

**ECONOMIST
IMPACT**

Multiple Myeloma in Central Europe and the Baltics:

**Supporting early and equitable
access to care to improve
patient outcomes**



Supported by

Johnson & Johnson

Contents

- 3** About this report
- 5** Executive summary
- 10** Introduction
- 15** Health systems' barriers and opportunities in addressing the new face of myeloma
 - 15** Streamlining the care pathway
 - 22** Accessing innovation: how to bridge disparities?
 - 31** Better data collection to enhance health systems' responsiveness
 - 34** Leveraging the leadership of haematologists and haematology societies
 - 35** Improving partnerships with patient organisations
- 37** Conclusion and calls to action
- 40** References

About this report

Multiple Myeloma in Central Europe and the Baltics: Supporting early and equitable access to care to improve patient outcomes is an Economist Impact white paper, commissioned by Johnson & Johnson Innovative Medicine. The report provides an independent analysis of multiple myeloma and its growing burden in the Central Europe and the Baltics (CE&B) region. The report evaluates the current care pathways for myeloma in 10 countries in the region (Bulgaria, Croatia, the Czech Republic, Estonia, Hungary, Latvia, Lithuania, Serbia, Slovakia and Slovenia), explore gaps in management, and identifies opportunities for improving patient outcomes. The insights in this report are based on an extensive literature review and desk research, expert panel discussions, and in-depth interviews with relevant clinical experts, scientific leaders, policy stakeholders and patient advocates. The editorial team at Economist Impact would like to thank the following individuals (listed alphabetically) for generously contributing their time and insights, which have been critical to the creation of this report:

Ms Mira Armour – Co-founder and CEO, MijelomCRO – The Croatian Myeloma Patients Association, Croatia

Dr Sandra Bašić-Kinda – Haematologist, University Hospital Centre Zagreb, Croatia

Prof Jelena Bila – Chair of the Serbian Myeloma Group; Head of the Ward for Multiple Myeloma and related Plasma Cell Disorders; Clinic of Haematology, University Clinical Centre of Serbia; Medical Faculty, University of Belgrade, Serbia

Prof Robert Babel'a – Professor of Public Health and Vice-Chancellor responsible for research and development at the Slovak Medical University in Bratislava, Slovakia

Ms Snežana Doder – President, Association of Myeloma Patients Serbia

Ms Ieva Dregviene – Chairperson, Association "Kraujas", Lithuania

Prof Roman Hájek – Professor of Oncology, Head of Department of HaematoOncology, University Hospital Ostrava and Faculty of Medicine, University Ostrava, the Czech Republic

Prof Ľubica Harvanová – Haematologist, Clinic of Haematology and Transfusiology, University Hospital Bratislava, Slovakia

Dr Ivan Kindekov – Haematologist, Department of Haematology, Military Medical Academy, Bulgaria

Prof Sandra Lejniece – Director of Study Programme, Department of Internal Diseases Rīga Stradiņš University; Chief of Chemotherapy and Haematology clinic in Riga East University Hospital, Latvia

Dr Diana Loigom – Haematologist, North Estonia Medical Centre Foundation, Estonia

Ms Kristina Modic – Executive Director, Slovenian Lymphoma and Leukemia Patient Association, Slovenia

Ms Kate Morgan – Co-Chief Executive Officer, Myeloma Patients Europe

Prof Gábor Mikala – Haematologist, South Pest Central Hospital, National Institute for Haematology and Infectious Diseases, Hungary

Ms Alice Onderková – Coordinator, Multiple Myeloma Patient Club, the Czech Republic

Dr Valdas Pečeliūnas – Director, National Cancer Institute of Lithuania; Haematologist, Hematology, Oncology and Transfusion Medicine Center, Vilnius University Hospital Santaros Klinikos, Lithuania

Dr Jana Skoupa – Independent Hospital & Health Care Professional, Member of the Czech Pharmacoeconomic Society, the Czech Republic

Prof Matjaž Sever – Haematologist, Head of Hematopoietic Stem Cell Transplant & Professor at the Medical Faculty, University Medical Centre Ljubljana, Slovenia

Mr Martin Smatana – Associate Fellow, Health and Economic Growth Programme, GLOBSEC; Lecturer, Slovak Medical University, Slovakia

Dr Gergely Varga – Haematologist, Department of Internal Medicine and Haematology, Semmelweis University, Hungary

Dr László Váróczy – Haematologist, University of Debrecen, Hungary

Dr Vilmantė Vaitekėnaitė – Medical doctor, Haematology, Oncology and Transfusion Medicine Centre, Vilnius University Hospital Santaros Klinikos, Lithuania

Ms Raminta Vilkevičienė – Board Member, Association “Kraujas”, Lithuania

Economist Impact bears sole responsibility for the contents of this report. The findings and views expressed in the report do not necessarily reflect the sponsor’s views. The report was written by Radha Raghupathy and edited by Gerard Dunleavy and Maria Ronald. The Economist Impact research team consisted of Rob Cook, Gerard Dunleavy, Julia Maciel de Rodrigues and Radha Raghupathy. While every effort has been taken to verify the accuracy of this information, Economist Impact cannot accept any responsibility or liability for reliance by any person on this report or any of the information, opinions or conclusions set out in this report.

Executive summary



For many patients, multiple myeloma – an incurable blood cancer – has transformed from a fast-moving and fatal disease to a chronic illness. The advent of innovative therapies and better provision of holistic care have resulted in significantly improved survival rates and health-related quality of life (HRQoL).¹ A proportion of patients with myeloma even enjoy a functional cure.² However, many patients in countries in the Central Europe and the Baltics (CE&B) region have not fully benefited from these advances. Health systems are not equipped to deal with the new face of myeloma; several gaps exist in the provision of multidisciplinary care and in the funding of novel therapies. While primarily a disease of the elderly, the rising incidence in younger adults raises new issues, including reproductive, financial and employment concerns, which health systems continue to grapple with.³⁻⁶

In this study, we evaluate the care pathway for multiple myeloma in 10 countries in the CE&B region, including Bulgaria, Croatia, the Czech Republic, Estonia, Hungary, Latvia, Lithuania, Serbia, Slovakia and Slovenia. We explore gaps in the holistic management of myeloma and propose an evidence-based roadmap to improving outcomes.

Key insights from our research include:

The health burden of myeloma in the CE&B region is rising.

The rise in the incidence of myeloma in Central and Eastern Europe is striking. Analysis of the Global Burden of Disease (GBD) data from 1990 and 2019 showed a 42.1% and 37.5% increase in the age-standardised incidence rate (ASIR) of myeloma in Eastern and Central Europe, respectively. Eastern Europe was among the top three regions experiencing the greatest increases in ASIR globally. Furthermore, while the global age-standardised death rate (ASDR) has been stable (among men) and decreasing (among women), the ASDR of myeloma in Central and Eastern Europe has increased by roughly 32% between 1990 and 2019 – indicating disparities in access to myeloma care.⁷ Data on the economic burden of myeloma in the CE&B region are sparse, and the impact of better holistic care on direct and indirect costs has not been well-studied.⁸

The CE&B region lags Western Europe in myeloma outcomes.

The difference in myeloma outcomes between Western Europe and the CE&B region is stark.⁹ A global study comparing different regions and countries for the myeloma Quality of Care Index (QCI) calculated the QCI in Western Europe to be 83.2 in 2019 as compared to 61.5 for the CE&B region. The QCI is a composite measure that takes into account four ratios: mortality to incidence, prevalence to incidence, Disability-Adjusted Life Years (DALYs) to prevalence, and Years of Life Lost (YLL) to Years of Life Lost due to Disability (YLD). The higher the score, the better the quality of care.¹⁰

Lower investments in healthcare, delayed rollout of advances in diagnosis and treatment, and health systems challenges in CE&B contribute to this disparity.¹¹ All our countries of interest have universal healthcare funded through wage contributions and/or taxation.¹² However, government spending on healthcare as a percentage of the gross domestic product (GDP) in the CE&B region is lower than that of Western Europe. For example, in 2021, government healthcare spending in the United Kingdom (UK) equalled 10.3% of GDP per capita, almost double that in Hungary and Lithuania, at 5.3% and 5.4%, respectively.¹³



Countries in the CE&B region also lag behind their European peers in terms of speed of access to innovative therapies. The W.A.I.T. Indicator 2022 Survey showed that the time duration between the European Medicines Agency's (EMA) approval of innovative therapies and their availability as reimbursable treatment options for patients was longer in a majority of CE&B countries as compared to the European Union (EU) average. The shortest delay between market authorisation and patient access was 128 days in Germany. In Croatia, the delay was estimated at 499 days, but most CE&B countries recorded a delay greater than the EU average of 517 days. Of our study countries, the delay is greatest in Serbia (811 days).¹⁴

Access to comprehensive multidisciplinary care in CE&B is limited.

Given its many manifestations affecting different organs, strong multidisciplinary care is essential to improve myeloma outcomes.¹⁵ In the CE&B region, haematologists note that most engagement with other specialists, such as nephrologists and orthopaedic surgeons, is done on an informal basis. Multidisciplinary care is concentrated in a few major hospitals, with peripheral hospitals having less access to physiotherapists, psychologists and social workers. Experts also attest to inadequate palliative care services, again with a higher concentration of such services in major hospitals. Issues among myeloma survivors need more attention, especially among the emerging cohort of younger adults with myeloma who face unique challenges related to fertility, reproduction, finances and re-entering the workforce.⁵

There is a lack of emphasis on value-based health care in the region, and robust disease-specific registries linked to payer data do not exist.

Reimbursement for first-line treatment for myeloma is not in line with the European Haematology Association-European Society for Medical Oncology (EHA-ESMO) recommendations in many of the countries studied.¹⁶ In the relapsed setting, while individual innovative therapies are often reimbursed, there is a lack of coverage for optimal combinations of these innovative drugs, which have been shown to improve outcomes.¹⁷ Part of this challenge may be attributed to rigid methodologies applied during Health Technology Assessment (HTA). Broad value-based assessments that consider the impact of therapies on quality of life and economic productivity that go beyond budget line impact are lacking, leading to fewer reimbursements of innovative treatments.¹⁸ Managed Entry Agreements (MEAs), which serve as cost/risk-sharing arrangements between pharmaceutical companies and payers, are primarily finance-based MEAs, involving price concessions and volume caps, especially when utilised to reimburse innovative therapies. Performance-based MEAs, when used, often lack high-quality data collection to study the impact of therapies on outcomes.¹⁹ The Czech Republic has a myeloma-specific disease registry, "Registry of Monoclonal Gammopathies", which some centres in Slovakia are also contributing to.²⁰ However, across the region, the development and implementation of myeloma-specific registries face challenges such as sustenance of funding, workforce allocation and confidentiality issues in data transfer. Thus far, myeloma-specific registries have yet to be effectively leveraged to support performance-based MEAs. Furthermore, data on the economic burden of myeloma are not included in these registries.

Based on these findings, we propose the following calls to action to improve the provision of comprehensive care for myeloma in the CE&B region:

Facilitate early diagnosis and specialist referral.

Facilitating early diagnosis of myeloma in CE&B needs improved awareness among physicians and the public, combined with universal access to basic laboratory tests that can confirm suspect cases. Establishing guidelines for optimal timeframes for referral and treatment, while concurrently streamlining the referral pathway, would expedite myeloma management and reduce the likelihood of irreversible organ damage.¹⁵

Invest in strengthening healthcare systems to improve the care pathway.

Myeloma is a complex disease that requires specialised care from multidisciplinary teams, including haematologists, oncologists, nurses and other healthcare professionals. Investing in strengthening healthcare systems ensures that patients have access to these specialised services, leading to better management of the disease and improved patient outcomes.

Healthcare systems in CE&B countries should be optimised to provide better ambulatory care for myeloma. Better outpatient management of myeloma would hinge on supporting decentralisation of care with a hub-and-spoke model, developing a specialist nurse service for task-sharing, and a gradual move towards home-based administration of certain injectable drugs that can be given subcutaneously.²¹⁻²⁵ These efforts, combined with improving the infrastructure for multidisciplinary care, including rehabilitation, palliative care and survivorship, will benefit the care pathway of not just myeloma but a broad spectrum of chronic diseases.

Improve access to innovation.

A structured HTA is critical to the reimbursement decision-making framework, especially in countries with publicly funded healthcare systems. However, HTA processes in the majority of countries in CE&B rely heavily on Incremental Cost-Effectiveness Ratios (ICER) to determine reimbursement. Balancing the price of a new medication against its perceived value to patients and broader society is complex, yet restricting reimbursement decisions to ICER assessments is currently limiting patient access to guideline-recommended myeloma treatment options in CE&B. HTAs require a more holistic and multidisciplinary process that incorporates economic, social, organisational and ethical considerations to guide decision-making.



Improving access to innovative treatments will require more holistic HTAs and the development of better funding models. MEAs are often used in CE&B to facilitate access to more expensive therapies, but most of them are finance-based MEAs, which are based on confidential discounts and capping. There is a need for more performance-based MEAs to facilitate value-based healthcare.²⁶ In addition, countries must strive to increase their attractiveness for clinical trials by improving their administrative capacity, supporting healthcare staff to run trials, and creating awareness among patients to improve enrolment.

Enhance estimates of the burden of myeloma and the impact of comprehensive care.

Improving estimates of the burden of myeloma requires the development of more robust disease-specific registries across the region that link to payer data. To achieve this goal, government investment in technology, infrastructure and human resources for data collection is crucial. Mandating the reporting of myeloma to these disease-specific registries will also help improve the completeness of data. The development of automated data collection systems with the capability to transfer information from electronic health records directly into registries will improve the efficiency of data management. Efforts to link myeloma-specific registries to payer data, such as in the ongoing development of the Czech National Information System and the Lithuanian Cancer Registry, will facilitate the estimation of direct

costs. More robust databases, which include both direct and indirect costs, can help to accurately estimate the impact of treatment. This will also serve as a foundation for the development of better performance-based MEAs and value-based payment models for innovation.²⁷ The CE&B region can be a forerunner in this space, given the small populations, existing national cancer registries and unified payment data.²⁸

Strengthen stakeholder collaboration towards the delivery of high-quality care.

Effective collaboration between all stakeholders, including policymakers, healthcare professionals, patients and pharmaceutical companies, is key to offering the best myeloma care. Experts describe how patient organisations across the region are pioneering the development of rehabilitation programmes with the support of health ministries, improving support for adults with myeloma, and seeking funding for the development of new programmes such as CAR-T cell therapy. Funding offered by pharmaceutical companies has facilitated the growth of the “Registry of Monoclonal Gammopathies” in the Czech Republic.²⁰ Haematologists have been actively engaging with policymakers to improve access to innovative therapies. In the Czech Republic, they have taken the initiative to raise awareness among policymakers regarding game-changing therapies versus “me-too” regimens. Hungarian haematologists have developed national guidelines that elucidate the gap between EHA-ESMO recommendations and local access to treatments.

