Project HealthCare

GOVERNMENT-CENTRIC FISCAL ANALYTICAL FRAMEWORK FOR EVALUATING BURDEN OF DISEASE IN CROATIA:

MULTIPLE MYELOMA

Slovak Republic

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Prepared by: Robert Babela & Silvester Krcmery (Comenius University, Bratislava)

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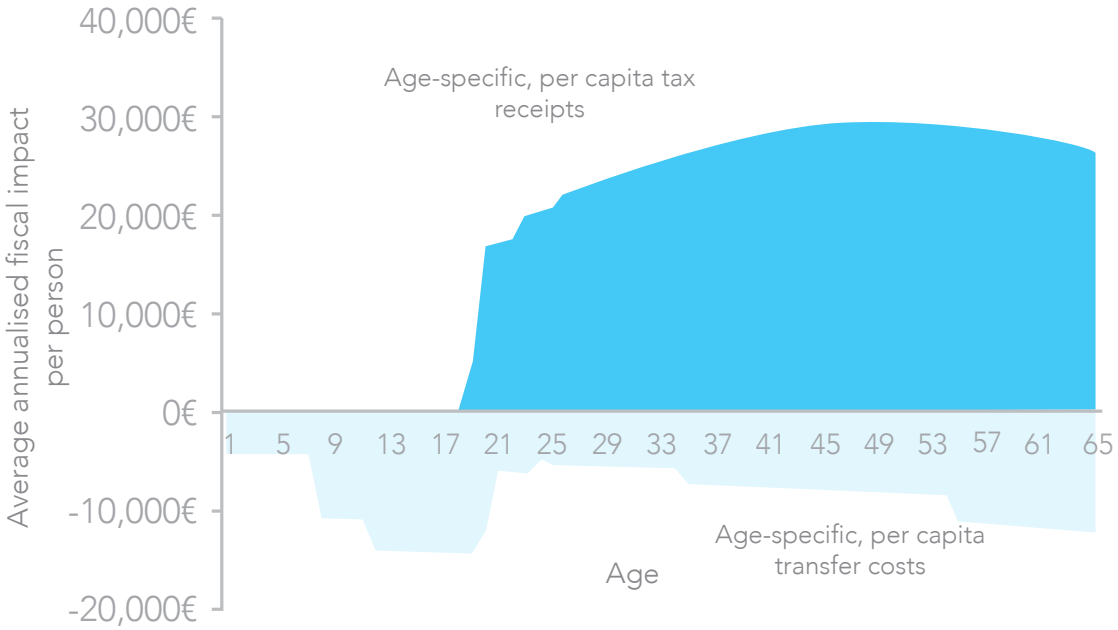
Introduction to Fiscal Modelling in Health: Concepts, Rationale, and Basic Principles

Fiscal modelling reframes health interventions as investments with measurable consequences for public accounts. Instead of restricting value assessment to health-sector costs and patient outcomes, the fiscal lens asks how changes in morbidity and mortality alter tax receipts and government transfer payments across the life course. Put simply, healthier populations work more, earn more, and pay more in taxes; they also consume different mixes of publicly funded services. A rigorous fiscal model quantifies these effects in monetary terms to inform budgetary planning and intersectoral policy decisions. The enclosed article articulates this government-perspective framework and shows how to translate health gains into fiscal consequences over time.

At the core of fiscal modelling is a shift in perspective. Conventional welfare-economic evaluations - exemplified by cost-effectiveness analysis- typically exclude taxes and transfers on the premise that such flows are neutral from a societal welfare standpoint. A finance ministry cannot take that view. Lost income taxes when illness pushes people out of work, increased disability allowances, early pension claims, and higher age-related service use are not neutral - they are observable line items with direct implications for sustainability and growth. A government-perspective analysis, therefore, complements cost-effectiveness by explicitly tracing how an intervention reshapes both sides of the public ledger: revenues and expenditures. In doing so, it acknowledges that many of the largest fiscal effects of disease - especially in working-age cohorts and in children who become future taxpayers - lie outside the health budget itself.

The life-course view underpins this approach. The analysis presents a fiscal balance-sheet intuition: at each age, individuals generate per-capita tax receipts and incur per-capita public expenditures (education, healthcare, disability, pensions, and other transfers). Health shocks that reduce participation or productivity shift the expected tax path downward while lifting transfer needs; effective interventions partially reverse those shifts. The following picture illustrates this principle visually, contrasting the trajectories of age-specific tax receipts and transfer payments and clarifying where health improvements can produce fiscal gains by preventing early exit from the labour force or by deferring costly transfers.



