clinical practice and develop patient-focused educational materials, so myeloma specialists can understand and communicate MRD with patients.
- Continue exploration of biomarkers to further prognostic capability and inform treatment decision-making.

§ In this survey from the Multiple Myeloma Research Foundation, 89% of respondents were employed from academic centers as opposed to private practice or a hybrid setting.

UNMET NEED 2: COMPLEX TREATMENT DECISION-MAKING IN MULTIPLE MYELOMA

Access to therapies is hindered by local reimbursement policies and lack of access to clinical trials, contributing to global disparity in care

Access to therapies is globally disparate. Despite positive outcomes in research, some populations are unable to derive benefit from it due to insufficient financial resources to access treatment.³¹⁻³³

In Latin America for example, economic disadvantage, high rates of comorbidity, and higher disease aggression contribute to disparity in multiple myeloma care **(Case Study 2).**^{32,11}

Programs have been initiated in Kenya to provide training to practitioners in the diagnosis and treatment of multiple myeloma.⁸⁹

A retrospective analysis of 219 patient charts over an 11-year period was conducted in Kenya, in which thalidomide and dexamethasone were the most commonly prescribed initial chemotherapy agents.⁹⁰ The observed outcomes were a median overall survival of 29 months and 5-year overall survival of 21%.⁹⁰ Although prescribing patterns in Kenya are similar to those observed in Nigeria,⁹¹ they differ markedly from those in Ghana, for example, where vincristine-, doxorubicin-, and melphalan-based regimens predominate as initial treatments.⁹²

CASE STUDY 2: DISPARITIES IN ACCESS TO TREATMENT ACROSS LATIN AMERICA

In an analysis of 245 patients, of which 84.7% were considered of low socioeconomic status, induction treatment without novel drugs was common and associated with a poorer overall survival (HR 1.49; 95% CI 1.08 - 2.06; $P=0.016$).³¹

Treatment in Latin America is limited in many cases to the use of thalidomide and dexamethasone with or without cyclophosphamide, and transplant access is also poor. In a retrospective cohort analysis of 1,103 Latin American patients with multiple myeloma, only 33.9% of patients underwent transplantation, and first-line treatment regimens were predominantly thalidomide- (54.9%) or bortezomib-based (29.1%).³² Access to therapies, such as lenalidomide is often limited due to high costs of therapy, reimbursement policy, and reduced access to clinical trials.³²

In a retrospective study in Mexico, patients receiving private health care demonstrated better response rates and survival. These real-world data emphasize the importance of developing strategies that improve access to drugs and transplants globally.³³

Access to basic backbone treatments are also reported to be limited in European countries,⁴² hence access remains a major unmet need in the global multiple myeloma community.

Racial, ethnic, and insurance-related disparities also limit utilization of highly effective multiple myeloma treatments in wealthy nations.

A retrospective study of 1,002 patients with multiple myeloma at a US tertiary referral center found that patients on Medicaid, alongside Black patients, were more likely to experience unplanned treatment interruption, further emphasizing the need for more equitable care provision.³⁴



CALL-TO-ACTION: IMPROVE APPLICABILITY AND RELEVANCE OF CLINICAL TRIAL DATA IN CLINICAL PRACTICE

- *Develop strategies that improve access to the best available therapies globally, seeking equitable outcomes for every myeloma patient, by encouraging greater investments in research and development, clinical trial infrastructure, as well as the coverage of standard of care treatments and specialized procedures.*

¹¹ Reference cited includes data from the pivotal trial: de Moraes Hungria VT, Martínez-Baños DM, Peñafiel CR, et al. Multiple myeloma treatment patterns and clinical outcomes in the Latin America HaematoOncology (HOLA) Observational Study, 2008-2016. *Br J Haematol.* 2020;188:383-393.

UNMET NEED 2: COMPLEX TREATMENT DECISION-MAKING IN MULTIPLE MYELOMA

Consensus on treatment and disease markers will guide treatment regimen individualization

There is an opportunity to redefine the treatment selection pathway by introducing novel therapies and improving access to treatments. As the myeloma community progresses towards cure, a clear consensus is required on the most appropriate therapies to be used based on the needs of individual patients. Several risk stratification models have been developed to support this.² One example is the IMWG (International Myeloma Working Group) risk stratification guidance, which provides a series of recommendations for patients with multiple myeloma based upon their risk factors.⁹³ It considers a number of important markers including genetic-, disease-, and patient-related factors.⁹³ Further collaboration within the multiple myeloma community will be necessary to achieve consensus on risk stratification measures. This would support hematologists in selecting treatment pathways and optimizing care for every patient.

The complexity of genetic factors, which change over the course of treatment, are thought to contribute considerably to drug resistance and relapse in multiple myeloma.⁹⁴ Further, the ability to predict treatment response and individualize care is limited by the absence of reliably predictive biomarkers.^{26,94} It is unlikely that a single targeted treatment would be effective for all patients, due to the genetically heterogenous nature of the disease.⁹⁴ The largest study on this topic to date identified 63 driver genes that recurrently mutate, initiating and/or driving disease progression.⁹⁴

Looking forward, deeper and more thorough investigation is necessary to effectively accelerate progress towards cure. Among the multiple myeloma community, collaboration will hasten the achievement of consensus on treatment selection algorithms, and the optimal biomarkers which guide them.



The largest study on predictive biomarkers to date identified **63 driver genes** that recurrently mutate, initiating and/or driving disease progression.⁹⁴

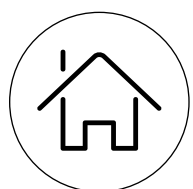


CALL-TO-ACTION: ENHANCE UNDERSTANDING OF TREATMENT RESPONSE FOR AN INDIVIDUALIZED APPROACH

- *Redefine the treatment algorithm, incorporating novel therapies to drive the treatment landscape towards cure, creating a clear consensus from the multiple myeloma community on risk-stratification measures.*



UNMET NEED 3: LIMITED APPLICABILITY AND DIVERSITY OF CLINICAL TRIALS



UNMET NEED 3: LIMITED APPLICABILITY AND DIVERSITY OF CLINICAL TRIALS

Multiple myeloma trials often do not reflect real-world populations, limiting generalizability of results into clinical practice

Randomized controlled trials remain the gold standard for regulators, who approve treatments based on strong statistical validity within the trial population.

Real-world populations can vary significantly,⁴⁰ and the highly heterogeneous nature of patients with multiple myeloma further exacerbates this disconnection between trial data and treatment individualization strategies.