Introduction

Multiple myeloma is a cancer that arises from plasma cells in the bone marrow – the cells responsible for making antibodies to fight infections. Among blood cancers, myeloma has the second highest incidence, accounting for 10% of blood cancers globally and 15% of cases in the Western world.²⁹ While the mean age of onset for myeloma is between 70 and 75 years, 37% of patients are younger than 65 years – and the incidence in younger adults is rising.^{3,30,31} The average number of Years of Life Lost (YLL) per patient with myeloma is about 16.8 years across all age groups. For patients between 40 and 49 years of age, YLL are about 27 years and for those under 40 years of age, YLL are as high as 36 years. In addition to a lower life expectancy, myeloma-related complications result in significant morbidity and disability. Patients with myeloma have more/severe symptoms including pain and fatigue compared

to those with other blood cancers; they also have poorer quality of life compared to several other blood cancers and solid tumours.^{29,32-35}

The acronym CRAB describes the common clinical manifestations of myeloma – hyperCalcaemia, Renal failure, Anaemia and Bone disease. Delayed diagnosis of myeloma results in more severe end-organ damage with patients presenting with debilitating symptoms such as bone fractures, compression of the spinal cord with paralysis, severe anaemia, kidney failure needing dialysis, and repeated infections.³⁶ Early diagnosis and treatment of myeloma is therefore crucial to limit end-organ damage and improve outcomes. Diagnosing myeloma requires blood tests, a bone marrow biopsy and bone imaging.³⁶

The advent of novel therapies and autologous stem cell transplantation has revolutionised the landscape of myeloma, transforming it from a fatal disease to a chronic one for many patients. The median survival of myeloma has increased significantly from ~3 years in 2000 to ~10 years at present.^{1,2,37} The use of more potent therapies earlier in the treatment course results in deeper responses, longer progression-free and overall survival – a proportion of patients treated with this approach may even achieve a functional cure.²

Among blood cancers, myeloma has the second highest incidence, accounting for 10% of blood cancers globally and 15% of cases in the Western world.

Currently approved novel agents for myeloma treatment include immunomodulators (IMiDs: thalidomide, lenalidomide and pomalidomide), proteasome inhibitors (PI: bortezomib [V], carfilzomib [K] and ixazomib [Ixa]), monoclonal antibodies (daratumumab [Dara], isatuximab and elotuzumab), bispecific antibodies (teclistamab, talquetamab and elranatamab), Chimeric Antigen Receptor-T cell therapies (CAR-T: ciltacabtagene autoleucel and idecabtagene vicleucel) and selective inhibitors of nuclear export (selenixor). For patients eligible for autologous stem cell transplant, the European Haematology Association-European Society for Medical Oncology (EHA-ESMO) guidelines recommend either the quadruplet daratumumab, bortezomib, thalidomide, dexamethasone (Dara-VTd) or the triplet bortezomib, lenalidomide, dexamethasone (VRd) as induction therapy, followed by transplant with melphalan conditioning and then lenalidomide maintenance. For transplant-ineligible patients, one of three combinations is recommended as induction: daratumumab, lenalidomide, dexamethasone (Dara-Rd)/daratumumab, bortezomib, melphalan, prednisolone (Dara-VMP)/VRd.^{16,38} Bone-strengthening treatments are also given to all patients with myeloma and bone disease in order to reduce the risk of fractures and disabilities.^{39,40}

Myeloma has the greatest symptom burden and lowest health-related quality of life (HRQoL) among patients with blood cancer.⁴¹ The use of comprehensive multidisciplinary care, including rehabilitation, psychosocial and supportive management, is crucial in mitigating symptoms of disease-related complications, including organ failure and bone fractures, as well as treatment-related side effects such as fatigue, neuropathy and gastrointestinal symptoms.⁴² Improving the care pathway for

myeloma can generate cost-savings for patients and payers, while improving outcomes and quality of life.²⁸ Achieving the deepest clinical response with the optimal induction therapy, delayed progression and fewer overall lines of therapy have been consistently associated with improved HRQoL in patients with myeloma.⁴³

Despite the advent of novel therapies and autologous stem cell transplants that have greatly improved survival rates and HRQoL in patients with myeloma, access to these improvements hasn't been universal. Real-world evidence has shown significant differences in clinical care for myeloma between Western and Central and Eastern European countries.⁹

Mortality rates due to myeloma continue to be higher in Eastern as compared to Western Europe, suggesting differences in the rollout of advances in diagnosis, treatment and management between the two regions.¹¹ A global study examined the myeloma Quality of Care Index (QCI). The QCI is a composite measure that takes into account four ratios: mortality to incidence, prevalence to incidence, Disability-Adjusted Life Years (DALYs) to prevalence, and YLL to Years of Life Lost due to Disability (YLD), where higher scores indicate better quality of care. The study found significantly higher scores in Western Europe, with a QCI of 83.2 as compared to 61.5 for the Central Europe and the Baltics (CE&B) region.¹⁰

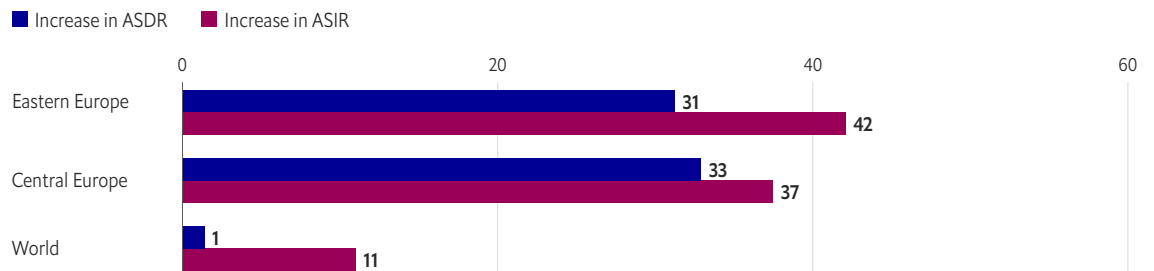
Our study will evaluate the care pathway for multiple myeloma in 10 countries in CE&B region, including Bulgaria, Croatia, the Czech Republic, Estonia, Hungary, Latvia, Lithuania, Serbia, Slovakia and Slovenia, explore gaps in disease management, and propose an evidence-based roadmap to improving outcomes.

The rising health burden of myeloma

The global incidence of myeloma is rising. A study of the trend of myeloma incidence using the Global Burden of Disease (GBD) data between 1990 and 2019 showed a 12% increase in the age-standardised incidence rate (ASIR) of myeloma from 1.72 per 100,000 people in 1990 to 1.92 per 100,000 people in 2019. Central Europe had a greater rise in the ASIR than the global average; the ASIR was 2.13 per 100,000 in 2019 (95% CI:1.7-2.5), which represents a 37.5% (95% CI:6.3-58.9%) increase in the ASIR between 1990 and 2019. As for Eastern Europe, the ASIR was 1.57 per 100,000 (95% CI:1.4-1.8) in 2019, which translates to an increase of 42.1% (95% CI: 21.5-60.3%) in the same timeframe.

Eastern Europe was among the top three regions of the world with the highest rise in the ASIR of myeloma between 1990 and 2019, and Estonia was among the top three countries for the same during this timeframe.⁷ The increasing incidence in Central and Eastern Europe has been attributed to greater awareness of the disease, rising prevalence of risk factors and higher rates of diagnosis.⁷ Advancing age, male sex, black race, physical inactivity, obesity, diabetes mellitus and a family history of the disease are all risk factors for myeloma.⁴⁴ Epidemiological studies in Croatia also suggest a positive correlation between proximity to oil and gas fields and the probability of developing myeloma.⁴⁵

Figure 1: Percentage increase in age-standardised incidence and death rate (ASIR and ASDR) of myeloma between 1990 and 2019 in Central and Eastern Europe compared to the global average⁷



Notes:

Central Europe: Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Czechia, Hungary, Montenegro, North Macedonia, Poland, Romania, Serbia, Slovakia, Slovenia; Eastern Europe: Belarus, Estonia, Latvia, Lithuania, Moldova, Russia, Ukraine

ASIR: age-standardised incidence rate; ASDR: age-standardised death rate

In contrast to the improving global mortality rates for myeloma, Central and Eastern Europe are experiencing a rise. The global age-standardised death rate (ASDR) of myeloma has shown a decline for women between 1990 and 2019, while remaining steady for men. However, the ASDR has increased by roughly 32% between 1990 and 2019 in Central and Eastern Europe. Estonia was among the top three countries showing the greatest percentage increase in ASDR for myeloma in this timeframe.⁷

The trends in myeloma incidence and mortality between 2001 and 2019 in individual countries were evaluated in another epidemiological study, which used various global databases, including the WHO Global Cancer Observatory (2020), Cancer Incidence in Five Continents (CI5) databases, the WHO Mortality Database, the Association of the Nordic Cancer Registries (NORDCAN) and the Surveillance Epidemiology and End Results (SEER) Program (1990-2019).

Among the 48 countries included, Croatia was in the top three countries reporting the largest increase in myeloma-related ASDR among men. Latvia and Bulgaria were among the top three countries reporting the largest increase in ASDR among women.⁴⁴

By 2050, the number of new patients with myeloma over 60 years of age is expected to increase in all countries in the CE&B region, except Serbia, which is projected to have a minor decrease (4%), according to forecasts by the International Agency for Research on Cancer (IARC). An increase of 55% is foreseen for Slovakia and Slovenia, while Estonia, the Czech Republic and Hungary will see a rise in excess of 20%.⁴⁶ Owing to the larger number of patients, the total number of deaths due to myeloma in those over 60 years of age is expected to increase across all countries in the region.⁴⁷ These concerning trends and projections in disease burden highlight the need for urgent attention.

Figure 2: Estimated number of new myeloma cases from 2022 to 2050 (among those aged 60–85 years)⁴⁶

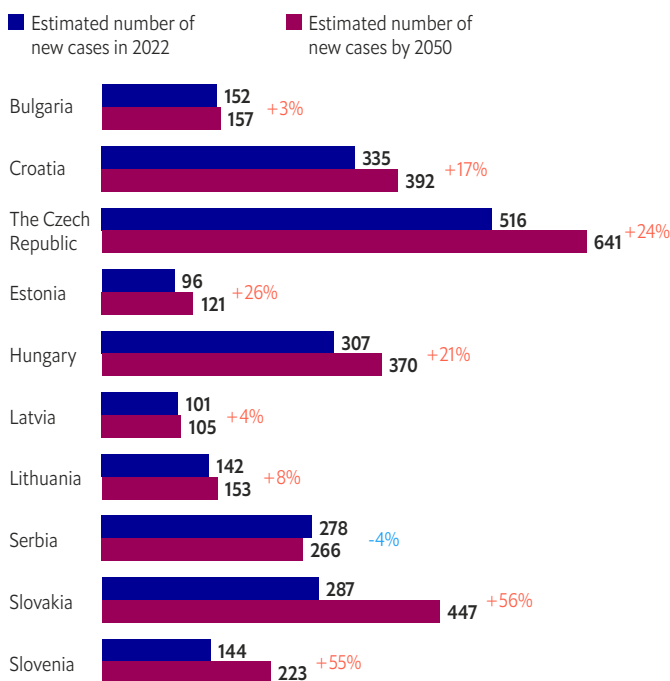
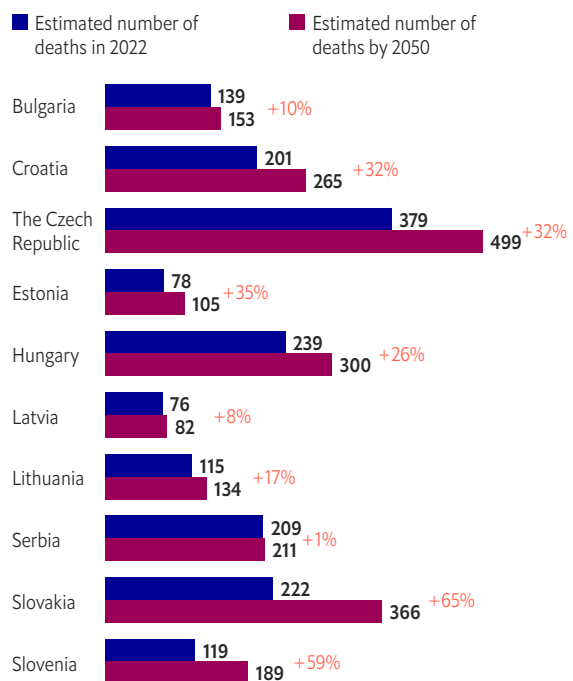


Figure 3: Estimated number of deaths due to myeloma from 2022 to 2050 (among those aged 60–85 years)⁴⁷



Economic burden of myeloma in the CE&B region: unknowns predominate

Limited information exists about the economic burden of myeloma in the CE&B region. A retrospective study of the economic burden of myeloma in Slovakia using health and social insurance records showed an increase in direct costs from €19.4m in 2014 to €24.8m in 2019. The proportion of pharmaceutical costs declined from 53.5% to 47.5% and that of inpatient care similarly fell from 18.8% to 12.3% in the same timeframe, while the portion of costs for diagnosis increased from 27.7% to 40.2%.⁸ Robert Babel'a, a health economist and Professor of Public Health and Vice-Chancellor responsible for research and development at the Slovak Medical University in Bratislava, Slovakia, led this analysis and shared that further data collection is ongoing. He also explains that from examining more than ten years of data, this trend appears to be continuing, with a concurrent decrease in the proportion of spending in the inpatient setting for patients with myeloma. He suggests the decreasing percentage of inpatient care costs reflects the impact of improved diagnostic techniques and early treatment.

Data suggest that improving the care pathway for myeloma can generate cost-savings for patients and payers, in addition to improving outcomes and quality of life.²⁸ However, the overall impact of better diagnostic techniques, innovative therapies and comprehensive care on the direct and indirect costs of myeloma in the CE&B region remains poorly studied. "The introduction of newer treatment regimens for myeloma has significantly improved progression-free survival. So instead of using seven to eight lines of treatment within ten years, we are now using two to three lines for each patient. With current treatments, about 10-15% of patients achieve a functional cure. We expect that number to be higher with the use of more innovative therapies moving to earlier lines. The potential for cure drastically changes the economic impact of treatment," opines Roman Hájek, Professor of Oncology and Head of Department of HaematoOncology at the University Hospital Ostrava and Faculty of Medicine, University Ostrava, the Czech Republic.

Prof Babel'a notes that economic analyses and policymakers need to take a long-term and holistic view when considering the economic impact of oncology treatments, saying, "It is worth investing in oncology as it will bring back an economic benefit in terms of productivity, but the challenge is you need to look at longer than the four years, which is how long one government typically lasts. So we have to change the mindset and narrative and say if you invest today, don't expect to have the results in four years, but if you look 10-15 years down the line, you will see a greater benefit for healthcare and social system, as well as for the whole society."

“With current treatments, about 10-15% of patients achieve a functional cure. We expect that number to be higher with the use of more innovative therapies moving to earlier lines. The potential for cure drastically changes the economic impact of treatment.”

Professor Roman Hájek, Professor of Oncology, Head of Department of HaematoOncology at the University Hospital Ostrava and Faculty of Medicine, University Ostrava, the Czech Republic

Health systems' barriers and opportunities in addressing the new face of myeloma

"We are practising medicine of the 21st century, but the health systems' organisation is that of the 18th century," remarks Jana Skoupa, an Independent Hospital & Health Care Professional, and Member of the Czech Pharmacoeconomic Society, the Czech Republic. With greater awareness, earlier diagnosis and many better treatments, administered orally or subcutaneously, myeloma management is moving from the inpatient to the outpatient setting.⁴⁸ There is therefore great pressure on health systems to improve ambulatory care capacity and make innovation accessible to patients despite tight budgets. The CE&B region is no exception to countries facing these challenges.