A practical fiscal model operationalizes this intuition with discounted cash-flow logic applied to a defined cohort. In its simplest form, the model is a government cost–benefit analysis. Costs are the present value of the intervention (and any consequent public service use); benefits are the present value of incremental direct and indirect tax revenues attributable to improved health and of transfer cost offsets that arise when disability, unemployment, or early retirement are avoided. Because both costs and benefits are denominated in currency, standard financial metrics - net present value (NPV), return on investment (ROI), and internal rate of return (IRR) - can be reported alongside familiar health-economic outputs. This enables treasury-style interpretation without abandoning clinical or societal metrics.

Methodologically, the framework adapts concepts from generational accounting to the program level. Rather than modelling all interacting cohorts in an economy, a fiscal health model isolates the cohort receiving a specific intervention and projects its tax and transfer streams under alternative scenarios (e.g., with vs. without the intervention). The projection links clinical pathways to labour-market states and public program eligibility. Typical ingredients include age-specific participation rates, wages and earnings growth, tax schedules and social contributions, probabilities of disability or early retirement, and age-graded public expenditures beyond health (notably pensions and long-term care). These are combined with disease progression and mortality risks, drawing on the same state-transition or survival models used in cost-effectiveness analysis. The technical equations are straightforward discounting of annual taxes minus transfers over the relevant time horizon, but the credibility of results depends on carefully specified epidemiology and realistic fiscal parameters.

The value of this framework lies in the questions it can answer. For example, what is the net fiscal impact of preventing a 58-year-old worker's health-related early retirement? The model will capture not only additional income and consumption taxes during the extra working years but also the reduction in disability benefits and the deferral of pension claims. Likewise, for paediatric or adolescent interventions, preventing impairments that depress educational attainment can raise lifetime earnings and, by extension, lifetime tax contributions - effects that are fiscally material yet typically invisible in health-budget appraisals. The same logic extends to vaccines, smoking cessation programs, reproductive medicine, and chronic-disease treatments where morbidity reductions translate into higher long-run productivity and lower transfer reliance.

Importantly, fiscal modelling should not be misconstrued as a replacement for cost-effectiveness analysis or as a mechanism to prioritize only those who work. The appraisal environment should be pluralistic. Health systems may aim to maximize health outcomes (e.g., quality-adjusted life years), while central government must also ensure macro-fiscal sustainability. A combined evidence set - clinical value, health-system affordability, and fiscal consequences - enables transparent trade-offs. Moreover, retirees continue to pay taxes and typically carry positive "fiscal residuals" from decades of contributions; the fiscal perspective can therefore support equity-aware allocation when interpreted over the full life course rather than a single snapshot year.

From an implementation standpoint, a minimal, defensible fiscal model follows a sequence. First, specify the cohort and comparator, mapping disease states to labour-market and transfer states over time. Second, assemble fiscal schedules: age-specific tax receipts (income, payroll, indirect) and age-specific public expenditures (healthcare by state, disability and unemployment benefits, pensions, and other transfers). Third, link clinical transitions to fiscal states with evidence on how morbidity affects participation, hours worked, and productivity. Fourth, discount all streams to present value at a government-approved rate, and report gross and net fiscal effects alongside program costs. Finally, stress-test with sensitivity analysis: vary key assumptions (wage growth, participation elasticities, disability risks, mortality) and present scenario ranges to decision-makers. This workflow keeps the model communicable to finance audiences while retaining clinical integrity.

The policy relevance is twofold. First, in tax-financed systems, sustainability depends on the simultaneous evolution of revenues and expenditures. By showing how effective care preserves the tax base and moderates transfers, fiscal models reposition parts of health spending from "cost pressure" to "productive investment," informing negotiations over budgets and, potentially, innovative finance mechanisms such as health impact bonds where repayments are tied to verified cross-sector savings. Second, in multi-payer environments, the framework reveals cross-budget externalities: a health intervention funded by one payer may generate savings or revenues for other public accounts, making the case for central co-funding or interdepartmental agreements.