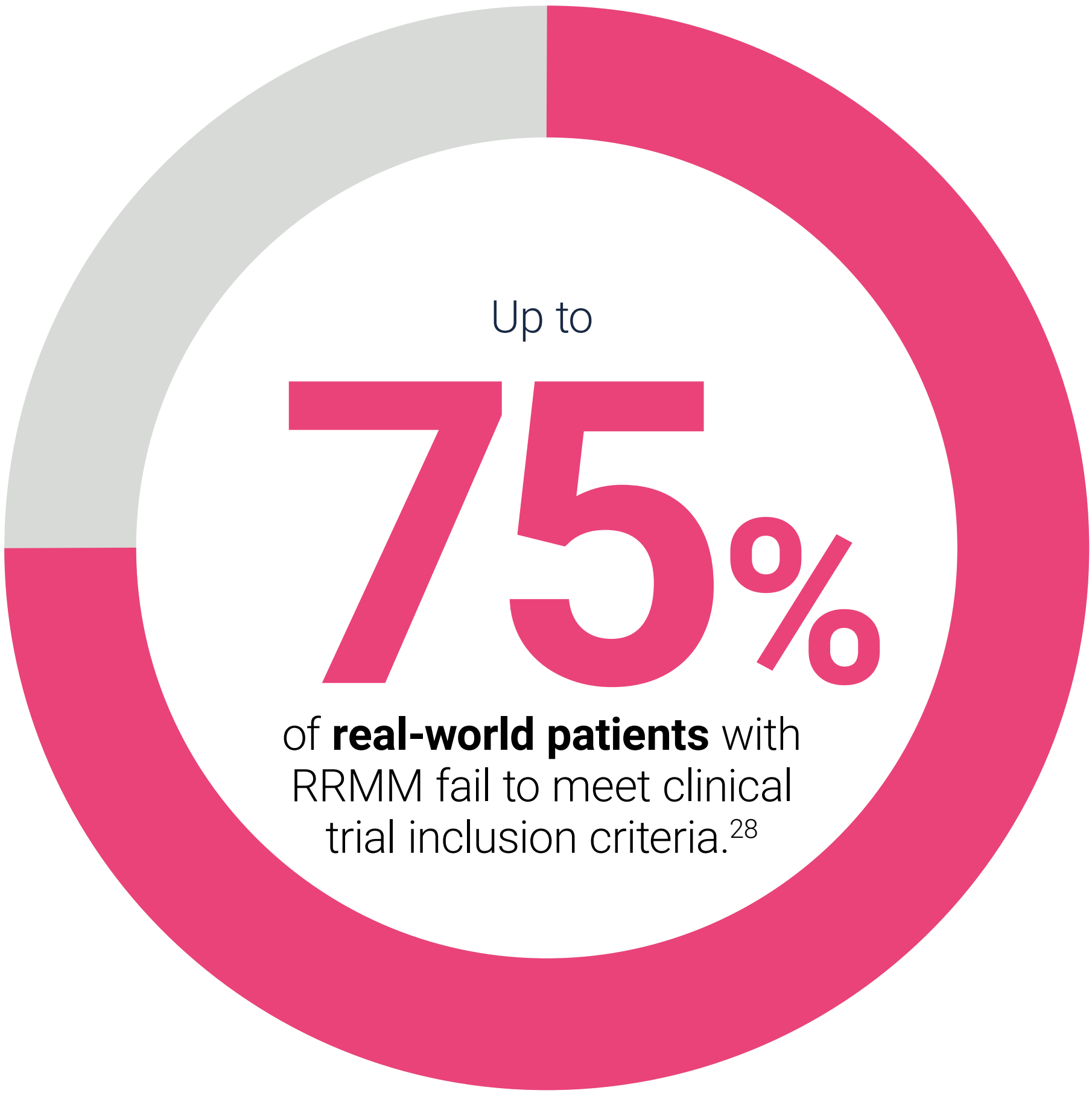
Approximately **40%** of all real-world patients with multiple myeloma **do not meet the inclusion criteria** for Phase 3 trials⁴⁰

Approximately 40% of patients with multiple myeloma in the real world do not meet the inclusion criteria for the Phase 3 trials on which regulatory approvals are based.⁴⁰ Ineligibility may be caused by any number of reasons, including poor performance status, inadequate organ function, adverse medical history, or comorbidity.⁴⁰ Unfortunately, this results in the underrepresentation of patient sub-populations within clinical trials.⁴⁰ Patients with RRMM are even less likely to qualify for trial inclusion, with up to 75% of real-world patients failing to meet inclusion criteria.²⁸ These patients have a 50% increased risk of mortality compared with those who are eligible for trial inclusion.²⁸

Despite this, physicians estimate that up to 90% of patients receiving first- or second-line treatments are elderly, and/or multi-morbid, and/or have a poor performance status.^{40,95} This is reflected in the data; for example, a prospective analysis of 3,007 patients showed that >50% of multiple myeloma diagnoses occur at >65 years of age.⁴¹ Similarly, a population-based study of 13,656 patients reported that >50% of patients with multiple myeloma have at least one comorbidity at time of diagnosis.⁹⁶

Naturally, regulators have encouraged the broadening of inclusion criteria in response.⁶² Working to accelerate the adoption of more inclusive enrollment practices, regulators will drive clinical trials to accept an increasingly diverse range of participants.⁶² These actions work to make trial data more reflective of the populations that practitioners will eventually treat following drug approval.

Physicians must analyze a considerable amount of information to consider how patient frailty, multi-morbidity, and underrepresentation will impact treatment strategy and selection.⁴⁰ These factors all contribute to increasing prescriptive complexity in an already challenging-to-manage disease.