"We are practising medicine of the 21st century, but the health systems' organisation is that of the 18th century. "

Dr Jana Skoupa, Member of the Czech Pharmacoeconomic Society, the Czech Republic

Streamlining the care pathway

Expediting diagnosis and treatment: what system-wide changes will help?

Myeloma is not a common disease, and its symptoms are often vague and variable. Symptoms include back pain, fatigue and kidney failure, all of which could be attributed to many other diseases. Because of its non-specific presentation, myeloma has one of the longest diagnostic intervals among all cancers. Delayed diagnosis is costly as patients often end up presenting with more advanced end-organ damage. Fractures due to destructive bone lesions, compression of the spinal cord resulting in limb weakness, and advanced renal failure are some of the severe end-organ complications that patients present with before they receive a myeloma diagnosis. While myeloma is a condition that can mostly be managed in the outpatient setting, the onset of complications often necessitates inpatient care and limits the treatment options available to the patient. Overall, there is higher morbidity, disability, mortality and healthcare costs due to late diagnosis. In addition, delayed diagnosis significantly impacts the physical and emotional well-being of carers.⁴⁹



In the CE&B region, delayed diagnosis remains a significant problem. A 2018 survey of experts conducted by Myeloma Patients Europe estimated that the median time from onset of symptoms to diagnosis was less than three months in countries like Ireland, Italy and Belgium, while in Bulgaria and Slovakia, it was estimated to be 6-12 months.⁵⁰ Studies in Hungary and Lithuania show a median diagnostic interval of around 4-5 months for myeloma.^{51,52} Based on a Europe-wide survey, 21% of patients reported that they saw three or more specialists before a diagnosis was made, while 9% of patients were diagnosed in the emergency room.⁵³

Raising awareness of the disease among the public and physicians is key to earlier diagnosis. Hungarian experts describe their efforts in raising awareness among general practitioners (GPs), nephrologists and orthopaedic surgeons who often encounter patients with myeloma first. Jelena Bila, Chair of the Serbian Myeloma Group; Head of the Ward for Multiple Myeloma and related Plasma Cell Disorders; Clinic of Haematology, University Clinical Centre of Serbia; Medical Faculty, University of Belgrade, tells us that since its foundation 15 years ago, "The Serbian Myeloma Group is constantly working on the education of medical professionals, myeloma patients and their families, incorporating all internationally recognised updates in

diagnostics and treatment, resulting in significant improvement regarding early recognition and prevention of myeloma complications." In Estonia, Diana Loigom, a haematologist at North Estonia Medical Centre, describes that haematologists host an annual event to provide training and information on haematological disorders like myeloma to GPs and other specialists. Prof Hájek reports that while delays to diagnosis are falling, "still about one-third of patients are diagnosed later than we wish." Czech and Slovakian myeloma experts have joined together to work on a project that aims to understand the symptoms with which patients present to the physician and the current diagnostic interval for myeloma. Current data will be compared to similar data collected ten years ago to understand the gaps and to design appropriate programmes to improve myeloma awareness.

"Improvement of the diagnostic infrastructure was one of six key calls to action in a white paper that gathered insights from physical therapists, nurses, patient support groups and haematologists on the most important actions needed to improve myeloma care in Hungary," says Gábor Mikala, a Haematologist at South Pest Central Hospital, National Institute for Haematology and Infectious Diseases, Hungary. He goes on to elaborate that "A late diagnosis can lead to terrible consequences such as long-term

dialysis. What we see in Hungary, especially in elderly patients with a late diagnosis, is that many of them unfortunately die in the first one or two months of their disease. This early mortality could be really handled only if we can identify patients earlier in the disease course, and this is something we have to accomplish with better involvement of the family physicians.”

Indeed, simply raising awareness would be ineffective in overcoming delays if it were not also accompanied by access to appropriate tools for diagnosis. Experts across the countries of study generally agreed that access to myeloma diagnostics has vastly improved, although a couple of exceptions were noted. Hungarian experts highlighted that GPs could not order serum protein electrophoresis (SPEP) or serum-free light-chain (SFLC) tests. Therefore, patients need to be referred to a haematologist upon initial suspicion of myeloma, which creates a bottleneck and delays in diagnosis. If patients present with kidney failure, the challenge can be greater. “SFLC is still not available in most Hungarian hospitals to evaluate renal failure to diagnose light chain myeloma. Therefore, patients will need to do a kidney biopsy, and the result is available in two weeks by which time the renal failure may be irreversible,”

highlights Gergely Varga, Haematologist at the Károly Rácz Doctoral School of Clinical Medicine, Semmelweis University, Hungary. Basic diagnostic tests for myeloma need to be made accessible across all hospitals and among all physicians to facilitate early detection and avoid irreversible end-organ damage.

Dr Varga describes how he manages patients suspected to have myeloma. “If there is a patient with myeloma and kidney failure, I fast-track the patient to be seen very quickly – on the same day or the next day. I do the bone marrow, see the smear in half an hour, and administer treatment within an hour,” he describes. However, such a fast-track arrangement relies on the motivations and contributions of individual physicians in Hungary – it does not exist system-wide. In contrast, Dr Loigom explains that Estonia has haematologists who can be contacted round-the-clock by telephone to fast-track referrals and management. A system of e-consultation also exists where the patient’s physician can email the system with the patient’s symptoms, medications and any blood tests that have been performed. Then, an appointment is scheduled with a haematologist based on the urgency of the situation.

“SFLC is still not available in most Hungarian hospitals to evaluate renal failure to diagnose light chain myeloma. Therefore, patients will need to do a kidney biopsy, and the result is available in two weeks by which time the renal failure may be irreversible.”

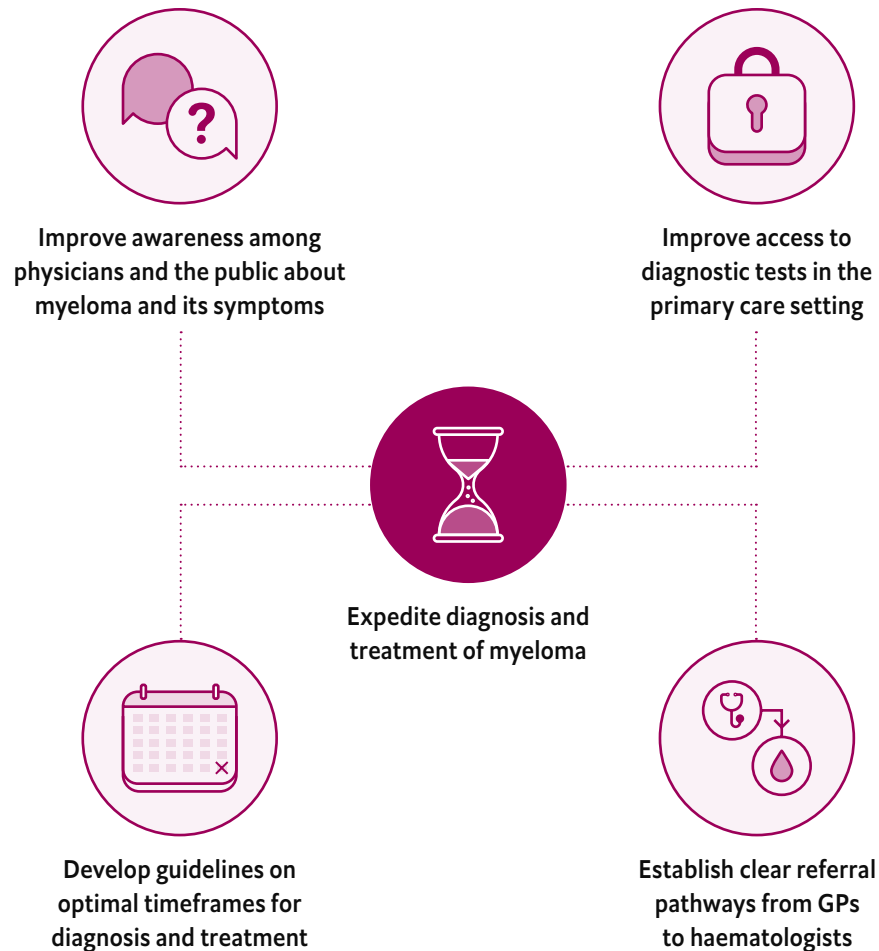
Dr Gergely Varga, Haematologist at the Károly Rácz Doctoral School of Clinical Medicine, Semmelweis University, Hungary

Developing guidelines for optimal care pathways of expedited management of patients with myeloma and impending organ damage will be critical in making a systematic change. The Australian optimal care pathway for myeloma, published in October 2021, is a good example in this regard. The guidelines have recommended timelines for prompt specialist referral of patients with suspected myeloma and rapid onset of treatment, especially for those with moderate to severe disease.¹⁵ The National Health Service (NHS) in Wales is also developing disease-specific guidelines on timeframes for diagnosis and

management of patients with suspected cancers, called the Suspected Cancer Pathway (SCP).⁵⁴ The use of such optimal treatment guidelines for other diseases such as lung cancer has shown a shorter time to diagnosis and treatment, potentially lower healthcare costs, increased patient satisfaction and provision of higher quality of care.⁵⁵

A coordinated effort to improve awareness, increase access to diagnostics, streamline referrals to specialists and establish optimal timeframes for therapy would improve the efficiency of care and myeloma outcomes.

Figure 4: Proposed approaches to expedite diagnosis and management of myeloma in the CE&B region



Source: Economist Impact



Centralised myeloma care or a hub-and-spoke model: what should we adopt to manage increasing outpatient care?

Experts note decreasing inpatient care for myeloma due to earlier diagnosis, less severe end-organ damage and the availability of several effective novel treatments that can be administered in the outpatient setting. As Prof Mikala explains, “In our hospital, the number of beds assigned for myeloma has decreased by about 50% over the past few years. Despite this reduction, we have managed to continue providing care effectively. This is possible due to the availability of novel agents and the expansion of outpatient facilities.” This shift to ambulatory care mirrors the trend seen in countries outside the CE&B region.^{56,57} Different countries in CE&B are tackling the rising ambulatory burden differently.

Some countries in the CE&B region still heavily rely on centralised care for outpatient management of myeloma. Experts in Hungary share that patients with myeloma are treated exclusively in designated centres. Local hospitals are not authorised to prescribe myeloma therapies. Patients need to travel long distances to access myeloma care, and there are significant financial implications for both patients and caregivers. Sandra Lejniece, Director of Study Programme at Rīga Stradiņš University's

Department of Internal Diseases and Chief of the Chemotherapy and Haematology clinic in Riga East University Hospital, describes a similar situation in Latvia where myeloma treatment can only be prescribed in four designated centres. Prof Hájek notes that in the Czech Republic, the myeloma centres of excellence provide treatment and are well-distributed across the country. However, there are regional differences in access to care, and sometimes patients need to travel as far as 80km to receive treatment.

The situation is different in Serbia, Estonia and Croatia, where care is more decentralised with the adoption of a hub-and-spoke model. The major specialist centres for myeloma diagnose patients and provide the treatment plan. Patients may then return to loco-regional hospitals to continue their treatment plan. They are re-evaluated as needed by the specialist centre. The haematologists in peripheral hospitals are supported through case discussions via weekly video conferences with the specialist centre.

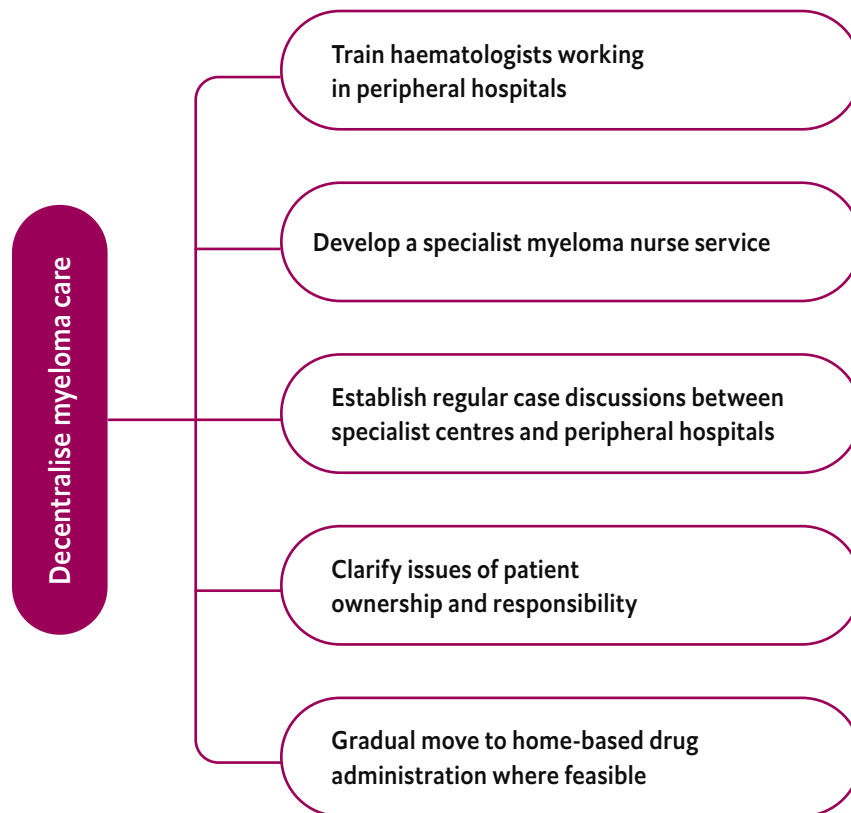
In the long run, decentralising routine ambulatory care for myeloma patients, similar to the practice in Serbia, Estonia and Croatia, is crucial to managing the increasing outpatient burden. Appropriate education, training and support for haematologists working in the periphery are key to these efforts. Issues such as patient ownership and responsibility for ongoing care

should be clarified at the outset. Developing a specialist nurse model would also greatly support physicians managing the increasing number of ambulatory visits. Australia, New Zealand, the United Kingdom (UK) and the United States are notable examples of countries that have myeloma nurse specialists (MNS) to effectively support holistic patient care.^{21,22}

Several countries in Europe, including Denmark, the UK and France, greatly expanded home-based myeloma treatments to reduce hospital visits during the Covid-19 pandemic.⁵⁸⁻⁶⁰ With some treatments, eligible and willing patients were trained to self-administer subcutaneous

injections, while specialist nurses delivered other therapies during a home visit. Moving certain treatments to home-based administration empowers patients, improves their HRQoL and may lower the burden on healthcare systems.²³⁻²⁵ Mira Armour, Co-founder and CEO of “MijelomCRO” – The Croatian Myeloma Patients Association, reports, “The transfer of good practice from where it is used, such as Oxford and Nottingham University Hospitals with their home-delivery or self-administration of some myeloma treatments, needs to be utilised more widely as soon as possible. We hope to see this becoming the norm.”

Figure 5: Proposed path to decentralising myeloma care



Source: Economist Impact

Transplantation for myeloma: how to augment capacity?