Two cautions are essential for credible use. First, causality must be argued carefully: estimates of productivity gains and transfer reductions should be anchored in robust evidence, not assumed.

Second, distributional implications should be examined explicitly. A portfolio oriented solely by near-term fiscal yield could under-serve high-need groups; the remedy is not to discard the fiscal lens but to present it alongside equity, clinical urgency, and ethical commitments so that decision-makers can balance objectives transparently. Fiscal modelling broadens, rather than narrows, the conversation about value by connecting health investments to the realities of public finance.

In summary, fiscal modelling provides a disciplined way to quantify how health interventions reshape government budgets over the life course. By integrating epidemiology with labour - market behaviors and public finance schedules, the framework expresses program consequences in terms familiar to treasuries - NPV, ROI, and IRR - while remaining compatible with established health-economic methods. Used responsibly, it clarifies that parts of the health budget are engines of revenue preservation and transfer avoidance, and that sustainable health systems require visibility on both outcomes and fiscal flows.

Inputs – data needed for the model

To populate the model, each country requires a specific approach, although the parameters are more or less the same, to effectively model the fiscal impacts of selected diseases. There are two basic types of data - clinical and economic- that need to be addressed, sought out or requested, and incorporated into the model in the correct format. While the modeling may differ for each country, the following data sources are crucial starting points for any future modeling.

PART 1: CLINICAL DATA – ASSOCIATED WITH MM

Component	Years	Age Groups (Y/N)	Details
Mortality	2009+	5 Years Age Groups	Man, Women, All, Total
Incidence	2009+	5 Years Age Groups	Man, Women, All, Total
Paid Sick Leave	2009+	10 Years Age Groups (nice to have)	Man/Women/Total Years/Total days/Total Costs/Cost per day/Average days on Sick Leave
Paid Disability	2009+	10 Years Age Groups (nice to have)	Man/Women/Total Under/Above 70%/ Total Number/ Costs
Disability years expectancy	2009+	10 Years Age Groups (nice to have)	Man/Women/Total Years
Healthcare spending	2009+	Nice to have, but not needed.	All MM patients. Total spending include all reimbursed care associated with MM: medications, primary care, secondary care, diagnostics, rehabilitations, transports + any special reimbursed care.

PART 2: ECONOMIC DATA – TOTAL POPULATION OF COUNTRY

Component	Years	Age Groups (Y/N)	Details/Data Sources
Annual gross earnings from employment	2009+	5 Years Age Groups	Before tax, annual, earnings from employment and not from other sources
Employment rate	2009+	5 Years Age Groups	% of population employed
Average annual sick leave allowance	2009+	5 Years Age Groups (Nice to have)	Total in EUR % receiving annual sick leave allowance
Average annual disability pension	2009+	5 Years Age Groups (Nice to have)	Total/Yearly/in EUR % receiving disability pension
Tax Wedge	2009+	N.A.	OECD/Eurostat
Indirect tax e.g. VAT	2009+	N.A.	ECD/Eurostat
Discount rate	Current or latest available	N.A.	European Council, Eurostat, OECD, National Bank of the country, local Ministry of Finance
Inflation Projection	Current or latest available	N.A.	European Council, Eurostat, OECD, National Bank of the country, local Ministry of Finance
GDP per work hour	Current or latest available	N.A.	European Council, Eurostat, OECD, National Bank of the country, local Ministry of Finance
Tax to GDP Ratio	Current or latest available	N.A.	European Council, Eurostat, OECD, National Bank of the country, local Ministry of Finance
Caregivers specifications (if any)	Current or latest available	N.A.	European Council, Eurostat, OECD, National Bank of the country, local Ministry of Finance

FINAL RESULTS

Fiscal Consequences of Multiple Myeloma in the Croatia: Overview from 2009 till 2030

Disclaimer:

Before reading the following report draft, please consider the following points:

1. This report and analysis are based on available data and projections. Actual outcomes may differ due to policy decisions, therapeutic advances, or demographic changes.
2. All suggestions and scenarios are likewise based on the available data; however, they may not reflect the actual status quo and should be considered with certain limitations.
3. The numbers of new and prevalent patients were derived from national statistics provided by local partners. The data are undergoing ongoing verification and may differ from the final figures in the future Croatia publication.