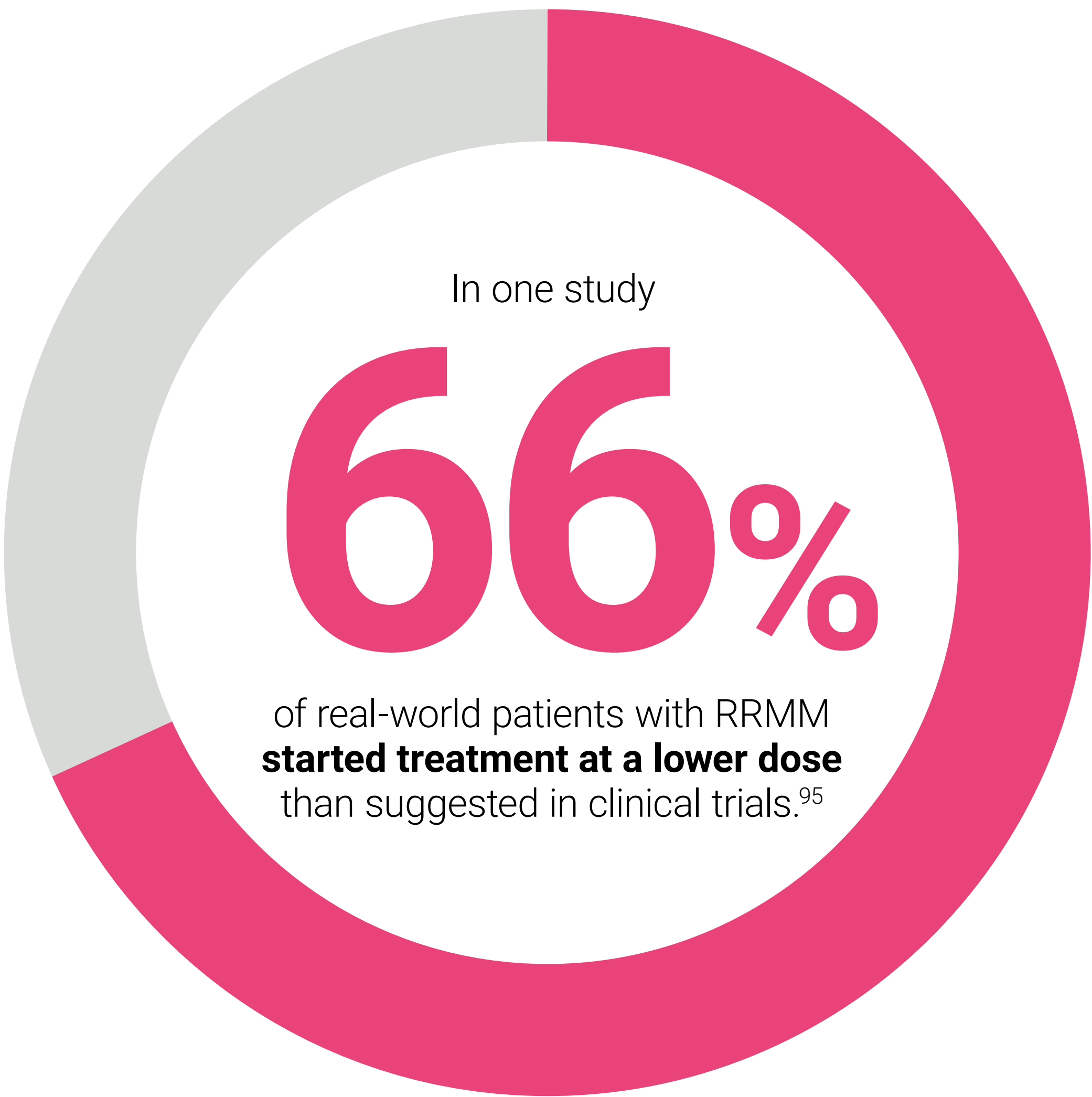
UNMET NEED 3: LIMITED APPLICABILITY AND DIVERSITY OF CLINICAL TRIALS

Treatment tolerability may be lower in the real world than in clinical trials

Treatment-associated toxicities have been shown to be extremely burdensome in the real-world setting. These can limit the duration of treatment more substantially than in clinical trials, adversely impacting clinical outcomes.⁴⁰

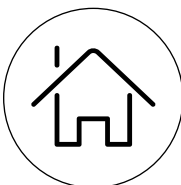
Maximum doses tolerated by real-world patients may be lower than those administered in clinical trials.⁹⁷ A retrospective cohort study of lenalidomide dosing in patients with RRMM over 65 found the majority of patients started treatment at a dose lower than the 25-mg daily dose suggested by clinical trial data.⁹⁵ The study also found that 66% of patients began treatment on doses of 10 mg or less.⁹⁵ The most common reasons for lower dosing were renal dysfunction and $\geq$ Grade 3 fatigue.⁹⁵ These data indicate that many patients experience challenges tolerating the recommended dosage of treatment. In real-world practice, many newly diagnosed elderly patients with multiple myeloma receive doublet (vs triplet) combination treatment.⁴¹

Treatment regimens need to be carefully constructed, accounting for the risk of adverse events or toxicity, and clearly communicated to each individual patient.



CALL-TO-ACTION: IMPROVE APPLICABILITY AND RELEVANCE OF CLINICAL TRIAL DATA IN CLINICAL PRACTICE

- *Improve the generalizability of trial data, by working to modify standard inclusion and exclusion criteria.*
- *Design smaller studies for specific patient sub-populations (e.g., frail patients), furthering the ability to individualize treatment strategies.*
- *Consider differences in treatment discontinuation and toxicity between the real world and in clinical trials to support careful development of treatment strategies, accounting for the risk of adverse events and toxicity in each individual patient.*
- *Collect real-world evidence (e.g., via observational studies, physician surveys, etc.) in parallel to clinical trials across a diverse range of geographies and socioeconomic populations, so that myeloma specialists can create optimal, individualized treatment strategies based on comprehensive and representative data.*



UNMET NEED 3: LIMITED APPLICABILITY AND DIVERSITY OF CLINICAL TRIALS

Multiple myeloma sub-populations require care to be individualized, with an adaptive approach to treatment

Receiving the treatment with the highest survival rates may not always guarantee patient well-being.⁹⁸ Frailty, anxiety, and pain can impact quality of life more than clinical characteristics.⁹⁸ Therefore, the consideration of how treatment affects quality of life is instrumental in the real-world setting, as treatment success is clearly dependent on a multitude of factors beyond what is investigated in clinical studies, i.e., survival.

“There’s less focus on elderly, unfit patients in clinical trials...If you have an 80 year-old, you won’t give them the full dose of a drug. We’re doing that every day in practice, but it’s really lacking the research behind it. It’s done very subjectively and not objectively.”

- Multiple Myeloma Specialist Hematologist, UK³⁵

As the therapeutic landscape in multiple myeloma continues to evolve, there is an increasing need to understand frailty as a means of risk-benefit decision-making. Rather than chronological age, frailty assessments can be used to evaluate health status, and can be used to individualize treatments.⁹⁸ Analysis of trials of drugs approved by the FDA (Food and Drug Administration) between 2015 and 2022 found that integration of frailty assessments into multiple myeloma clinical trials was highly varied.⁹⁹ The most commonly used tools to assess frailty included the IMWG frailty index (41.8%) and the simplified frailty score (39.5%).⁹⁹ However, the contrast in definition and categorization of frailty between these tools limits their potential impact on outcomes, due to a lack of uniformity in patient categorization.⁹⁹ The UK Myeloma Research Alliance FiTNEss trial is the first prospective randomized trial to integrate frailty assessments into treatment decision-making within a randomized, controlled setting in multiple myeloma.¹⁰⁰ Although the results of this trial are still pending, assessment of frailty continues to be incorporated into trial design.¹⁰⁰

Clinical trials that focus on enrolling and optimizing treatment for frail patients with standardized assessment tools are needed to further improve outcomes in multiple myeloma.

Concurrent generation of real-world evidence may support the applicability of trial results for more individual patients

In clinical decision-making, controlled and real-world studies together provide information of paramount importance.²⁸ Ongoing real-world data generation and collection support the applicability of data gained from clinical trials in real-world settings.

The INSIGHT MM study is the largest observational study of its kind, evaluating real-world effectiveness of treatments in 4,000 patients from 15 countries.¹⁰¹ This study was initiated in response to the shifting and growing complexity of the multiple myeloma treatment landscape. Other examples of real-world data collection include the MMRF CoMMpass study, which collected clinical and genomic information from 1,150 patients across the entire course of their disease,¹⁰² the PREAMBLE study,¹⁰³ and the MMRF CureCloud initiative.¹⁰⁴

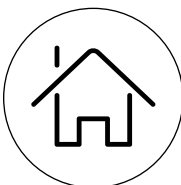
Regulatory initiatives, such as the European Health Data Space platform created by the European Commission, continue to reflect the need for real-world evidence to best make use of tools through the utilization of patient data.¹⁰⁵

Further collaborative efforts are underway to generate real-world data, including the HARMONY BigData Platform.¹⁰⁶ Its aim is to accelerate the development of treatments for patients with hematological malignancy through the collection of data from different sources/providers, including registry data. Data are then utilized by several initiatives to improve care.¹⁰⁶ Consolidated, population-based cancer registries are fundamental to the collection of high-quality real-world data.²⁸ However, current initiatives for data and insight generation are occurring locally, not internationally. This highlights a further opportunity for global collaboration to better understand the shifting and changing treatment paradigm in the real world.