Access to autologous stem cell transplants varies across the countries studied. Across the majority of countries in our study, experts report that patients have timely access to transplants. Ivan Kindekov, a Haematologist at the Military Medical Academy's Department of Haematology, Bulgaria, describes how autologous transplantations, provided in the country's university clinics, are situated strategically, explaining that "There are currently three centres for transplantations which are distributed in such a way as to cover the entire health map of the country." However, Ľubica Harvanová, a Haematologist at University Hospital Bratislava's Clinic of Haematology and Transfusiology,

Slovakia, describes challenges facing her centre in terms of the provision of autologous stem cell transplantation. "The main barrier seems to be the availability of beds in hospitals. Our centre in Bratislava also performs allogeneic transplantation for the whole of Slovakia, which adds to the strain on bed availability. Conversely, other centres only perform autologous stem cell transplantation and do not face this particular issue," she notes. To overcome barriers to accessing autologous stem cell transplants, Prof Harvanová emphasises the need to develop outpatient programmes.⁶¹ Her centre has performed two outpatient transplants so far. However, expanding this endeavour will require training, capacity development, close monitoring for complications and engagement with insurance companies to facilitate reimbursement.

Prof Mikala describes a unique situation in Hungary where some centres have freed-up transplant capacity. This is partly due to tandem transplantation (performing two transplants sequentially for patients with myeloma) being restricted to select high-risk cases following the advent of effective novel agents. Such freed-up capacity can be used to develop CAR-T cell programmes that require cell-harvesting procedures similar to transplantation.

Comprehensive multidisciplinary care: how to cover blind spots?

Multidisciplinary care, where all treating specialists discuss and make joint decisions regarding patient management and thereby deliver patient-centric care, is recommended to improve myeloma outcomes.¹⁵ Patients with myeloma often need care from nephrologists, orthopaedic surgeons, radiation oncologists, palliative care specialists, nurses, rehabilitation teams and social workers in addition to haematologists. However, access to different specialists in a coordinated and expedited fashion



is a challenge across health systems in CE&B. Dr Varga notes “I usually pick up the phone to call the nephrologist if a patient in front of me has renal complications and together we fast-track the patient to be seen efficiently and quickly. Having a multidisciplinary team (MDT) meeting can have its own challenges, especially if physicians are waiting for the MDT to decide on management when patients need therapy imminently.” Slovakian experts describe good coordination between nephrologists and surgeons, while coordination between neurologists and psychologists is less robust. In Croatia, smaller hospitals have less access to multidisciplinary care, especially with regard to psychologists, physiotherapists and social workers.

Experts across all countries studied attest to significant gaps in palliative and end-of-life care. Prof Harvanová shares that “The availability of palliative care is a significant issue in Slovakia. For instance, in Bratislava, there’s only one palliative care department, along with a few centres for long-term patients and a few hospices. This shortage of resources greatly affects palliative care not only in the capital but also across the entire country.” According to Sandra Bašić-Kinda, a Haematologist in the University Hospital Centre Zagreb, Croatia, “The absence of insurance coverage for palliative care services has been a challenge in Croatia, but the country is working towards improving services.” The enactment of successive national strategies for palliative care in Croatia has increased the number of coordinators in palliative care contracted by the Croatian Health Insurance Fund from 29 to 42 between 2016 and 2020, while the number of palliative care beds has increased from 48 to 88 per million.⁶² Despite the growth in palliative care capacity, further improvements are needed as Dr Bašić-Kinda reports, “We still do not have enough hospital beds for palliative care.” Prof Lejniece

describes Latvia as having only one palliative care department, but that “a new initiative for home-based palliative care is showing promise”.

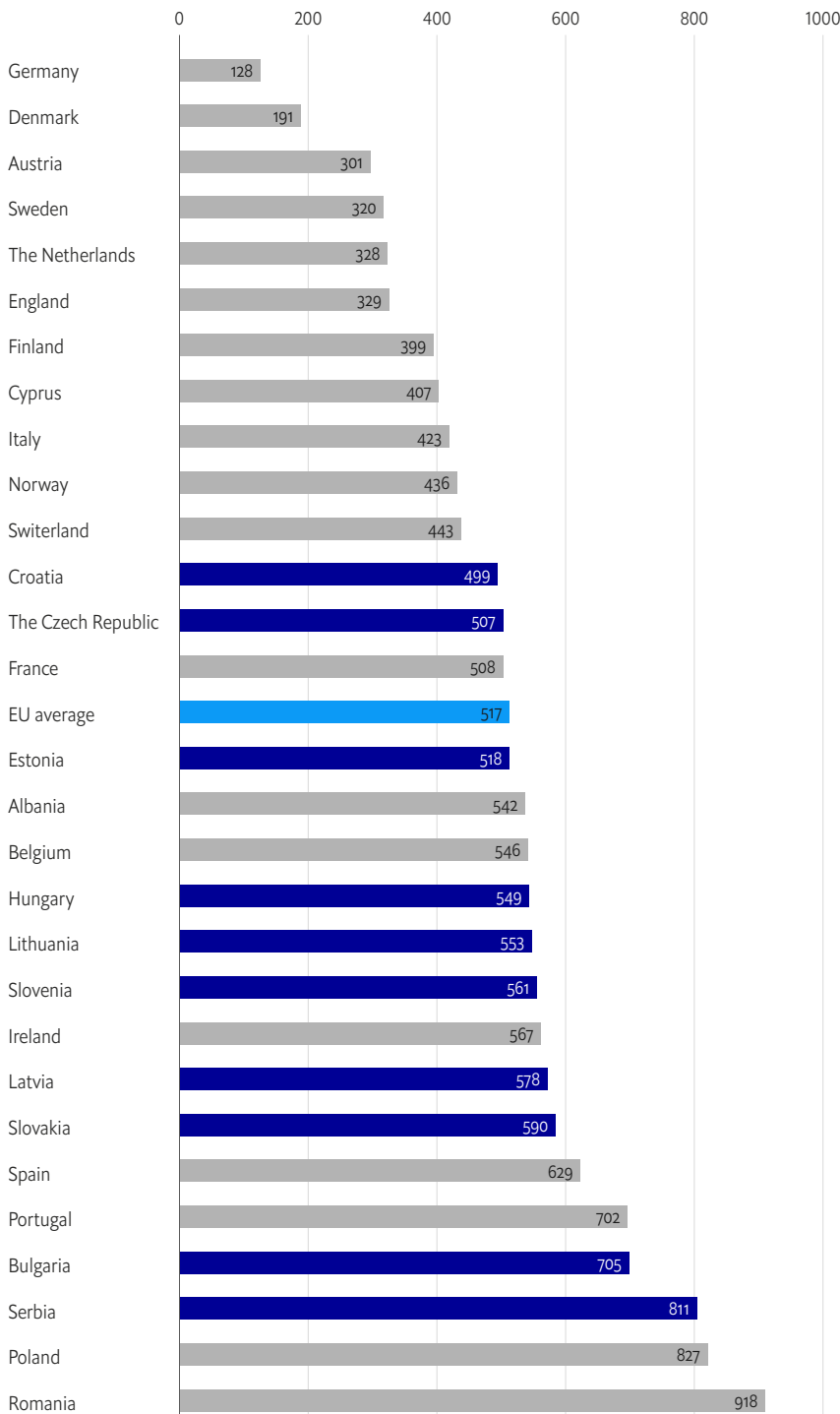
With a greater number of people aged 30 to 50 years developing myeloma, there is a pressing need to improve survivorship care and facilitate their reintegration into the workforce.^{5,6} Kristina Modic, Executive Director of the Slovenian Lymphoma and Leukemia Patient Association, Slovenia, opines that “Special consideration is needed for young myeloma patients, who have distinct needs in terms of treatment, support and reintegration into daily life post-treatment. Many face financial challenges due to their inability to work, highlighting the need for support from both the healthcare and social systems.” Kate Morgan, Co-Chief Executive Officer of Myeloma Patients Europe, informs that Myeloma Patients Europe, which is a consortium of myeloma patient support organisations, is establishing a new group dedicated to understanding the unique challenges of, and advocating for, younger myeloma patients.

Accessing innovation: how to bridge disparities?

Delayed approval and reimbursement decisions for innovative therapies in the CE&B region

The W.A.I.T. Indicator 2022 Survey highlights the variation in European countries between EMA approval of a product and its availability as a reimbursed treatment option for patients. The survey examines 168 innovative medicines authorised by the EMA between 2018-2021. The average length of time to market access is higher in most countries in the CE&B region as compared to the EU average. Of the countries studied for this report, the delay between market authorisation and patient access to new medicines is greatest in Serbia (811 days).¹⁴

Figure 6: Length of average market access delays by country (in days)



Source: IQVIA, EFPIA Patient W.A.I.T. Indicator 2022 Survey¹⁴

Several approved innovative therapies for myeloma are not readily available in our countries of interest, especially in earlier treatment lines where they offer significant benefits. Even where the drug is reimbursed, long delays are seen between drug approval and reimbursement by individual countries in line with findings in the W.A.I.T. Indicator survey. The time interval between EMA approval and coverage for daratumumab was 30 and 39 months in Estonia and the Czech Republic, respectively. The interval between EMA approval and coverage for ixazomib was 27 months in the Czech Republic.⁶³ Raminta Vilkevičienė, a Board Member of Association “Kraujas”, Lithuania, describes the situation regarding reimbursement of myeloma therapies in her country. “In 2022, a 10-year analysis of drug availability for multiple myeloma patients was performed. During this time, 13 new drugs were registered by the EMA for treating myeloma, but by 2022, only three of these medicines were available in our country. The reimbursement process for these drugs took at least four years, and for one of them, it took seven years,” she highlights.

These delayed approval and reimbursement decisions contribute to significant disparities in access to myeloma therapies between Western Europe and CE&B countries.⁶⁴ A 2019 study of cancer therapies across the EU included all the countries in our study except Serbia and Estonia. The countries were grouped into lower-, middle- and upper-tier gross domestic product (GDP) per capita – all our countries fell in the lower tier. The use of innovative medicines in myeloma was low or very low in lower-tier countries in 2018. Myeloma had the greatest inequalities in the use of innovative therapies between the tiers of countries across all cancer types studied.⁶⁵

Current status of reimbursement and access to myeloma therapies in CE&B

Table 1 details the reimbursement status of first-line treatment combinations recommended by the EHA-ESMO, across countries in the CE&B region and EU5 (France, Germany, Italy, Spain and the UK [availability in England was used to represent the UK]). These data further highlight disparities in treatment between CE&B and the rest of Europe. Generally, access to recommended treatments is greater in the EU5 countries compared to the CE&B region. Slovenia has the greatest availability of guideline-recommended treatments in the CE&B region, while Serbia doesn't reimburse any recommended treatment combinations in the first line. While Lithuania currently has the second lowest level of access to these treatments in the first line, Vilmantė Vaitekėnaitė, a Medical Doctor at the Haematology, Oncology and Transfusion Medicine Centre, Vilnius University Hospital Santaros Klinikos, Lithuania, shares that Dara-VTd will be reimbursed for patients eligible for autologous stem cell transplant from September 2024.

According to Matjaž Sever, Head of Hematopoietic Stem Cell Transplant & Professor at the Medical Faculty, University Medical Centre Ljubljana, Slovenia, essentially all innovative therapies for myeloma are available in Slovenia, including monoclonal and bispecific antibodies. Three bispecific antibodies were being used on a compassionate basis, of which one is now approved and available for regular prescription, followed by the other two by the end of the year. Patients are also referred to Germany to receive CAR-T cell therapy. The reasons for such good access in Slovenia include effective work by regulatory authorities and careful patient selection by doctors to ensure that the reimbursed therapies are used in a cost-effective manner. When a new drug is introduced in the market, physicians choose patients who have the most severe disease and are most likely to benefit from the treatment to receive it. Prof Sever explains, "Such patient selection is based on team discussions in the main tertiary care centre. If peripheral hospitals have patients that can benefit from such innovative therapies, these cases are also discussed in the tertiary centre

Table 1: Availability of first-line treatments in line with EHA-ESMO recommendations

■ Reimbursement ■ No Reimbursement ■ Reimbursement with restrictions

	CE&B region										EU5				
	BG	CZ	ES	HR	HU	LV	LT	RS	SK	SI	DE	EN	FR	IT	SP
Patients eligible for autologous stem cell transplant															
Induction: Dara-VTd	N^	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	Y	Y
Induction: VRd	Y	Y	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y
Maintenance: Lenalidomide	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y
Patients ineligible for autologous stem cell transplant															
Dara-Rd	Y	N	N	N*	N	N	N	N	N*	Y	Y	Y	Y	Y	Y
Dara-VMP	N	N	N	N*	N	N	Y	N	Y	Y	Y	N	Y	Y	Y
VRd	N	Y	Y	Y	Y	Y	N	N	Y	Y	Y	R	N	N	N

Countries: BG: Bulgaria; CZ: The Czech Republic; ES: Estonia; HR: Croatia; HU: Hungary; LV: Latvia; LT: Lithuania; RS: Serbia; SK: Slovakia; SI: Slovenia; DE: Germany; FR: France; EN: United Kingdom; IT: Italy; SP: Spain

Treatment options
 Dara-VTd: daratumumab, bortezomib, thalidomide, dexamethasone; VRd: Bortezomib, lenalidomide, dexamethasone; Dara-Rd: Daratumumab, lenalidomide, dexamethasone; Dara-VMP: Daratumumab, bortezomib, melphalan, prednisolone

^Daratumumab, bortezomib, dexamethasone are reimbursed but thalidomide is not reimbursed

*Reimbursement expected mid-2024

Source: MPE Atlas and expert interviews

and a recommendation letter is given to the treating physician. There are no clear guidelines or official limits on the number of patients that can receive treatment; physicians make decisions based on clinical need.” Prof Harvanová describes the situation with access in Slovakia, “While access to innovative drugs in newly diagnosed multiple myeloma follows guidelines, inadequate access to these drugs is noted in relapsed refractory multiple myeloma. Many innovative agents cannot be used in the second line, they are only available in the third or fourth line of treatment and not in optimal combinations.”

In some CE&B countries with poor access to recommended first-line options, applications can be filed by individual patients to request reimbursement for specific drugs. For example, in Hungary, experts say that doctors can submit applications requesting reimbursement

of a drug on a case-by-case basis. However, the timeframe for approvals can be lengthy – patients with critical end-organ damage may succumb to the disease during the wait. Experts also allude to a lack of transparency in how the reimbursement is awarded and report a high administrative burden. Snežana Doder, President of the Association of Myeloma Patients Serbia, discusses access to treatments in Serbia, “Drugs included in the so-called positive list of Republic Fund for Health Insurance are reimbursed and costs of such treatment is covered by the Fund.” However, patients face challenges accessing treatments that are not on the reimbursement list, and as already highlighted in Table 1, there is a lack of access to guideline-recommended treatment in Serbia. Ms Doder, shares that, “in the case of exhausted treatment options, special applications can be made in accordance with Article 9 health care regulation so that patients can access drugs that don't appear on the positive list.” Prof Bila further references using Article 9, which is based on the opinion of a board consisting of three haematologists, to provide optimal treatment options in front-line in certain ultra high-risk patients.