Executive Summary

This report presents a comprehensive fiscal impact analysis of Multiple Myeloma (MM) in Croatia from 2009 to 2030, assessed from the perspective of the Croatian government. Using the Connolly et al. fiscal framework implemented through a 22-sheet Excel model, the analysis quantifies the total burden imposed on public finances through direct healthcare expenditures, lost tax revenues, and the indirect economic impact of caregiver burden.

The total fiscal burden of multiple myeloma in Croatia reached €44.99 million in 2024 (Mean estimator), having grown by 296% from €9.37 million in 2009. This represents a compound annual growth rate of approximately 11.3% over fifteen years. Projections indicate the burden will reach €60.3 million by 2030, a further 34% increase from 2024 levels.

Healthcare costs dominate the fiscal burden at 88.6% of the total (€39.88 million in 2024), reflecting the high cost of novel MM therapies reimbursed by the Croatian Health Insurance Fund (HZZO). This inverted cost structure – where direct healthcare costs exceed indirect costs – contrasts sharply with most chronic diseases where indirect productivity losses typically dominate. The remaining 11.4% comprises lost tax revenues from patient absenteeism (€3.15 million, 7.0%), caregiver employment reduction (€0.91 million, 2.0%), caregiver absenteeism (€0.59 million, 1.3%), patient morbidity (€0.41 million, 0.9%), and mortality (€0.03 million, 0.1%), with minimal excess social transfer costs.

An important caveat applies to the healthcare cost component. HZZO expenditure on high-cost medicines (posebno skupi lijekovi, or PSL) is reported at gross prices before contractual rebates from marketing authorization holders (MAHs). HZZO annual reports show that MAH refunds represented between 15% and 34% of gross PSL expenditure during 2021–2024. Since MM therapies fall predominantly within the PSL category, the actual net cost borne by HZZO is likely materially lower than the €39.88 million reported in the model. This means the fiscal burden presented in this report represents an upper-bound estimate of the healthcare cost component, and the true ROI of MM healthcare investment is likely more favorable than the figures reported here.

The sensitivity analysis confirms that healthcare costs are overwhelmingly the dominant driver of model uncertainty: a ±30% change in healthcare costs shifts the total burden by ±26.6%, while changes in wages, patient numbers, or tax parameters each produce effects of ±1–3.4%. The central estimate of €44.99 million is highly robust to variation in indirect cost parameters.

ROI analysis demonstrates that for every €1.00 invested in MM healthcare, the Croatian state recovers approximately €0.14 in preserved indirect economic value over a 5-year horizon, rising to €1.14 in total fiscal value per euro invested. When adjusted for the PSL rebate mechanism, the effective ROI is likely higher. Combined implementation of three intervention scenarios (10% caregiver reduction, 10% mortality reduction, 10% productivity improvement) could generate €6.69 million in cumulative savings over 2024–2030.

The analysis underscores that multiple myeloma represents a significant and growing fiscal challenge for Croatian public finances. This challenge must be understood within the broader context of Croatia's demographic transition – a population of 3.87 million with an average age of 44.5 years, nearly 900,000 citizens over 65, and a projected loss of 150,000 working-age individuals by 2030 – which amplifies the fiscal consequences of every disease that reduces workforce participation. Coordinated policy attention across healthcare reimbursement, caregiver support, and workforce retention is essential to manage the trajectory of this burden.

1. Introduction and Context

1.1 Global and National Disease Burden Context

Multiple myeloma represents a significant and growing hematological malignancy challenge both globally and within Croatia, characterized by the clonal proliferation of malignant plasma cells in the bone marrow leading to end-organ damage including bone lesions, renal insufficiency, anemia, and hypercalcemia. As the second most common blood cancer after non-Hodgkin lymphoma, multiple myeloma affects approximately 0.76% of the population during their lifetime, with incidence rates showing steady increases globally due to population aging and improved diagnostic capabilities. The disease primarily impacts older adults, with a median age at diagnosis of 68 years in Croatia, creating substantial economic consequences during what should be productive contribution years for experienced workers and active grandparents supporting multi-generational families.

The global incidence of multiple myeloma has increased by 126% between 1990 and 2016, with age-standardized incidence rates rising from 1.0 to 1.4 per 100,000 population. This trend reflects not only population aging but also improved diagnostic techniques including serum-free light chain assays, advanced imaging modalities, and increased awareness leading to earlier detection. The disease shows significant geographic variation, with

higher rates in developed countries potentially reflecting better diagnostic capabilities rather than true epidemiological differences. Southern European countries, including Croatia, have historically reported moderate incidence rates, though this has increased considerably as diagnostic infrastructure has improved following EU accession.