CALL-TO-ACTION: INCREASE PRIORITIZATION OF OUTCOMES RELATED TO PATIENT EXPERIENCE

- Drive collection of quality-of-life assessments as key clinical trial endpoints, to better understand patient experience and build a more complete and balanced picture of how efficacy and treatment response align with patient needs.
- Publicize and communicate the patient experience in clinical trials, to broaden understanding of the impact on multiple myeloma trials on quality of life.
- Establish routine integration of patient opinions to improve better representation of patient needs and insights into study design, selecting more meaningful endpoints in clinical trials.
- Elevate the patient voice and quality of life as an essential goal of therapy, i.e., by developing simple, standardized tools to regularly assess quality of life in clinical practice, for example, through enhanced utilization of simplified PROs.
- Generate real-world data on quality-of-life measures (e.g., health-related quality of life and PROs) to complement clinical trial data for a holistic picture.



UNMET NEED 3: LIMITED APPLICABILITY AND DIVERSITY OF CLINICAL TRIALS

Disparity in trial inclusion criteria disproportionately excludes patients from economically disadvantaged countries

Analysis by MPE of the period between January 2001 and September 2020 found that, of 3,229 trials, only 6% included patients from Central and Eastern Europe.⁴² Furthermore, 7 countries in Central and Eastern Europe were found to have no access to multiple myeloma clinical trials whatsoever.⁴²

This trend also extends globally. A systematic review of multiple myeloma clinical trials that resulted in FDA approvals between 2005 to 2019, which met their primary endpoint and enrolled patients outside the US, found that high-income countries enrolled patients in 100% of trials identified.⁴³ Patients from upper-middle- and lower-middle-income countries were, on the contrary, represented in 61% and 28% of trials, respectively.⁴³ No patients from low-income countries were enrolled.⁴³ These analyses clearly highlight stark geopolitical and economic disparity in trial recruitment. Equitable health care requires broadened trial inclusion, in order to optimize and individualize treatment for every patient, no matter where they are in the world.

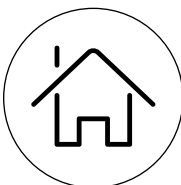
A major contributor to this inequality in multiple myeloma care could be the lack of access to generic backbone therapies, which are often central to the inclusion of patients in new research.⁴² This represents a further obstacle for sponsors in selecting where to locate trials.

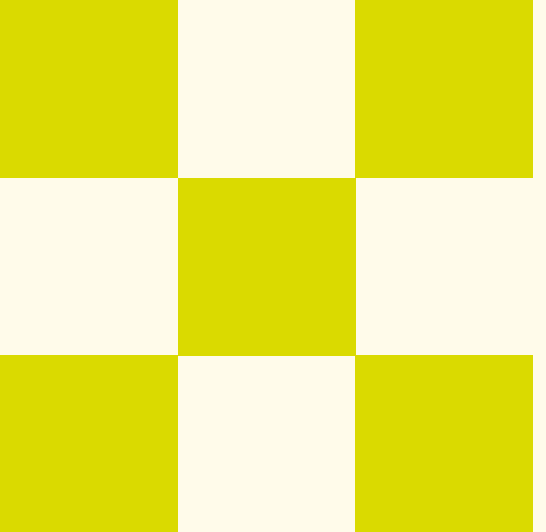
The cost of supplying treatment, in a country where it is not routinely covered, often makes trials impossible without substantial funding.⁴² Further, in countries where standardization of care is lacking due to access limitations, the chance of patients being eligible for trial inclusion is low.⁴² Local availability of appropriate trial resources can play a major role in trial participation, as smaller and rural institutions may not have the infrastructure available or staffing to undertake research.⁴² The rate of innovation in multiple myeloma trials is high, and with access to specialized treatment centers already limited, the ability for low-income countries to run precision trials is diminishing.⁴²



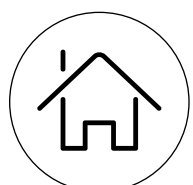
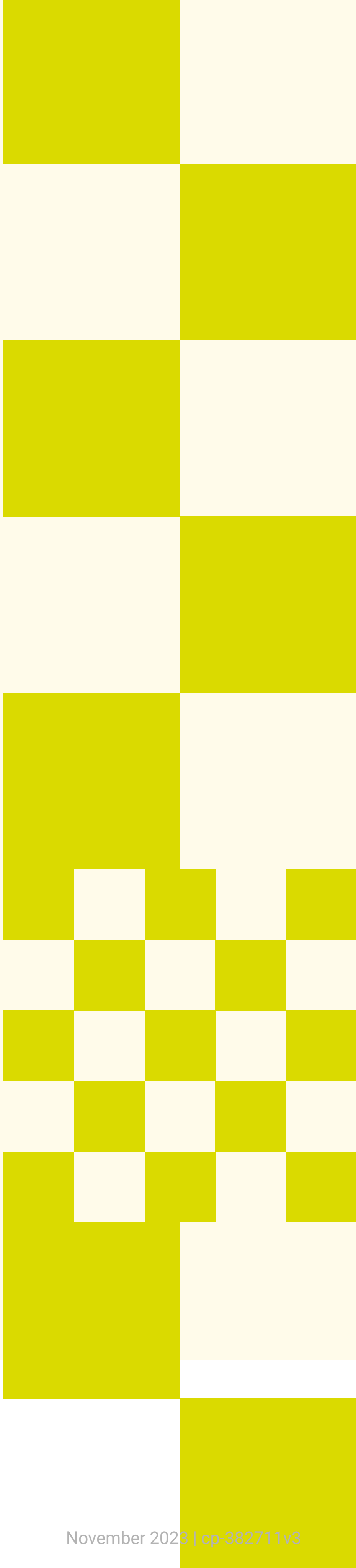
CALL-TO-ACTION: AREAS OF FOCUS: REINFORCE ACCESS, DIVERSITY, AND EQUALITY ACROSS CLINICAL TRIAL POPULATIONS

- Create a clinical trial network that offers clear regulatory standards and guidance, combined with the necessary infrastructure and staff education to support the expansion of clinical trials into underserved communities.
- Enforce collaboration between medical societies and research institutions to help countries prioritize available resources and improve access to treatments.
- Communicate and educate on trial availability, objectives, and execution to broad audiences, enabling discussion between HCPs and patients to ensure more diverse participation in clinical trials.
- Increase awareness of sub-population and minority underrepresented groups in trials to drive broader representation of these groups.
- Highlight the impact in global care disparity by using clear metrics, targeting policymakers, regulators, payors, and broad non-specialist audiences.





UNMET NEED 4: INCONSISTENT HOLISTIC MANAGEMENT OF MULTIPLE MYELOMA



UNMET NEED 4: INCONSISTENT HOLISTIC MANAGEMENT OF MULTIPLE MYELOMA

Survivorship in multiple myeloma starts at diagnosis due to the life-long burden associated with the disease.

Continuous scientific and clinical innovation has transformed the multiple myeloma landscape.²⁶ It is no longer rare for patients to live for 10-15 years after diagnosis.^{26,46} However, the lack of curative treatment means that, while the duration of life is extended, patients usually remain on medication. Living longer is the primary goal for many patients with multiple myeloma. However, focus on quality of life is increasing, notably through the use of patient-identified outcomes.

“I’ve been ill for 11 years, there is not one second in a day that I’m not confronted by my illness because I have pain with every step I take, but nobody sees it.”