There are challenges in funding allocation and drug pricing that impact drug access in CE&B, even when reimbursement is available. A performance audit was performed by the Ministry of Health (MoH) in Latvia in 2022, which noted a lack of stable allocation of funds for cancer drug purchases. Once drugs are approved for reimbursement, wholesale and pharmacy markups are added to the manufacturing price and a Value Added Tax (VAT) of 12% is applied, increasing the amount of money that the state needs to pay. In contrast, Lithuania and Estonia have a fixed markup once a certain price threshold is reached, thereby lowering the cost of medicines as compared to Latvia.⁶⁶



Promoting holistic HTAs for more robust decision-making on reimbursements

Health Technology Assessment (HTA) agencies are still in nascent stages in many of the countries under study, contributing to the lack of, or delayed, reimbursements. Most countries rely on Incremental Cost-Effectiveness Ratios (ICER) to support HTA decisions. An official ICER threshold is used in Bulgaria, the Czech Republic, Estonia, Hungary, Latvia, Lithuania and Slovakia. Croatia and Slovenia require a cost-effectiveness analysis but do not have a threshold defined. A higher GDP per capita was found to be correlated with a lower ICER threshold for reimbursement.^{67,18}

There is a need for more broad value-based assessments to determine reimbursement as opposed to solely relying on cost-effectiveness measures. The State Institute for Drug Control (SÚKL) in the Czech Republic determines reimbursement rates based on a drug's clinical effectiveness, cost-effectiveness and financial impact on the healthcare system.⁶⁸ However, according to Prof Hájek, "In the end, it all comes down to budget impact more than anything else." In Slovakia, legislative amendments were introduced in 2022 regarding the scope and conditions for reimbursement of medication

costs. Managed Entry Agreements (MEAs) are now handled by the MoH rather than health insurance companies, and the process has been simplified. The Quality-Adjusted Life Year (QALY) or ICER thresholds for innovative medicines and drugs for rare diseases has now been increased to 10x the GDP per capita. With these changes, 57 new medicines were brought into the Slovakian market in 2022.⁶⁹ To improve access to innovative therapies, Lithuania established a new HTA process in 2020, which includes clinical value, pharmacoeconomic evaluations, and ICER thresholds.⁷⁰ However, Ms Vilkevičienė says that "Implementing this HTA mechanism has been impeded by the lack of personnel with expertise to perform high-quality economic evaluations," further noting that "No university in Lithuania offers a study programme to train economists specialised in this field." Prof Harvanová explains that there is limited communication between myeloma specialists and experts engaged in the HTA process, the MoH and insurance companies in Slovakia. Frequent changes in personnel in the government and the MoH also impact the ability to engage effectively, and with continuity, to implement the necessary changes.⁶⁹

As Martin Smatana, Associate Fellow, Health and Economic Growth Programme, GLOBSEC and Lecturer at the Slovak Medical University in Slovakia, notes "The current HTA systems fail to account for all aspects of quality of life, such as social impact, social expenses and changes in economic productivity. Rectifying this and moving towards a more holistic assessment is crucial to ensure that we're not undervaluing the benefits these drugs bring to the country as a whole." Patient involvement in HTA processes is not widespread in the region.⁷¹ Providing patients with the opportunity to offer their unique perspectives and experience would be a step in the right direction towards more holistic value assessments.

“The current HTA systems fail to account for all aspects of quality of life, such as social impact, social expenses and changes in economic productivity. Rectifying this and moving towards a more holistic assessment is crucial to ensure that we’re not undervaluing the benefits these drugs bring to the country as a whole.”

Martin Smatana, Associate Fellow, Health and Economic Growth Programme, GLOBSEC; and Lecturer, Slovak Medical University, Slovakia

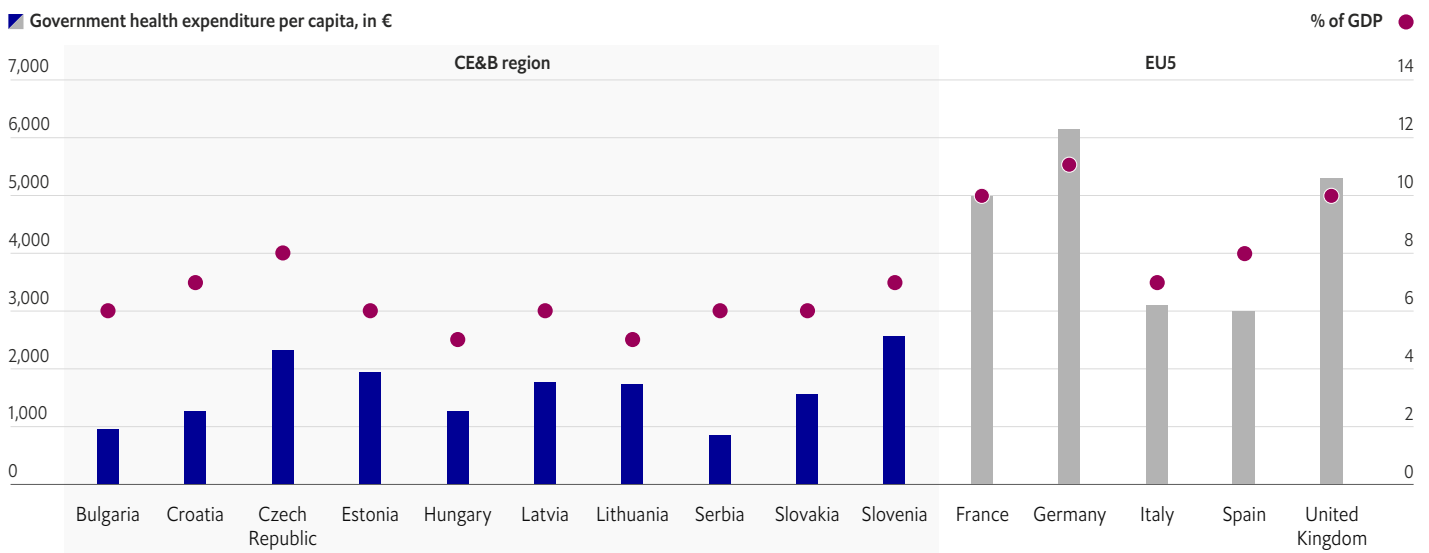
The EU HTA regulation, which will come into force in 2025, could further support national agencies. This regulation will allow for cooperation between EU countries in performing joint clinical assessments and joint scientific evaluations of emerging health technologies, thereby establishing a unified approach throughout the EU. Only clinical domains will be assessed under the joint umbrella; economic evaluations, reimbursement and pricing decisions will be made at the country level.⁷² Mr Smatana discusses the benefits of this unified approach to HTAs in the EU, explaining that “Many countries in Central and Eastern Europe don’t have the capacities, the expertise, or money to do complex clinical assessments in a timely manner, so this approach may bring about quicker evaluations for countries in this region.” However, Mr Smatana, as well as other experts in our panel, raised concerns about this unified approach and whether the scope of the assessments would remain limited to clinical assessment or would also include reimbursement recommendations. Experts fear that such an approach would be out of touch with the economic realities of the CE&B region.

Improving funding models to improve access to innovative therapies

“About 20 years ago, multiple myeloma was a very simple and inexpensive disease. Fortunately, we have a lot more information and many, many new and effective medications for the disease now, but they are quite expensive. So, one of the most important challenges in myeloma care is to fund reimbursement for these medications,” highlights László Váróczy, a Haematologist at the University of Debrecen, Hungary.

Increasing government investments in healthcare could improve funding for these medications. Figure 7 gives an overview of healthcare financing in the CE&B region and EU5 countries. In general, the total healthcare spending per capita and the percentage of GDP spent in the public health systems are lower in the CE&B region, as compared to EU5 countries, partly explaining the inequitable access to therapies. In 2021, government healthcare spending in the UK equalled 10.3% of GDP per capita, which was almost double the percentage spent on healthcare in Hungary and Lithuania, at 5.3% and 5.4%, respectively.¹³

Figure 7: Government health expenditure (per capita and as % of GDP) in CE&B and EU5 countries



Source: World Health Organization. Global Health Expenditure Database, 2021

MEAs are cost/risk-sharing agreements between drug manufacturers and payers that can also help improve access to innovative treatments. There are finance- or performance-based MEAs — either implemented at the patient or population level. Financial agreements focus on lowering the budget impact through confidential price concessions and volume caps. Performance-based agreements analyse the data on the performance of drugs; ongoing coverage for a drug is contingent on data collection demonstrating product performance.¹⁹

Legislation covering MEAs is active in all the countries of our study.²⁶ Countries in the CE&B region are heavily reliant on finance-based MEAs to improve access to innovative treatments. Data on the use of performance-based MEAs is not available freely in the public domain. In a 2018-2019 OECD survey, Hungary reported seven active performance-based MEAs, which were either payment-by-result or Conditional Treatment Continuation (CTC) agreements, while Lithuania reported one performance-based MEA – a CTC. Even where performance-based MEAs are used in these countries, the primary aim is to provide access to novel therapies that have received fast-track approvals while reducing the budgetary impact. Often, high-quality data are not collected to assess payment-by-result endpoints, and treatment continuation from prescriptions is taken as a surrogate marker. In Estonia, data from electronic medical records and e-prescriptions are used to determine the results of treatment. The Czech Republic uses insurance claims data for this purpose. Prospective data collection for MEAs is performed in Lithuania where payers, providers and pharmaceutical companies are joint data custodians.¹⁹

Better approaches are essential to strengthen the healthcare system and improve access. Considering the increasing costs of cancer drugs, Dr Skoupa suggests that “Pricing adjustments and cost-control mechanisms are needed to



deliver sustainable accessibility and affordability.” Simultaneously, establishing good mechanisms for collecting real-world evidence is key to understanding the impact of innovative therapies and developing performance-based models and value-based pricing for sustainable access. The barriers to collecting such evidence for performance-based MEAs in CE&B are multi-fold. There is a huge administrative burden on payers. Due to workforce constraints, data collection is a challenge. There are significant costs to developing and maintaining databases, and IT infrastructure is limited. Uncertainties around the financial impact of this additional research often disincentivise pharmaceutical companies from collecting the data.¹⁹ “Most of the time, the only meaningful outcome data available are whether the patient is alive or dead,” notes Dr Skoupa.

Insights can be drawn from performance-based models developed in other countries to strengthen systems in the CE&B. In the UK, the Cancer Drugs Fund (CDF) uses Managed Access Agreements (MAA) to fund innovative therapies where data uncertainties have been identified by the National Institute for Health and Care Excellence (NICE). There are Data Collection Arrangements to address uncertainties in data and Commercial Access Agreements that specify the prices and commercial conditions under which the NHS will purchase the drugs during the MAA. If the data requirements are met, the NHS will provide coverage for the drug.¹⁹ Such an arrangement places the onus on the pharmaceutical companies to ensure that data collection is robust. Encouraging more performance-based MEAs with evidence development in CE&B will need better collaboration with the pharmaceutical companies, improved infrastructure and human resources for data collection, as well as incentives for data collection efforts. Ultimately, governments or other relevant stakeholders should allocate funding and take on the onus of data collection from pharmaceutical companies to limit conflict of interest.

According to Mr Smatana, Slovakia is moving in this direction, and steps have been taken to improve the standard data flow between providers and health insurance companies. New data requests have been introduced ensuring that every time a doctor prescribes medicine, relevant information, such as the diagnosis, drug group, and sometimes even the specific drug ID, is included. These data are ultimately transferred to the MoH to ensure that agreed-upon terms for performance-based models are properly reflected and accounted for. Developing value-based payment systems remains critical to recognising the impact of real innovations and improving patient outcomes.²⁶ Since January 2022, new mechanisms have been set in place in the Czech Republic to facilitate better reimbursement of new drugs. For highly innovative medical products, the period of the first temporary reimbursement has been extended from two to three years, and for the second temporary reimbursement, it has been extended from one to two years. However, if costs exceed the budget impact outlined by the marketing authorisation holder, that company would need to reimburse the insurance fund. There is also an obligation for companies to offer follow-up treatment if permanent reimbursement is declined after the 5-year period.⁶⁸ For highly innovative products receiving temporary reimbursement, the drug company will need to establish a local registry to ascertain whether the safety and efficacy in the real world are in line with published data.

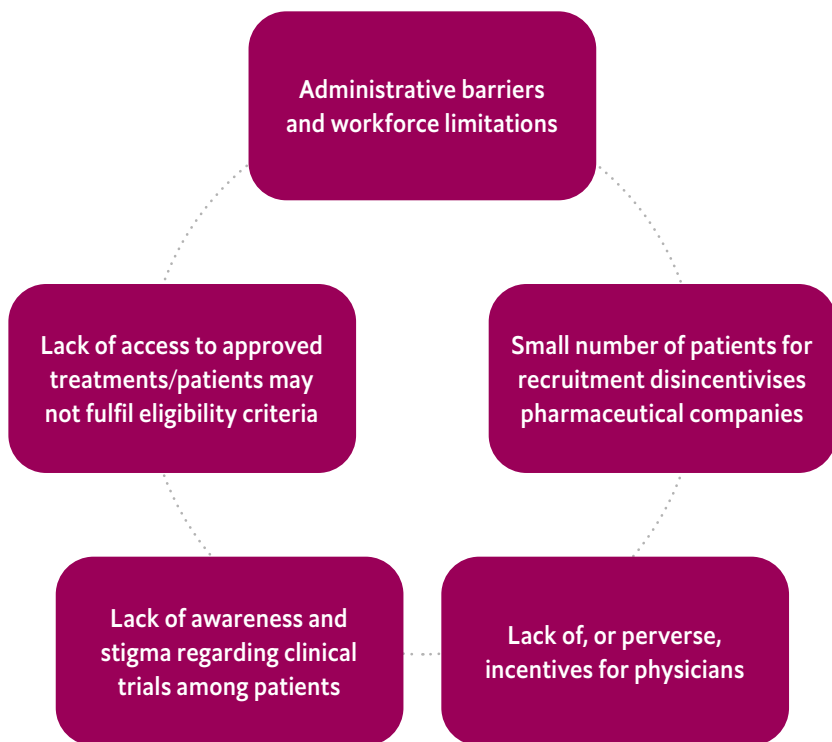
Facilitating participation in clinical trials

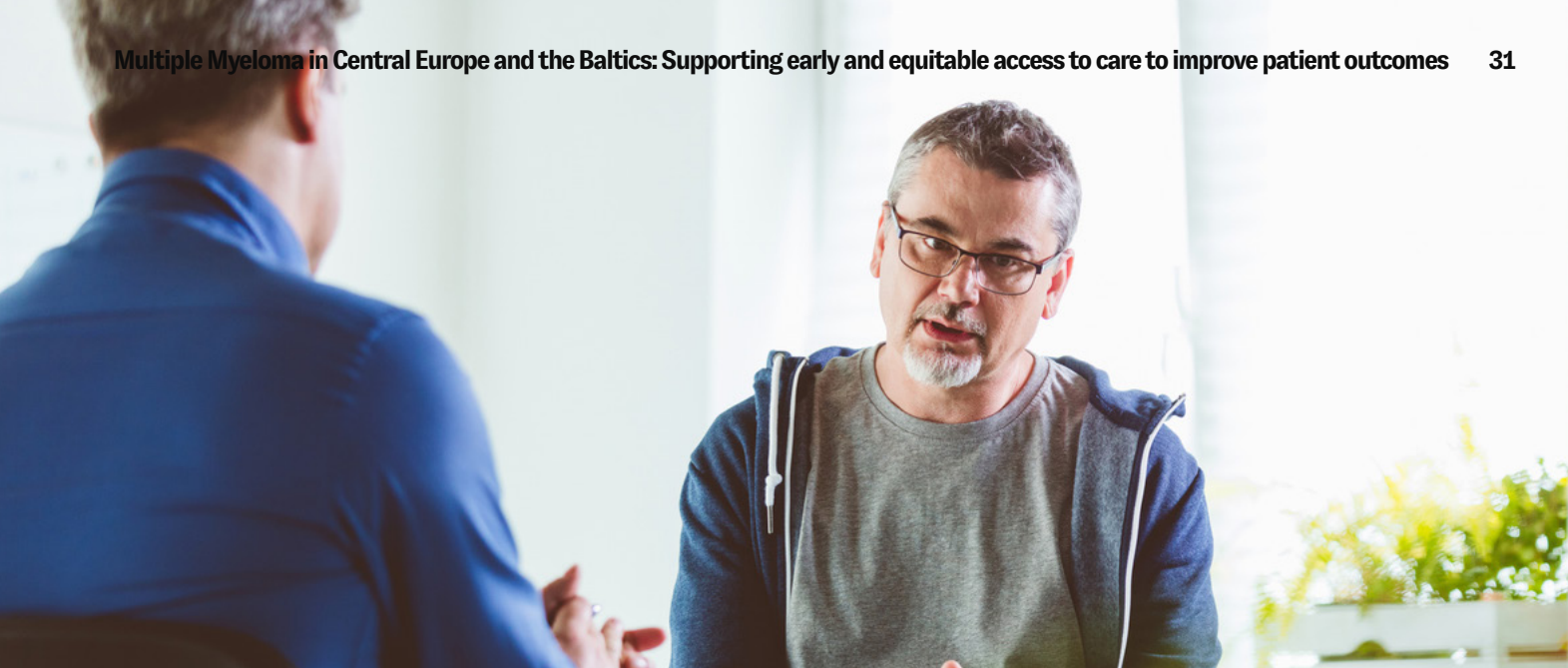
Over 3,000 clinical trials have been conducted for myeloma treatment over the past two decades, but only 6% of them included patients from Central and Eastern Europe.⁷³ The Myeloma Patients Europe’s Central and Eastern Europe (CEE) Working Group conducted a study examining the barriers to clinical trials in the region. Between 2001 and 2020, the Czech Republic was involved in the largest number of myeloma trials in the region (128 trials). Hungary was involved in 66 trials, Bulgaria in 24, Lithuania in 18, Serbia in 13, Slovakia in 12, Croatia and Estonia in 8, Latvia in 5 and Slovenia in 2. The Czech Republic, Hungary and Bulgaria were the most efficient in conducting myeloma research in Central and Eastern Europe.⁷⁴

Our experts spoke about various barriers that impact clinical trials enrolment in the CE&B region (see Figure 8). CE&B countries must look for ways to enhance their attractiveness for clinical trials. Within the region, the Czech Republic has a robust administrative and healthcare workforce to support clinical trials and can act as a regional benchmark. With access to trained administrative and legal personnel, the Czech Republic has a streamlined clinical trial negotiation and agreement process. Academics in the Czech Republic collaborate closely with counterparts in Western Europe and have a large volume of publications, making their centres more attractive to running clinical trials. “We need to raise awareness among policymakers and hospital administrators about how important clinical trials are for general development including getting access to new drugs, developing experience managing patients, having publications and increased global visibility — there are a lot of benefits. Leaders in countries where clinical trials are emerging, like in the Baltics, do not understand the amount of administrative work required for trials. There are no data managers employed, which means that physicians and nurses have to take care of patients and also streams of paperwork. Eventually, they burn out. If they realise this, clinical trials will flourish; if not, there will be no development,” opines Prof Hájek.

Insights can also be drawn from New Zealand, a small country with a population of 5.1m. Currently, New Zealand has 122 active clinical trials in cancer, of which nine are in myeloma.⁷⁵ The country has published a health research strategy (2017-2027) that the MoH and the Ministry of Business, Innovation and Employment will jointly oversee. One of the strategic priorities is to strengthen the clinical research environment by establishing a strong research workforce, embedding research into clinical networks and promoting industry investments.⁷⁶

Figure 8: Barriers to clinical trials for multiple myeloma in the CE&B region





Better data collection to enhance health systems' responsiveness

Improving national cancer registries is an essential, but not a comprehensive solution

Mandatory cancer reporting has facilitated the development of population-based cancer registries with nearly 100% coverage across all countries of our interest.⁷⁷⁻⁸⁴ Bulgaria was one of the earliest to launch its national cancer registry in 1952, collecting data from 13 cancer centres covering all 28 regions. The database has over 80 characteristics for each patient diagnosed with cancer and these are monitored dynamically. However, funding challenges have impacted the data collection process at the regional level since 2014. Bulgaria's MoH is working to stabilise funding to maintain the existing registry and develop 35 new electronic registries.⁸³ Several countries are facing similar funding challenges and struggling with outdated data. "The latest national registry data in Slovakia is from 2013 — this really needs updating," says Prof Babel'a. The Latvian Cancer Registry group was formed in 1993 and is responsible for registering and processing cancer data from Latvia.⁸¹ However, the registry is now outdated and the data registration platforms cannot ensure data capture and exchange in line with current requirements.⁸⁵

Not only are outdated data a problem with national registries, there are also limitations with the accuracy and validity of the available information. As Prof Mikala notes, often patients with suspected cancers are entered into the registries but they may end up not having a

myeloma diagnosis eventually. A study evaluating the quality of data in the Hungarian cancer registry between 2000 and 2019 found that the proportion of morphologically verified cancers in the database was 57.8%. The cancer registry recorded a significantly higher ASIR of cancers compared to IARC estimates, likely due to ill-defined International Classification of Diseases and Related Health Problems (ICD-9) codes used for data collection by the cancer registry.⁸² "Due to the lack of the robustness of these national cancer registries, it is difficult to use them for research purposes," explains Dr Váróczy.

Efforts are being made through national and international collaborations to improve the robustness of clinical registry data for better management of cancer. "At present, data from the hospital's electronic medical records are manually entered into the registry, but this is not a sustainable option. People are evaluating how automated input of data can be enabled from the medical record into the registry," observes Prof Hájek. The Czech National Cancer Plan 2030 aims to develop a fully computerised Czech National Cancer Information System. It will obtain population-level data from the Czech National Cancer Registry, payer-level data from the National Registry of Reimbursed Health Services and patient-level data from the Death Certificate System. The data will be used to augment and track population-level screening, and provide access to early specialist care and better palliative care services.²⁷

Lithuania may serve as an example to others if their ambitious plans play out. Valdas Pečeliūnas, Director of the National Cancer Institute of Lithuania and a Haematologist at the Hematology, Oncology and Transfusion Medicine Center, Vilnius University Hospital Santaros Klinikos, informs us that “We’ve commenced plans for the next generation of the registry. Our aim is to incorporate all available data from state databases to establish an automated cancer registry in real-time. While specialists will be involved in data creation, we’re currently acquiring access to, and integrating data from, various registers, including electronic medical records, electronic prescription systems, pathology centre systems and billing systems. These sources provide structured and standardised data, forming the basis for a comprehensive registry. Our goal is to create a ‘data lake’ with health data mapped to a common standard, which is part of our five-year plan. Specifically, we’re working on a project to map myeloma data to a common standard, leveraging artificial intelligence (AI) and large language models to analyse non-standardised medical records. We envision the cancer registry as the hub for analytical competencies in the cancer field, enabling data-driven decision-making.”

Europe’s Beating Cancer Plan has committed to developing the European Cancer Inequalities Registry (ECIR). Indicators studied will include smoking, obesity, physical activity rates, screening rates, access to various treatment modalities and cancer mortality. Disparities in cancer care based on geography (Western versus Central and East Europe), age, sex, ethnicity, sexuality and health literacy are also being explored. These efforts would be instrumental in bridging the access gap.^{86, 87}

Facilitating the growth of myeloma-specific clinical registries will promote value-based healthcare

Creating more robust and detailed disease-specific registries can facilitate a better understanding of real-world referral patterns, treatment access and outcomes. These registries can also evaluate the impact of innovative therapies, facilitating the development of performance-based MEAs and value-based healthcare. Countries like Slovenia are developing clinical registries for common cancers such as breast, prostate, lung, colorectal and skin melanoma, where extended information on clinical characteristics, treatment and outcomes are collected.⁸⁸ There is a need to extend such clinical registries to other cancers. For less common cancers such as myeloma, most efforts to develop registries currently come from treating physicians and their collaborations rather than the government.

The Czech Republic is a forerunner in the development of a collaborative myeloma-specific registry in the region. Their dedicated registry for plasma cell disorders called the “Registry of Monoclonal Gammopathies” has collected data on treatment and outcomes since 2007. Slovakian centres have also been involved in recruiting patients to this registry; more and more centres from Slovakia are now participating in this effort.²⁰ Szabolcs-Szatmár-Bereg County in Hungary has a dedicated registry



for blood cancers, which includes patients with myeloma along with epidemiological data.⁸⁹ National Myeloma Study Groups in Serbia, Slovenia and Croatia are founding members of, and participate in, the Balkan Myeloma Study Group (BMSG) registry.⁹⁰ To improve the robustness of these registries, insights can be drawn from the Danish Multiple Myeloma Registry (DMMR), which was established in 2005. Data regarding patient demographics, disease characteristics at presentation, complications, first- and second-line treatments, response and outcomes are collected. The data are linked to the country's Cancer Registry and the National Patient Registry, which facilitates comprehensive, longitudinal data collection.^{91,92}

Experts elaborated on various challenges to establishing and maintaining such myeloma clinical registries. In Hungary, Prof Mikala describes how four university hospitals and the national medical centre tried to merge their myeloma data to create a clinical registry. However, there were various impediments that derailed this effort. The data in the different hospitals were collected differently making merging a challenge. The legalities of data sharing were an even greater stumbling block. The General Data Protection Regulation (GDPR) passed by the EU in May 2018 is one of the toughest security and privacy laws in the world, and it imposes several obligations on organisations collecting and sharing data in the EU. In addition to restrictions on data sharing, it also regulates the engagement of individuals who maintain databases.⁹³ "Medical students who could previously be involved in database management are no longer eligible to do so based on the GDPR," notes Dr Bašić-Kinda.

"Starting a clinical registry is difficult but, in a way, also easy. A greater challenge is maintaining the registry. When you already have 10,000-15,000 patients in the registry, you need dedicated data managers to manage the registry. If there isn't adequate funding for staffing, the data quality will suffer and eventually the registry will die," opines Prof Hájek, one of the key members involved in establishing the Czech registry. At present, pharmaceutical companies support most of the costs of maintaining the Czech registry, according to Prof Hájek. Other support comes from international organisations and/or projects such as the EU-funded Healthcare Alliance for Resourceful Medicines Offensive against Neoplasms in Hematology (HARMONY), European Health Data & Evidence Network (EHDEN) and Haematology Outcomes Network in Europe (HONEUR). However, this is not an ideal arrangement. "Support must come from the MoH and the social insurance companies," states Dr Skoupa. "The data from the registry should also be used for developing MEAs for drug reimbursement, but insurance companies do not usually agree to this," she adds.

The voluntary nature of reporting to the clinical registry is another challenge to ensuring its robustness. Dr Bašić-Kinda describes the experience in Croatia, where a myeloma-specific cancer registry was started in 2016. Given the voluntary nature of reporting to the registry, data collection was a challenge, and efforts to maintain the registry were eventually suspended.

At present, data collected for these clinical registries are limited to disease, treatment and outcome parameters. "Even the high-quality myeloma registry in the Czech Republic lacks data on the economic burden of the disease, including indirect costs and quality-of-life data of patients," notes Dr Skoupa. These are areas that need more attention moving forward.



Leveraging the leadership of haematologists and haematology societies

Haematologists and haematology societies from CE&B countries have successfully raised awareness of myeloma, facilitating a speedier diagnosis and pathway to treatment. In addition, experts highlight the multi-pronged approach they are currently taking to improve treatment access. Dr Varga and colleagues recently published myeloma guidelines for Hungary, which highlight optimal treatments, options currently available in the country and what is reimbursed.⁹⁴ “This information will reach the local insurance companies and is hoped to galvanise action to broaden treatment options,” notes Dr Váróczy.

More engagement between researchers and physicians and the MoH and insurance companies can help raise awareness of the importance of the most effective treatments. “Some drugs that are approved and reimbursed are not game changers but ‘me-too’ regimens. It is important for us to raise awareness among

policymakers regarding which regimens are game changers so resources are spent effectively,” remarks Prof Hájek. The Czech Myeloma Society has been active in this regard, arranging pharmacoeconomic workshops where physicians discuss innovative therapies with insurance companies and the MoH to facilitate better understanding between stakeholders.

Haematologists must also spearhead the process of developing myeloma-specific registries, collecting real-world evidence and galvanising government support for funding to maintain these registries. Clinical trials should be another important area of focus. Raising awareness among policymakers about the optimal infrastructure for running successful clinical trials and the benefits of doing so can help more novel therapies reach patients. Experts also highlighted the cost-savings to both the healthcare system and patients through such participation.

Improving partnerships with patient organisations

Patient organisations across the CE&B region are engaged in improving disease awareness among the public, supporting myeloma care provision, facilitating patient-centric care and advocating for access to more innovative therapies. Improving cooperation among various stakeholders is key to the successful engagement of patient organisations in the myeloma care pathway. “In Slovenia, we cooperate well with various stakeholders involved but it is not always the case in other countries. It is important to create more awareness among stakeholders about the role of patient organisations and how they can be valued and partnered with,” notes Ms Modic. In Croatia, Mijelom CRO, a non-profit that provides support to myeloma patients, initiated a national prevention of late diagnosis programme, which was supported by professional associations of haematologists and GPs. Ms Armour shares that “The effort resulted in a tool aimed at primary care to help them in early diagnosis of multiple myeloma. This algorithm is being used in other specialities like nephrology and physiotherapy meetings, where myeloma patients are often being seen at the onset of active myeloma but when the disease is often not recognised.”

Myeloma care provision could be more robust in multidisciplinary support and palliative care. Patient organisations can work to fill this gap with government support. Examples of this work can be drawn from Slovenia where the MoH is co-financing a comprehensive rehabilitation programme developed by the Slovenian lymphoma and leukaemia patient association (L&L) in partnership with the Slovenian Haematology Society and in cooperation with rehabilitation experts, and contributing one-quarter of the cost through a public tender. Ms Modic describes that the goal is to eventually integrate this rehabilitation programme into the healthcare system.



The organisation also offers a web platform for patient and/or caregiver consultations with medical doctors, psychologists, social workers, nutritionists and peers. Forty-five-minute consultations are provided free of charge. More work can be done going forward in optimising palliative care support.

Patient-centric care is not prioritised in the region. The “Green Corridor” oncology pathway was established for expedited patient care in Latvia. An evaluation of this pathway highlighted that physician-patient communication was lacking and patients lacked information on treatment options and side effects.⁹⁵ “In all countries, medical doctors do not have enough time to explain everything. On the other hand, patients are in shock when they are diagnosed or relapsed and feel like they don’t receive all the information. This is where patient organisations with several support programmes and informative meetings, group and individual counselling and publications can come in to improve communication and support for patients,” describes Ms Modic.