- 70 year-old patient with multiple myeloma, The Netherlands.^{53‡}

Real-world understanding of the patient experience in multiple myeloma may be underappreciated, as quality-of-life data in multiple myeloma are primarily gained from clinical trials.⁴⁵ It has been well documented that patient quality of life decreases as their disease progresses.¹⁰⁷ However, each patient has a unique set of individual needs and values which greatly influence their experience and should be appropriately investigated and considered by their practitioner through open and honest conversation.⁴⁶

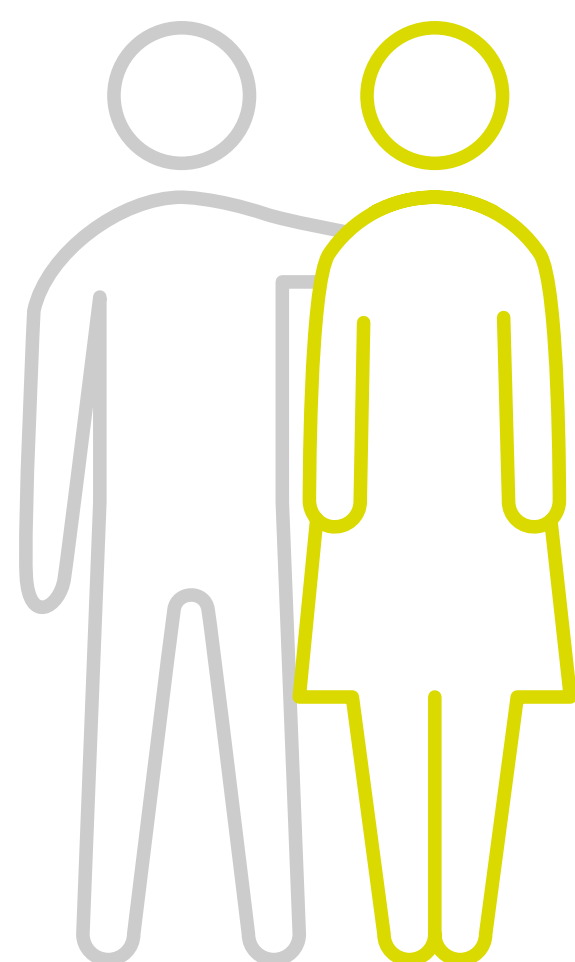
As patients progress through lines of therapy, treatment sequencing becomes less clear and the health challenges of patients with multiple myeloma are compounded due to impact of treatment and underlying disease.³⁵ Specialists are aware that an individualized approach to care which considers quality of life, as well as treatment efficacy, is key to the optimal management of patients with multiple myeloma. However, the heterogenous nature of patients with multiple myeloma and disease biology requires both individualization and adaptive support measures to optimize care.



Figure 3: Words used by hematologists, specialist nurses, and a patient advocate to describe the patient experience in various states of disease, showing it becomes increasingly diverse as multiple myeloma progresses. This further highlights the need for an individualized and holistic approach to meet patient needs.³⁵

‡ Anonymous insights gathered through a survey questionnaire via Myeloma Patients Europe (MPE) with patients living with multiple myeloma (n=4), across 4 countries in Europe. Survey conducted in April 2023.

UNMET NEED 4: INCONSISTENT HOLISTIC MANAGEMENT OF MULTIPLE MYELOMA



A study of patients with NDMM in Western Europe found that **90% of patients stopped leisure activities** such as **spending time with family and friends** 1 year after diagnosis⁴⁹

The effects of multiple myeloma and treatment on the body can limit the ability of patients to undertake normal activity. A study of patients with NDMM in Western Europe found that 90% of patients stopped leisure activities such as spending time with family and friends 1 year after diagnosis.⁴⁹ This may have a considerable impact on their psychological and psychosocial condition that worsens over time due to the effects of disease progression, increasing frailty and decreasing quality of life. A Portuguese study spanning 15 years demonstrated that, in addition to heightened diagnosis of depression in patients, the psychological impact of multiple myeloma resulted in longer hospital stays. Notably, higher rates of depression were seen in women.¹⁰⁸

The reduction in the ability of patients to undertake day-to-day activities can also significantly impact disease burden. A study in the US found that 55% of patients with multiple myeloma expressed feeling too tired to perform simple necessary tasks.¹⁰⁹ The physical impact of the disease clearly has the potential to affect psychological and psychosocial well-being as a result.

“You have no desire for any company except maybe the company of people who are going through the same thing.”

- 47 year-old female patient with multiple myeloma, Serbia^{53‡}

Patients with multiple myeloma often feel that physical, emotional, and social pain as a result of treatment remains under-addressed.⁴⁴ Discussions centered around quality of life should occur at every stage of the patient journey,¹¹⁰ to ensure care is continually adjusted and optimized to best meet the needs of each individual patient. However, the reality is that these conversations can be time-consuming and difficult for physicians to implement in practice, and there is more that can be done to address this difficulty.

PROs will likely prove to be a useful tool in identifying patient support needs and serve as a trigger from which interventions to directly address them can be initiated.¹¹¹ A small pilot study in Australia found that PRO integration into clinical practice for advanced cancer improved care and enhanced patient-physician communication,¹¹² showing how PROs can aid practitioners to identify patients who may require re-assessment and/or subsequent adjustment to their care.^{111,113}



CALL-TO-ACTION: AREAS OF FOCUS: ENSURE AWARENESS OF PATIENT NEEDS ALONG THE MM JOURNEY

- *Develop simple and standardized tools (such as simplified PROs) to be appropriately integrated into electronic medical records to consistently assess patient experience to meet their individual needs as they evolve over time.*
- *Guide patients to the correct HCP specialty by improving the integration of signposting throughout the multiple myeloma care pathway, e.g., via:*
 - *“Nurse navigators” to better guide patients to existing services within regions.*
 - *A centralized, global multiple myeloma portal to explore relevant and reputable services in each region.*
 - *A country-specific helpline to provide information and support to patients who would struggle to access online resources, with integrated interpretation services.*
 - *Creation of a network of patient group organizations for each country with support from established global multiple myeloma organizations such as the International Myeloma Foundation and MPE.*



[‡] Anonymous insights gathered through a survey questionnaire via Myeloma Patients Europe (MPE) with patients living with multiple myeloma (n=4), across 4 countries in Europe. Survey conducted in April 2023.

UNMET NEED 4: INCONSISTENT HOLISTIC MANAGEMENT OF MULTIPLE MYELOMA

Standardized, multidisciplinary teams must be integrated into care, in order to improve patient experience and associated outcomes

Hematologists require additional specialist support to comprehensively manage patients with multiple myeloma, and holistic care is necessary to support the psychological, social, physical, spiritual, and financial needs of patients. A strategy based around multidisciplinary team (MDT) engagement may accelerate progress and better support every individual patient. MDT approaches ensure patients can access support from a variety of professional specialists, drawing benefit from the unique contributions each provides.⁵¹ These multidisciplinary teams form a core group of specialists who continually discuss the clinical needs of the patient. Nurses are instrumental to these teams, and empowering transparency and collaboration between specialist healthcare personnel is widely understood to benefit care.⁴⁷ In a UK national cancer patient experience survey from 2010-2014, patients who had a clinical nurse specialist in their orbit of care reported better experiences with involvement in treatment decisions, coordination of care, found more respect and dignity in their treatment, and overall had a better experience in care.⁴⁸

The “wrap-around” approach to MDT has been widely adopted in other cancers. Studies have found that integration of an MDT in colorectal and lung cancer improved survival rates and treatment compliance.^{114,115} Exemplifying this further, advanced breast cancer guidelines recommend the provision of physical, social, spiritual, and financial support.¹¹⁶

**CASE STUDY 3:
QUALITY INDICATORS IN BREAST
CANCER CARE (EUSOMA)**

The European Society of Breast Cancer Specialists (EUSOMA) has developed quality indicators of particular interest in breast cancer care for the certification of treatment centers.¹¹⁷

These indicators outline MDT structure: minimum case, procedure, and staffing volumes. Also incorporated were detailed descriptions of the skills of, and resources needed by, the different members and specialists found in multidisciplinary teams.¹¹⁷

However, access to MDT care can be limited both by socioeconomic status and geographical locations, as allied teams of specialist health professionals are often based in large teaching hospitals.⁵⁰

As with breast cancer, tight collaboration between healthcare professionals could play a valuable role in the delivery of holistic patient care (**Case Study 3**).¹¹⁸ Furthermore, standardization of such approaches to the management of multiple myeloma could ensure high standards of care for every multiple myeloma patient.