Patient organisations have also been active in improving access to novel treatments. Mijelom CRO is organising a campaign in Croatia called “Smart Drugs for Smart Disease”, where representatives from the MoH, insurance agencies, medical fraternity and patients will meet to discuss improving access to myeloma therapies. The Association “Kraujas” in Lithuania has organised a public campaign called the “Calendar of Death”, which estimated the number of myeloma patients who have died over time due to inadequate treatment. L&L in Slovenia raised ~€1m for CAR-T therapy equipment. Patient organisations also collaborate across borders to establish advocacy groups in neighbouring countries to improve drug access. Despite these efforts, there is limited, if any, engagement of patients in the HTA processes of these countries, highlighting the need for more inclusive stakeholder engagement and decision-making.

As Ms Morgan describes, great progress has been made in how patient organisations work with other stakeholders in the healthcare ecosystem, but much more progress is needed. She shares, “Over the past 10 years, I’ve seen huge leaps in collaboration between the clinical and patient community and I think that will

only increase but it shouldn’t just be patients and clinicians that collaborate, it should be with payers, researchers and other stakeholders to make sure that we’re all working in the direction that improves outcomes for patients.”

Alice Onderková, Coordinator of the Multiple Myeloma Patient Support Group in the Czech Republic, shares that patient groups now have a greater opportunity to contribute to the reform of healthcare policies, reimbursement of treatments, and care optimisation for myeloma in the Czech Republic. “Since about 2018, there has been a significant progress. Patients and their representatives can be actively involved in these processes. Patients can be involved via a Patients Council, which is a permanent advisory body of the MoH, composed of representatives of patient organisations, which acts as an intermediary of the patients’ voice at the Ministry.” Ms Onderková also describes how the Department of Patient Rights Support has been operating at the Czech MoH since 2017, saying that “The department is dedicated to the systemic involvement of patients in management and processes in healthcare. It focuses primarily on supporting and collaborating with patient organisations as legitimate representatives of patients.”

Conclusion and calls to action

The advancements made in myeloma care are enviable, but are yet to reach a majority of patients in the CE&B region. Concerted efforts are needed to bolster comprehensive myeloma care in the region and improve disease outcomes. We need a better understanding of the impact of comprehensive care on the disease burden, a plan to strengthen health systems' capabilities to facilitate such care, and strong collaboration between stakeholders to deliver this care.

Facilitate early diagnosis and specialist referral

Improved awareness among physicians and the public, combined with universal access to basic laboratory tests to confirm the suspicion of myeloma, is essential to facilitating early diagnosis. Developing guidelines for optimal timeframes for referral and treatment, while streamlining the referral pathway, would expedite myeloma management and reduce the likelihood of irreversible end-organ damage.¹⁵

Invest in strengthening healthcare systems to improve the care pathway

Optimising healthcare systems for better delivery of ambulatory myeloma care will not only improve health outcomes, but also increase health systems' capacity for managing other diseases. To achieve this goal, countries should look to decentralise myeloma care using a hub-and-spoke model, develop strong specialist nurse programmes to support physicians and transition some injectable treatments to home-based administration.²¹⁻²⁵ Developing infrastructure for multidisciplinary care, including for rehabilitation, palliative care and survivorship, will offer benefits across a wide spectrum of chronic diseases. Croatian efforts to develop national strategies for palliative care that have resulted in greater capacity and better care delivery are a good example to follow.⁶² Greater government investment in healthcare systems, combined with better governance and timely reimbursement decisions for innovative treatments, will be pivotal to enhancing the care pathway and outcomes for patients.

Improve access to innovation

A structured HTA is crucial within the reimbursement decision-making framework, especially in countries with publicly funded healthcare systems. However, HTA processes in CE&B rely heavily on ICER to determine reimbursements. Balancing the price of a new medication against its perceived value to patients and broader society is complex, yet restricting reimbursement decisions to ICER assessments is limiting patient access to guideline-recommended myeloma treatment options in CE&B. HTAs require a more holistic and multidisciplinary process, incorporating economic, social, organisational and ethical considerations to guide decision-making.

Improving access to innovative treatments will require more holistic HTAs and the development of better funding models. MEAs are often used in CE&B countries to facilitate access to more expensive therapies, but a majority of them are finance-based MEAs, which are built on confidential discounts and capping. There is a need for more performance-based MEAs to facilitate value-based healthcare.²⁶ In addition, countries must strive to increase their attractiveness for clinical trials by improving their administrative capacity, supporting healthcare staff to run trials and creating awareness among patients to improve enrolment.

Enhance estimates of the burden of myeloma and impact of comprehensive care

There is a lack of data globally regarding the impact of comprehensive care on the health and economic burden of myeloma. Such real-world evidence is crucial to inform resource allocation. To accomplish better data collection in the CE&B region, efforts should focus on bolstering government investment in technology and infrastructure and incentivising a dedicated workforce to develop myeloma-specific registries. Reporting of myeloma should be made mandatory. Software solutions that enable automated data collection have the potential to support this effort and decrease pressures on an already stretched healthcare workforce.

Developing linkages of myeloma-specific registries with payer data will improve estimates of the economic burden and the impact of comprehensive care. Efforts of the Czech Republic in developing the Czech National Cancer Information System, which links population-level data from the Czech National Cancer Registry, payer-level data from the National Registry of Reimbursed Health Services and patient-level data from the Death Certificate System, can serve as a case study for further developments in this space in CE&B.²⁷ In addition, more efforts should be undertaken to assess indirect costs to understand the impact of myeloma on productivity. Whether the use of fewer lines of more effective myeloma treatment and the evolving paradigm of long-term therapy to maintain remissions can actually result in reduced economic burden is an important question to be answered.⁹⁶ Eventually, real-world evidence encompassing these domains should stimulate a move towards value-based payment models for innovation.

Strengthen stakeholder collaboration towards the delivery of high-quality care

Collaboration and cooperation between all stakeholders, including policymakers, healthcare professionals, patients and pharmaceutical companies, is crucial to overcoming systemic and economic barriers to offering the best myeloma care. L&L in Slovenia has pioneered a rehabilitation programme for cancer patients, which is now partly funded by the MoH and may eventually be fully integrated into the health system. Myeloma Patients Europe is focusing on an emerging group of younger myeloma patients to offer them survivorship support. Pharmaceutical companies continue to fund the growth of the Registry of Monoclonal Gammopathies in the Czech Republic. Stronger cooperation is needed between these stakeholders to make innovative therapies more accessible to patients. The Czech Republic has demonstrated how haematologists can take the lead in engaging with policymakers to raise awareness regarding game-changing innovative therapies instead of “me-too” regimens. Such efforts can facilitate better allocation of resources for reimbursement decisions. Hungarian experts are working towards influencing reimbursement decisions by highlighting treatment gaps in country-specific guidelines.

Treatment has advanced, survival has improved, and functional cures are possible in myeloma today. Through early diagnosis and the delivery of holistic multidisciplinary care, combined with providing access to the most effective therapies, longer survival and better productivity can be achieved among myeloma patients in all age groups. Greater investments in healthcare systems and the healthcare workforce are necessary in the CE&B region to see the full extent of improvement in myeloma outcomes. There are successful examples regionally and globally that countries in the CE&B region can use as case studies to facilitate capacity-building. The CE&B region can look to pioneer the development of better estimates of the economic burden of myeloma and the impact of high-quality comprehensive care. The smaller populations, existing national cancer registries, and ongoing efforts to link population-, payer- and patient-level data in CE&B countries can spearhead the efforts towards economic burden estimation. Prioritising these investments in the healthcare system will have long-term benefits in improving outcomes, not only for myeloma but also across many other chronic diseases and cancers.

References

1. Zamagni E, Barbato S, Cavo M. How I treat high-risk multiple myeloma. *Blood*. 2022;139(19):2889-903.
2. Landgren O, Kazandjian D. Modern Myeloma Therapy + Sustained Minimal Residual Disease-Negative = (Functional) Cure! *J Clin Oncol*. 2022;40(25):2863-6.
3. Mousavi SE, Ilaghi M, Aslani A, et al. A population-based study on incidence trends of myeloma in the United States over 2000–2020. *Scientific Reports*. 2023;13(1):20705.
4. Cancer Research UK. Myeloma incidence statistics [Internet]. London: Cancer Research UK. Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/myeloma/incidence#heading=Two>.
5. Bennink C, van der Klift M, Scheurer H, et al. Perspectives on returning to work of multiple myeloma patients: A qualitative interview study. *Eur J Cancer Care (Engl)*. 2021;30(6):e13481.
6. Forbat L. Multiple myeloma in people of working age in Czechia, Germany, and Poland: findings from a qualitative interview study. *Journal of Cancer Survivorship*. 2023.
7. Zhou L, Yu Q, Wei G, et al. Measuring the global, regional, and national burden of multiple myeloma from 1990 to 2019. *BMC Cancer*. 2021;21(1):606.
8. Babela R, Dugas J. Direct and Indirect Costs Associated with Multiple Myeloma in Slovakia: 5 Years Overview. *Value in Health*. 2022;25:S253.
9. Coriu D, Dytfeld D, Niepel D, et al. Real-world multiple myeloma management practice patterns and outcomes in selected Central and Eastern European countries. *Pol Arch Intern Med*. 2018;128(9):500-11.
10. Geng J, Zhao J, Fan R, et al. Global, regional, and national burden and quality of care of multiple myeloma, 1990-2019. *J Glob Health*. 2024;14:04033.
11. Santucci C, Patel L, Malvezzi M, et al. Persisting cancer mortality gap between western and eastern Europe. *Eur J Cancer*. 2022;165:1-12.
12. American Chamber of Commerce to the European Union. At a turning point: Healthcare systems in Central and Eastern Europe [Internet]. Written by Economist Impact. Available from: https://www.amchameu.eu/sites/default/files/publications/files/at_a_turning_point_healthcare_systems_in_central_and_eastern_europe_0.pdf.
13. World Health Organization. Global Health Expenditure Database [Internet]. Available from: <https://apps.who.int/nha/database/Select/Indicators/en>.
14. IQVIA. EFPIA Patient W.A.I.T. Indicator 2022 survey [Internet]. Available from: https://www.efpia.eu/media/s4qf1eqo/efpia_patient_wait_indicator_final_report.pdf.
15. Leukaemia Foundation, Australian Government Department of Health. Optimal care pathway for people with multiple myeloma. 2021. Available from: <https://www.cancer.org.au/assets/pdf/multiple-myeloma-1st-edition>.
16. Dimopoulos MA, Moreau P, Terpos E, et al. Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up(†). *Ann Oncol*. 2021;32(3):309-22.

17. Myeloma Patients Europe. Myeloma Access Atlas [Internet]. Brussels: Myeloma Patients Europe.
18. Augustyńska J, Skóra K, Leszczynska A, et al. EE524 The Incremental Cost-Effectiveness Ratio (ICER) Thresholds in Central and Eastern European Countries. *Value in Health*. 2022;25(12):S159.
19. Wenzl M, Chapman S. Performance-based managed entry agreements for new medicines in OECD countries and EU member states. 2019.
20. CMG group. Registry of Monoclonal gammopathies. Available at <https://rmg.healthregistry.org/index.php?pg=participants>.
21. International Myeloma Foundation. Nurse leadership board members [Internet]. Available at <https://www.myeloma.org/nlb-members>.
22. Myeloma Australia. The Myeloma Australia team [Internet]. Available at <https://myeloma.org.au/>
23. Lassalle A, Thomaré P, Fronteau C, et al. Home administration of bortezomib in multiple myeloma is cost-effective and is preferred by patients compared with hospital administration: results of a prospective single-center study. *Ann Oncol*. 2016;27(2):314-8.
24. Myeloma UK. Clinical service excellence programme. Introducing home treatment with bortezomib [Internet]. Available at <https://csep.myeloma.org.uk/csep-shared-practice-introducing-home-treatment-with-bortezomib-velcade/>.
25. De Angelis G, Fiorini A, Trapè G, et al. Subcutaneous Daratumumab at Home Is a Safe and Effective Procedure for Frail Patients with Multiple Myeloma: A Myelhome Project Report. *Blood*. 2023;142(Supplement 1):7242-.
26. Ferrario A, Arāja D, Bochenek T, et al. The Implementation of Managed Entry Agreements in Central and Eastern Europe: Findings and Implications. *Pharmacoeconomics*. 2017;35(12):1271-85.
27. Institute of Health Information and Statistics of the Czech Republic. Czech National Cancer Control Plan 2030 - Summary of analytical study [Internet]. Available from: <https://mzd.gov.cz/wp-content/uploads/2022/07/NOPL-CR-2030-annexe-1-summary-of-analytical-study.pdf>. 2022.
28. Choon-Quinones M, Zelei T, Barnett M, et al. Beyond medicines' barriers: exploring the true cost of multiple myeloma. *Journal of Medical Economics*. 2022;25(1):1167-75.
29. Turesson I, Bjorkholm M, Blimark CH, et al. Rapidly changing myeloma epidemiology in the general population: Increased incidence, older patients, and longer survival. *Eur J Haematol*. 2018.
30. Cancer Research UK. Myeloma incidence statistics [Internet]. London: Cancer Research UK. Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/myeloma/incidence#heading=Two>.
31. Palumbo A, Anderson K. Multiple myeloma. *N Engl J Med*. 2011;364(11):1046-60.
32. Tanguay M, Dagenais C, LeBlanc R, et al. Young Myeloma Patients: A Systematic Review of Manifestations and Outcomes. *Curr Oncol*. 2023;30(6):5214-26.
33. Kent EE, Ambs A, Mitchell SA, et al. Health-related quality of life in older adult survivors of selected cancers: data from the SEER-MHOS linkage. *Cancer*. 2015;121(5):758-65.
34. Shapiro YN, Peppercorn JM, Yee AJ, et al. Lifestyle considerations in multiple myeloma. *Blood Cancer Journal*. 2021;11(10):172.
35. Ramsenthaler C, Osborne TR, Gao W, et al. The impact of disease-related symptoms and palliative care concerns on health-related quality of life in multiple myeloma: a multi-centre study. *BMC Cancer*. 2016;16:427.
36. Rajkumar SV. Updated Diagnostic Criteria and Staging System for Multiple Myeloma. *Am Soc Clin Oncol Educ Book*. 2016;35:e418-23.
37. Puertas B, González-Calle V, Sobejano-Fuertes E, et al. Novel Agents as Main Drivers for Continued Improvement in Survival in Multiple Myeloma. *Cancers (Basel)*. 2023;15(5).
38. European Medicines Agency. Elranatamab overview [Internet]. Available at <https://www.ema.europa.eu/en/medicines/human/EPAR/elrefxio>.
39. Rajkumar SV, Kumar S. Multiple myeloma current treatment algorithms. *Blood Cancer J*. 2020;10(9):94.
40. NCCN clinical practice guidelines in Oncology-Multiple myeloma [Internet]. United States. National

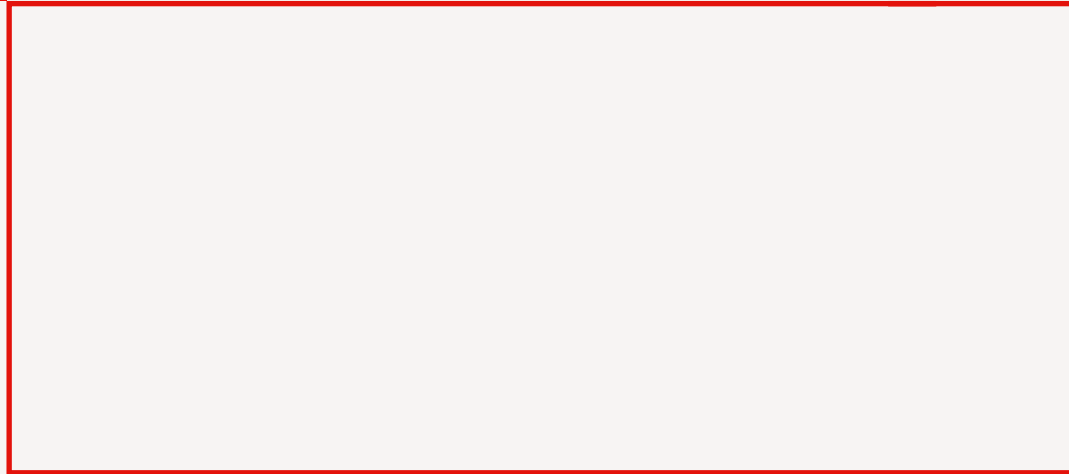
Comprehensive Cancer Network. Available from: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.