MDT support may offer an opportunity to reduce the burden of non-professional caregivers. One Western European study found 97% of patients with NDMM rely on such caregivers to provide holistic care, which places a high burden on their support network.⁴⁹ This subsequently impacts caregiver quality of life and may result in poorer care and outcomes for the patients whom they support.



A Western European study found **97% of patients with NDMM rely on caregivers to provide holistic care**⁴⁹

The burden of providing care can negatively impact caregivers – with 48% stating that they had been diagnosed with either stress, anxiety, or depression in the 1 year following diagnosis of the patient for whom they were providing care.⁴⁹



**CALL-TO-ACTION:
DRIVE CONSISTENT
INTEGRATION AND
ACCESS TO MDT AT
MULTIPLE MYELOMA
CARE CENTERS**

- *Develop guidance for the implementation and integration of holistic care models involving MDTs in multiple myeloma care centers to better support patients and reduce burden for patients and caregivers, utilizing technology where possible (e.g., telehealth communications) to support access to established MDTs for remote or rural communities.*
- *Encourage initiatives that work to integrate MDT approaches to care to improve patient experience and improve patient outcomes. Emphasize the importance of continuity of care within the MDT to further improve patient experience.*
- *Foster collaboration within the multiple myeloma community, defining standards of care to provide benefit to patients and their caregivers, improving their outcomes and their quality of life.*

UNMET NEED 4: INCONSISTENT HOLISTIC MANAGEMENT OF MULTIPLE MYELOMA

Improving HCP-patient communication strengthens the practice of shared decision-making

Shared decision-making (SDM) describes a process in which open and honest communication between patients and practitioners enables treatment choices which simultaneously optimize clinical outcomes and honor individual values and preferences.⁵² This is of significant importance in diseases where there is no single, evidence-based choice of treatment, as in multiple myeloma.

For SDM to be effective, physicians must deeply understand and effectively communicate the risks and benefits associated with treatment options.⁵² Similarly, patients must feel empowered in sharing their goals and concerns.⁵² A study of patients with hematologic malignancies in two public health institutions in Mexico investigated SDM. It found that less than a third of patients felt they had received adequate information in order to make decisions, or had their healthcare or psychosocial needs met.¹¹⁹

For patients, physicians remain the primary source of myeloma-related information, according to one global survey.⁵⁸ Many patients express the desire to learn more from their physicians in order to make more deeply informed decisions about their health. As multiple myeloma is a disease of the elderly, with a global median age of diagnosis of 70 years,⁸ patients may have a deferential relationship with their practitioner, taking a more passive role in their own care.¹²⁰ Patient-doctor interactions have progressed over the last 50 years to become more patient-centered.¹²⁰ However, disparate health literacy and health education availability may act as a barrier to patient-doctor communication.

CASE STUDY 4: HEALTHTREE UNIVERSITY FOR MULTIPLE MYELOMA

HealthTree University represents a gold-standard example of patient education in multiple myeloma.¹²⁶

As a free service, the program consists of over 40 lectures from multiple myeloma specialists, covering a myriad of topics to support patients from diagnosis, including support with making treatment decisions.¹²⁶

The lecture titled “Becoming an Empowered Patient” emphasizes the importance of disease education, providing helpful questions for patients to ask their doctor at the point of diagnosis.¹²⁶

The website’s “notebook” feature allows patients to keep a record of useful information, while the quiz function helps in the testing and retention of knowledge.¹²⁶

For patients without access to a multi-disciplinary team or specialist to provide them with accurate information, this resource can relieve the burden and worry of self-researching. It provides reliable, relevant, and clear information in a single location.

Further, as patients of lower socioeconomic status often have poorer levels of health literacy,¹²¹ the potential empowerment of these patients by deeper integration of SDM may be limited.

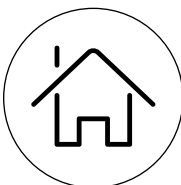
Many initiatives have been launched to support communication of the complex needs of patients with multiple myeloma, including the Myeloma Monitor App in Canada,¹²² LivingWith® in the US,¹²³ LLS Health Manager,¹²⁴ an SDM app developed by CaPPRe in collaboration with Myeloma Australia,¹²⁵ and patient programs from the HealthTree Foundation **(Case Study 4).**¹²⁶

These tools may be helpful for recording a patient’s experience with multiple myeloma, with focus on tracking symptoms, medical results, adverse effects, and quality of life, and completing preference surveys, in addition to providing questions to ask physicians. Despite these efforts, there remains a widespread lack of easily accessible tools that leverage best practice experiences to develop conclusions and recommendations that improve SDM in clinical practice. MPE is currently conducting research to develop evidence-based knowledge and recommendations for best practice in multiple myeloma SDM from patient and clinician perspectives.



CALL-TO-ACTION: ESTABLISH THE VALUE OF SDM IN CLINICAL PRACTICE

- Patient advocacy organizations can partner with healthcare institutions and medical societies to help raise awareness of SDM among the multiple myeloma community and, more specifically, myeloma treatment teams.
- Conduct a real-world study in SDM, specific to multiple myeloma, to further validate its use within clinical practice.
- Develop SDM tools for both HCPs and patients, aid communication, and improve HCP-patient relationships, such as through the use of key question guides.
- Incorporate SDM into multiple myeloma HCP training programs, helping to raise awareness of the importance of SDM and improving understanding among HCPs.



The Collaboration Council is committed to encouraging and accelerating progress in multiple myeloma, through actively identifying unmet needs and inspiring innovative solutions to address them. Through multidisciplinary engagement across the spectrum of care, the global multiple myeloma community can start to imagine a future where cure might be possible for many more patients living with multiple myeloma.

Together we can shape the future of myeloma care.

This report was supported by VMLY&R Health



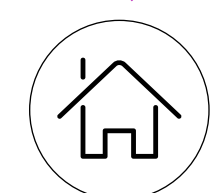
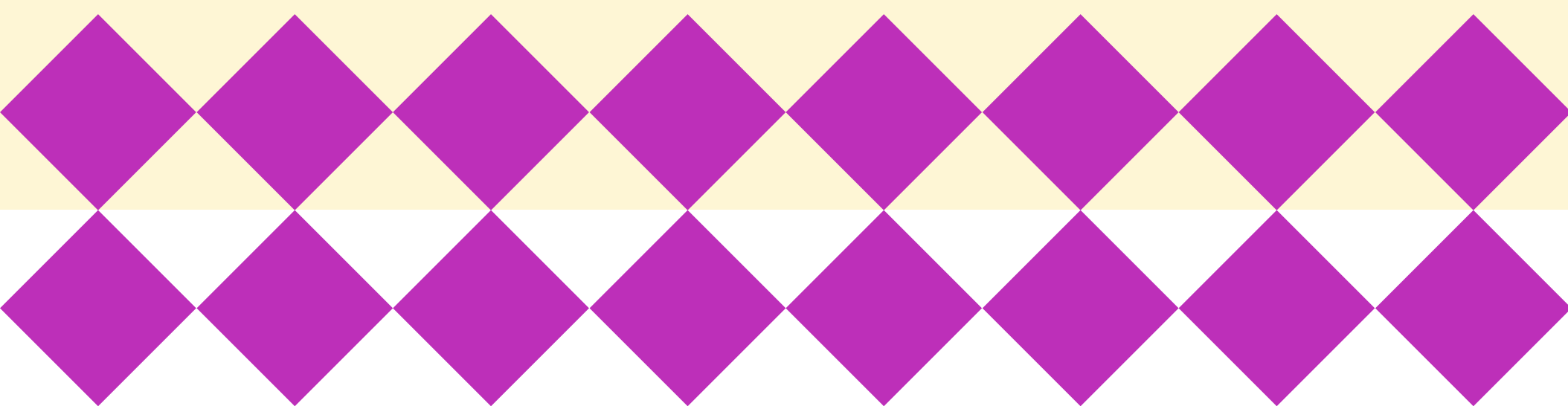
APPENDIX I: LITERATURE SEARCH STRATEGY

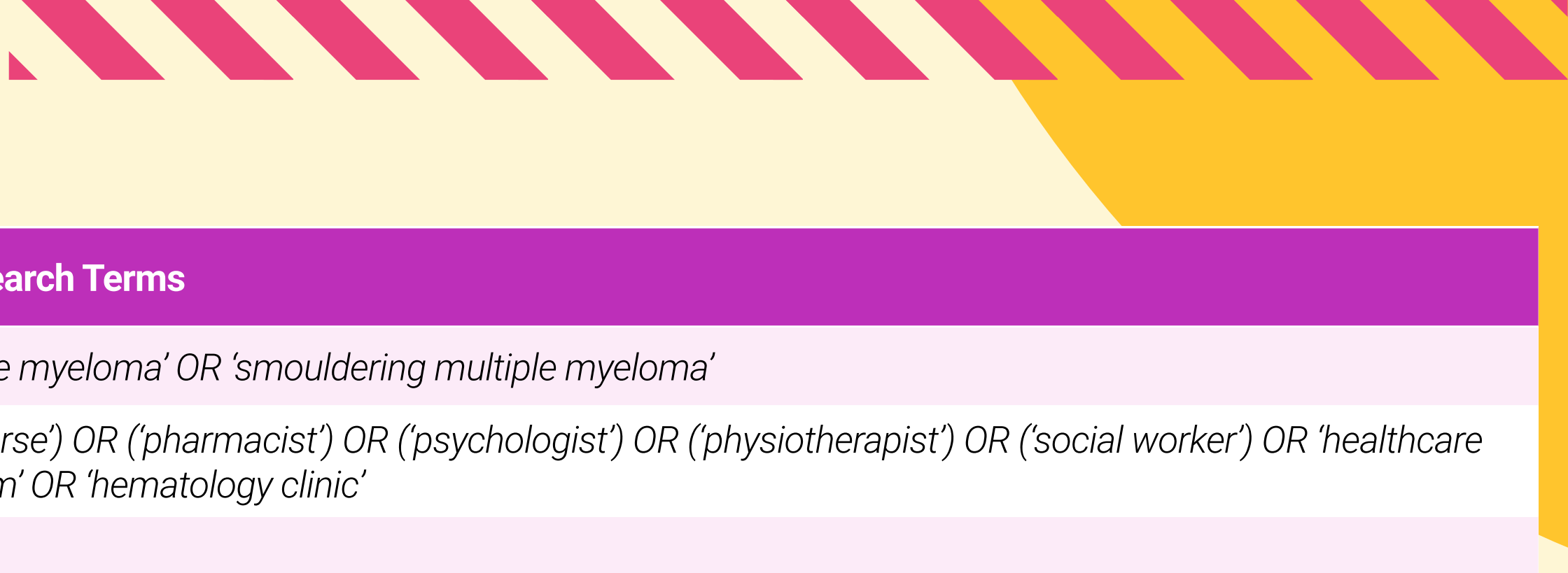
Literature search strategy

- Database used: EMBASE
- Publication dates were limited from 2019-2023
- No limitation on the publication type (i.e., journal article/ conference abstracts). Company-sponsored study/public study reports were included as appropriate
- UK and US spellings were included (e.g., haematology and hematology) within all searches, EMBASE searches accounted for this
- All included publications were peer-reviewed
- The scope of this research was global

Supplemental research

- Key areas of focus and unmet needs were identified as a result of the overarching search strategy
- Identified unmet needs and areas of focus were presented to the Collaboration Council during one virtual and one hybrid engagement
- During the meetings, the Collaboration Council members were invited to provide their insights and expertise to iterate the unmet needs
- Following feedback from the Collaboration Council, supplemental research was conducted to substantiate data
- Many Collaboration Council members provided additional references for inclusion





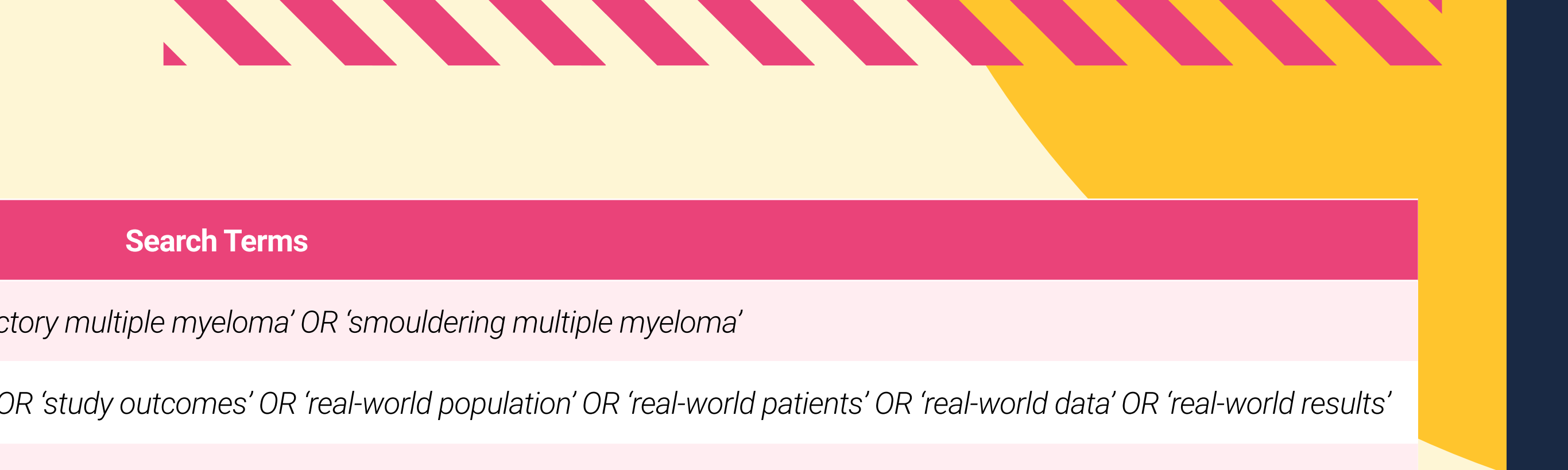
Unmet need 1: Delays in timely diagnosis of multiple myeloma