41. Jagannath S, Mikhael J, Nadeem O, et al. Digital Health for Patients With Multiple Myeloma: An Unmet Need. *JCO Clin Cancer Inform.* 2021;5:1096-105.
42. Sørensen J, Sørensen TV, Andersen KH, et al. Early, Patient-Centered, and Multidisciplinary Approach in Newly Diagnosed Multiple Myeloma: What Are We Talking About? A Case Description and Discussion. *Palliat Med Rep.* 2022;3(1):369-73.
43. Fonseca R, Tran D, Laidlaw A, et al. Impact of Disease Progression, Line of Therapy, and Response on Health-Related Quality of Life in Multiple Myeloma: A Systematic Literature Review. *Clin Lymphoma Myeloma Leuk.* 2023;23(6):426-37.e11.
44. Huang J, Chan SC, Lok V, et al. The epidemiological landscape of multiple myeloma: a global cancer registry estimate of disease burden, risk factors, and temporal trends. *Lancet Haematol.* 2022;9(9):e670-e7.
45. Gazdek D, Strnad M, Mustajbegovic J, et al. Lymphohematopoietic malignancies and oil exploitation in Koprivnica-Krizevci County, Croatia. *Int J Occup Environ Health.* 2007;13(3):258-67.
46. International Agency for Research on Cancer. Estimated number of new cases from 2022 to 2050, Both sexes, age [60-85+], Multiple myeloma. *Cancer Tomorrow.* Lyon: World Health Organization; 2024.
47. International Agency for Research on Cancer. Estimated number of deaths from 2022 to 2050, Both sexes, age [60-85+], Multiple myeloma. *Cancer Tomorrow.* Lyon: World Health Organization; 2024.
48. Hannig LH, Nielsen LK, Ibsen R, et al. The impact of changed treatment patterns in multiple myeloma on health-care utilisation and costs, myeloma complications, and survival: A population-based comparison between two time periods in Denmark. *Eur J Haematol.* 2021;107(1):63-73.
49. Smith L, Carmichael J, Cook G, et al. Diagnosing myeloma in general practice: how might earlier diagnosis be achieved? *British Journal of General Practice.* 2022;72(723):462-3.
50. MPE Atlas. 2018 Atlas access survey [Internet]. Available at <https://atlas.mpeurope.org/surveys-data/atlas-2018-survey>.
51. Varga G, Mikala G, Andrikovics H, et al. How long does a myeloma patient currently wait for the diagnosis in Hungary? *Orv Hetil.* 2014;155(39):1538-43.
52. Dapkevičiūtė A, Šapoka V, Martynova E, et al. Time from Symptom Onset to Diagnosis and Treatment among Haematological Malignancies: Influencing Factors and Associated Negative Outcomes. *Medicina (Kaunas).* 2019;55(6).
53. Myeloma Patients Europe. Myeloma diagnosis across Europe [Internet]. 2022. Available at https://www.mpeurope.org/wp-content/uploads/2022/09/MPE-report_Myeloma-Diagnosis-Across-Europe.pdf.
54. GIG. CYMRU. NHS Wales. Suspected Cancer Pathway [Internet]. Available at <https://executive.nhs.wales/functions/networks-and-planning/cancer/workstreams/suspected-cancer-pathway/>.
55. Otty Z, Brown A, Sabesan S, et al. Optimal Care Pathways for People with Lung Cancer- a Scoping Review of the Literature. *Int J Integr Care.* 2020;20(3):14.
56. Borgsten F, Gatopoulou X, Pisini M, et al. Healthcare resource utilisation and sickness absence in newly diagnosed multiple myeloma patients who did not undergo autologous stem cell transplantation: Trends in Sweden with the changing treatment landscape. *Eur J Haematol.* 2021;107(1):92-103.
57. Gil K, Abbasi S, Mehta K, et al. Trends in Inpatient Chemotherapy Hospitalizations, Cost and Mortality for Patients with Acute Leukemias and Myeloma. *Clin Hematol Int.* 2022;4(1-2):56-9.
58. Mittaine-Marzac B, De Stampa M, Marquestaut O, et al. Treatment for multiple myeloma in hospital at home: clinical characteristics and patient care pathways. *Home Health Care Serv Q.* 2022;41(2):165-81.
59. Kirkegaard J, Lundholm BW, Rosenberg T, et al. Home is best. Self-administration of subcutaneous Bortezomib at home in patients with multiple myeloma - A mixed method study. *Eur J Oncol Nurs.* 2022;60:102199.
60. Djebbari F, Panitsas F, Sharpley FA, et al. Myeloma care adaptations in the UK during SARS-CoV-2 pandemic: Challenges and measurable outcomes. *Eur J Haematol.* 2020;105(5):662-6.
61. Kodad SG, Sutherland H, Limvorapitak W, et al. Outpatient Autologous Stem Cell Transplants for Multiple

- Myeloma: Analysis of Safety and Outcomes in a Tertiary Care Center. *Clin Lymphoma Myeloma Leuk.* 2019;19(12):784-90.
62. Vočanec D, Džakula A, Lončarek K, et al. Integration processes within the Croatian palliative care model in 2014 - 2020. *Health Policy.* 2022;126(3):207-15.
 63. Organisation for Economic Co-operation and Development. Addressing challenges in access to oncology medicines [Internet]. Available from: <https://www.oecd.org/health/health-systems/addressing-challenges-in-access-to-oncology-medicines.htm>.
 64. Myeloma Patients Europe. Central and Eastern European (CEE) workgroup on access [Internet]. Available at <https://www.mpeurope.org/access-and-policy/cee-workgroup-on-access/>
 65. Hofmarcher T, Brådvik G, Svedman C, et al. Comparator Report on Cancer in Europe 2019 – Disease Burden, Costs and Access to Medicines. Lund: IHE, 2019. Available from: <https://www.efpia.eu/media/580501/comparator-report-on-cancer.pdf>.
 66. Latvijas Republikas Valsts kontrole. Oncology-priority without result [Internet]. Riga 2023. Available at <https://www.lrvk.gov.lv/en/news/we-do-not-provide-early-detection-of-oncological-diseases-and-the-necessary-medicines-compensation-for-patients-now>.
 67. The World Bank Data. GDP per capita [Internet]. Available at <https://data.worldbank.org/indicator/NY.GDP.PCAP.CD?locations=1W>.
 68. Bryndová L, Šlegerová L, Votápková J, et al. Czechia: Health System Review. *Health Syst Transit.* 2023;25(1):1-216.
 69. European Observatory on Health Systems and Policies. Slovakia: Country Health Profile 2023 [Internet]. Available from: <https://eurohealthobservatory.who.int/publications/m/slovakia-country-health-profile-2023>.
 70. State Medicines Control Agency of Lithuania. Health technology assessment [Internet]. Vilnius: State Medicines Control Agency of Lithuania. Available from: <https://vvkt.lrv.lt/en/health-technology-assessment/>.
 71. Jakab I, Dimitrova M, Houžez F, et al. Recommendations for patient involvement in health technology assessment in Central and Eastern European countries. *Front Public Health.* 2023;11:1176200.
 72. European Commission. Implementing the EU Health Technology Assessment Regulation [Internet]. Available at https://health.ec.europa.eu/system/files/2023-09/hta_regulation-implementation_factsheet_en.pdf.
 73. Fortuna G. Multiple myeloma patients face late diagnosis, unequal access to therapies [Internet]. Brussels: Efficacité et Transparence des Acteurs Européens. Available from: <https://www.euractiv.com/section/health-consumers/news/multiple-myeloma-patients-face-late-diagnosis-unequal-access-to-therapies/>.
 74. Myeloma Patients Europe. Myeloma Patients Europe report finds huge inequalities in access to myeloma clinical trials in Central and Eastern Europe [Internet]. Available from: <https://www.mpeurope.org/2022/11/29/myeloma-patients-europe-report-finds-huge-inequalities-in-access-to-myeloma-clinical-trials-in-central-and-eastern-europe/>.
 75. Australian New Zealand Clinical Trials Registry. About us [Internet]. Available from: <https://www.anzctr.org.au/Support/AboutUs.aspx>.
 76. Ministry of Business, Innovation and Employment, Ministry of Health. New Zealand Health Research Strategy 2017–2027: Summary of submissions and consultation [Internet]. Available from: <https://www.health.govt.nz/system/files/documents/publications/nz-health-research-strategy-2017-2027-summary-submissions-feb17.pdf>.
 77. Croatian Institute of Public Health. Croatian National Cancer Registry - Cancer Incidence in Croatia [Internet]. Available from: https://www.hzjz.hr/wp-content/uploads/2021/12/Bilten44_2019.pdf.
 78. Institute of Public Health of Serbia. Department for Prevention and Control of Noncommunicable Diseases - Malignant Tumors in Republic of Serbia [Internet]. Available from: <https://www.batut.org.rs/download/publikacije/MaligniTumoriURpubliciSrbiji2021.pdf>.
 79. Linkos. Cancer Epidemiology and cancer registries in the Czech Republic [Internet]. Available from: <https://www.linkos.cz/english-summary/national-cancer-control-programme/cancer-epidemiology-and-cancer-registries-in-the-czech-republic/#:~:text=The%20Czech%20Republic%20keeps%20on,the%20entire%20period%20under%20consideration>.
 80. National Cancer Institute. Cancer Registry [Internet]. Available from: <https://www.nvi.lt/cancer-registry/>.

81. Stengrevics A. Cancer-registry data in Latvia. *Lancet*. 1997;350(9076):523.
82. Wéber A, Mery L, Nagy P, et al. Evaluation of data quality at the Hungarian National Cancer Registry, 2000-2019. *Cancer Epidemiol*. 2023;82:102306.
83. Innovative Partnership for Action Against Cancer. Bulgarian National Cancer Registry: the Experience of the Population-Based Cancer Registry in Bulgaria [Internet]. Available from: <https://www.ipaac.eu/roadmap/detail/44>.
84. Zadnik V, Žagar T. Epidemiology and cancer registry. Oncology Institute Ljubljana. Available from: <http://www.slora.si/en/register-raka-rs>.
85. Organisation of European Cancer Institutes. Improving cancer coordination and screening in Latvia and Slovakia [Internet]. Available from: <https://oeci.eu/ProjectDetails.aspx?id=7#:~:text=In%20Latvia%2C%20cancer%20registries%20are,components%20of%20an%20organized%20programme>.
86. Van Poppel H, Battisti NML, Lawler M, et al. European Cancer Organisation's Inequalities Network: Putting Cancer Inequalities on the European Policy Map. *JCO Glob Oncol*. 2022;8:e2200233.
87. European Cancer Organisation. Inequalities Network [Internet]. Available from: <https://www.eurocancer.org/topic-networks/7:inequalities.html>.
88. Institute of Oncology Ljubljana. Clinical cancer registries [Internet]. Available from: <https://www.onko-i.si/eng/rrs/cr>.
89. Jakó J, Szerafin L. [Epidemiologic features of myeloma in Szabolcs-Szatmár-Bereg county, Hungary. Analysis of data of a 33-year period]. *Orv Hetil*. 2016;157(34):1357-60.
90. Balkan Myeloma Study Group. Available from: <https://balkanmyeloma.org/index.html>.
91. Gimsing P, Holmström MO, Klausen TW, et al. The Danish National Multiple Myeloma Registry. *Clin Epidemiol*. 2016;8:583-7.
92. Abildgaard N, Freilich J, Anttila P, et al. Use of Linked Nordic Registries for Population Studies in Hematologic Cancers: The Case of Multiple Myeloma. *Clin Epidemiol*. 2023;15:987-99.
93. GDPR.EU. What is GDPR, the EU's new data protection law? [Internet]. Available from: <https://gdpr.eu/what-is-gdpr/>.
94. Varga G, Mikala G, Váróczy L. A myeloma multiplex kezelési javaslat 2024-ben.
95. European Observatory on Health Systems and Policies. Latvia: health system summary 2022 [Internet]. Available from: <https://eurohealthobservatory.who.int/publications/i/latvia-health-system-summary>.
96. Dimopoulos MA, Jakubowiak AJ, McCarthy PL, et al. Developments in continuous therapy and maintenance treatment approaches for patients with newly diagnosed multiple myeloma. *Blood Cancer J*. 2020;10(2):17.

While every effort has been taken to verify the accuracy of this information, Economist Impact cannot accept any responsibility or liability for reliance by any person on this report or any of the information, opinions or conclusions set out in this report. The findings and views expressed in the report do not necessarily reflect the views of the sponsor.



LONDON

The Adelphi
1-11 John Adam Street
London WC2N 6HT
United Kingdom
Tel: (44) 20 7830 7000
Email: london@economist.com

GENEVA

Rue de l'Athénée 32
1206 Geneva
Switzerland
Tel: (41) 22 566 2470
Fax: (41) 22 346 93 47
Email: geneva@economist.com

SÃO PAULO

Rua Joaquim Floriano,
1052, Conjunto 81
Itaim Bibi, Sao Paulo - SP
04534-004
Brasil
Tel: +5511 3073-1186
Email: americas@economist.com

NEW YORK

900 Third Avenue
16th Floor
New York, NY 10022
United States
Tel: (1.212) 554 0600
Fax: (1.212) 586 1181/2
Email: americas@economist.com

DUBAI

Office 1301a
Aurora Tower
Dubai Media City
Dubai
Tel: (971) 4 433 4202
Fax: (971) 4 438 0224
Email: dubai@economist.com

WASHINGTON DC

1920 L street NW Suite 500
Washington DC
20002
Email: americas@economist.com

HONG KONG

1301
12 Taikoo Wan Road
Taikoo Shing
Hong Kong
Tel: (852) 2585 3888
Fax: (852) 2802 7638
Email: asia@economist.com

SINGAPORE

8 Cross Street
#23-01 Manulife Tower
Singapore
048424
Tel: (65) 6534 5177
Fax: (65) 6534 5077
Email: asia@economist.com