Index	Search Component	Search Terms
1	Disease area	'multiple myeloma' OR 'newly diagnosed multiple myeloma' OR 'relapsed refractory multiple myeloma' OR 'smouldering multiple myeloma'
2	Study subject	('physician' OR 'doctor' OR 'hematologist' OR 'surgeon') OR 'healthcare professional' OR ('nurse') OR ('pharmacist') OR ('psychologist') OR ('physiotherapist') OR ('social worker') OR 'healthcare provider' OR 'researcher' OR 'non-specialist' OR 'general practitioners' OR 'healthcare system' OR 'hematology clinic'
3		#1 AND #2
4		'education' OR 'awareness' OR 'diagnostic delay' OR 'delayed diagnosis' OR 'misdiagnosis' OR 'public health' OR 'screening programmes' OR 'screening programs' OR 'treatment outcomes' OR 'referral' or 'specialist care' OR 'time to diagnosis'
5	Study type	#3 AND #4
6		'survey' OR 'questionnaire' OR 'perspective' OR 'attitude' OR 'perception' OR 'satisfaction' OR 'opinion' OR 'preference' OR 'review' OR 'retrospective study' OR 'retrospective analysis' OR 'observational study' OR 'referral' OR 'referral process'
7		#5 AND #6
8	Exclusion terms	('randomized controlled trial' OR 'randomized controlled study' OR 'case series' OR 'case study')
9		#7 NOT #8
10		#9 AND 'article'/it

Unmet need 2: Complex treatment decision-making in multiple myeloma

Index	Search Component	Search Terms
1	Disease area	'multiple myeloma' OR 'newly diagnosed multiple myeloma' OR 'relapsed refractory multiple myeloma' OR 'smouldering multiple myeloma'
2	Study subject	('physician' OR 'doctor' OR 'hematologist' OR 'surgeon') OR 'healthcare professional' OR ('nurse') OR ('pharmacist') OR ('psychologist') OR ('physiotherapist') OR ('social worker') OR 'healthcare provider' OR 'researcher' OR 'non-specialist' OR 'general practitioners'
3		#1 AND #2
4		"complexity' OR 'difficulties' OR 'challenges' OR 'heterogeneity' OR 'heterogeneous'
5		#3 AND #4
6		'treatment options' OR 'treatment algorithms' OR 'treatment sequencing' OR 'combination therapy' OR decision-making OR 'precision medicine' OR 'precision oncology' OR 'optimal treatment' OR 'tailored approach' OR 'patient-centric' OR personalized care'
7	Study type	#5 AND #6
8		'survey' OR 'questionnaire' OR 'perspective' OR 'attitude' OR 'perception' OR 'satisfaction' OR 'opinion' OR 'preference'
9		#7 NOT #8
10	Exclusion terms	('randomized controlled trial' OR 'randomized controlled study' OR 'case series' OR 'case study')
11		#9 NOT #10
12		#11 AND 'article'/it





Unmet need 3: Limited applicability and diversity of clinical trials

Index	Search Component	Search Terms
1	Disease area	'multiple myeloma' OR 'newly diagnosed multiple myeloma' OR 'relapsed refractory multiple myeloma' OR 'smouldering multiple myeloma'
2	Study subject	'trial results' OR 'trial data' or 'trial outcomes' OR 'study results' OR 'study data' OR 'study outcomes' OR 'real-world population' OR 'real-world patients' OR 'real-world data' OR 'real-world results'
3		#1 AND #2
4		'Disparities' OR 'disparity' 'Generalizability' OR 'generalization' OR 'application' OR 'External validity' OR 'Underrepresented populations' OR 'participation'
5		#3 AND #4
6	Study type	'survey' OR 'questionnaire' OR 'perspective' OR 'attitude' OR 'perception' OR 'satisfaction' OR 'opinion' OR 'preference' OR 'review'
7		#5 AND #6
8	Exclusion terms	('randomized controlled trial' OR 'randomized controlled study' OR 'case series' OR 'case study')
9		#7 NOT #8
10		#9 AND 'article'/it

Unmet need 4: Inconsistent holistic management of multiple myeloma

Index	Search Component	Search Terms
1	Disease area	'multiple myeloma' OR 'newly diagnosed multiple myeloma' OR 'relapsed refractory multiple myeloma' OR 'smouldering multiple myeloma'
2	Study subject	('hospital' OR 'tertiary care' OR 'secondary care' OR 'cancer center') OR 'care center' OR 'site of care' OR 'community care' OR 'cancer clinic'
3		#1 AND #2
4		'Multidisciplinary team' OR 'Cancer care team' OR 'outpatient services' OR 'Health related quality of life' OR 'Shared decision making' OR ('patient-centered' OR 'person-centered') OR 'Treatment decisions' OR 'Patient decision making' OR 'holistic care' OR 'support groups' OR 'counselling' OR 'supportive care' OR 'holistic therapy' OR 'holistic approach' OR 'psychological support' OR 'social support' OR 'physiotherapy' OR 'mindfulness' OR 'mental health support' OR 'health-related discussions' OR 'consultation discussions' OR 'quality of life discussions'
5		#3 AND #4
6	Study type	'survey' OR 'questionnaire' OR 'perspective' OR 'attitude' OR 'perception' OR 'satisfaction' OR 'opinion' OR 'preference' OR 'review'
7		#5 AND #6
8	Exclusion terms	('randomized controlled trial' OR 'randomized controlled study' OR 'case series' OR 'case study')
9		#7 NOT #8
10		#9 AND 'article'/it





Disparities in multiple myeloma care

Index	Search Component	Search Terms
1	Disease area	<i>'multiple myeloma' OR 'newly diagnosed multiple myeloma' OR 'relapsed refractory multiple myeloma' OR 'smouldering multiple myeloma'</i>
2	Study subject	<i>'trial results' OR 'trial data' or 'trial outcomes' OR 'study results' OR 'study data' OR 'study outcomes' OR 'real-world population' OR 'real-world patients' OR 'real-world data' OR 'real-world results'</i>
3		<i>#1 AND #2</i>
4		<i>'Disparities' OR 'disparity' 'Generalizability' OR 'generalization' OR 'application' OR 'External validity' OR 'Underrepresented populations' OR 'participation'</i>
5		<i>#3 AND #4</i>
6	Study type	<i>'survey' OR 'questionnaire' OR 'perspective' OR 'attitude' OR 'perception' OR 'satisfaction' OR 'opinion' OR 'preference' OR 'review'</i>
7		<i>#5 AND #6</i>
8	Exclusion terms	<i>('randomized controlled trial' OR 'randomized controlled study' OR 'case series' OR 'case study')</i>
9		<i>#7 NOT #8</i>
10		<i>#9 AND 'article'/it</i>



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