In the Croatian context, with a population of 3.87 million experiencing rapid demographic transition and significant emigration challenges, the registered prevalence of multiple myeloma reached 2,285 patients in 2024 according to latest HZZO records (April, 2026), corresponding to a point prevalence of approximately 59 per 100,000 population. The recorded prevalence has grown materially over the past 15 years (1,280 patients in 2009; 1,842 in 2019), reflecting both improved survival under modern therapies and progressively better diagnostic ascertainment. The incidence rate of approximately 11 per 100,000 annually means 420-430 new cases are diagnosed each year, with each new diagnosis representing not just a clinical challenge but a cascade of economic consequences affecting patients, families, employers, and government budgets. The true prevalence has likely been underestimated historically due to diagnostic limitations in rural areas and among elderly populations where symptoms may be attributed to normal aging rather than underlying malignancy.

1.2 Croatia's Position in the Regional Context

Croatia's management of multiple myeloma reflects both remarkable achievements and persistent challenges within the European Union healthcare landscape, shaped by the country's unique position as one of the newer EU members with a healthcare system in transition. The country has made significant strides in adopting novel therapeutic approaches, with all major treatment classes now available including proteasome inhibitors like bortezomib and carfilzomib, immunomodulatory drugs such as lenalidomide and pomalidomide, and more recently, monoclonal antibodies including daratumumab and isatuximab. However, the pathway from regulatory approval to patient access remains lengthy, with typical delays of 12-18 months between European Medicines Agency approval and Croatian Health Insurance Fund reimbursement decisions, during which patients may progress or die without access to potentially life-extending treatments.

The five-year survival rate in Croatia has improved dramatically from approximately 35% in 2009 to 60-65% by 2024, reflecting both therapeutic advannces and improved supportive care including better management of bone disease, renal complications, and infectious complications. This improvement, while remarkable, still lags behind Western European averages of 70-75% achieved in countries like Germany, France, and the Nordic nations. The survival gap of 10-15 percentage points translates directly into hundreds of premature deaths annually, with each death representing not only human tragedy but also substantial economic losses through foregone productivity, lost tax revenues, and the destruction of human capital accumulated over decades of education and experience.

The organization of multiple myeloma care in Croatia follows a centralized model with specialized expertise concentrated in major university hospitals in Zagreb, Split, Rijeka, and Osijek, creating both opportunities and challenges for optimal disease management. The country's five main hematology-oncology centers provide specialized care, but geographic disparities mean that patients from eastern Slavonia or the Dalmatian islands may travel 300+ kilometers for treatment, incurring additional costs and potentially delaying care. Rural patients face particular challenges, with studies showing they present with more advanced disease, receive fewer lines of therapy, and experience worse outcomes than their urban counterparts. This geographic inequality in access contributes to the overall disease burden and represents a modifiable factor that could improve both clinical and economic outcomes.

1.3 Croatia's epidemiological, demographic and economic context

This analysis applies the government perspective fiscal consequences framework, a comprehensive approach that evaluates how health conditions influence government accounts through both expenditures and foregone revenues across all affected sectors. Unlike traditional cost-effectiveness analyses that focus narrowly on clinical outcomes and healthcare costs from a payer perspective, this framework captures the full economic footprint of disease including cross-sectoral impacts that ripple through the economy. The methodology recognizes that governments, unlike healthcare systems or insurers, must consider not just what they spend but also what they fail to collect when disease prevents economic participation.

The framework has been extensively validated across multiple disease areas and countries, consistently demonstrating that the full fiscal impact of disease extends far beyond healthcare expenditures to encompass lost tax revenues that may exceed direct costs, social transfer payments that strain welfare systems, intergenerational effects as working-age caregivers reduce employment to support ill family members, and macroeconomic

impacts through reduced consumption and investment. In the context of multiple myeloma, this approach reveals how a disease affecting primarily older adults can nevertheless generate substantial economic losses through premature exit from the workforce, as many patients are diagnosed while still employed, and through the cascade effects on family members who become caregivers. The application of this framework to multiple myeloma in Croatia required careful adaptation to local economic conditions, tax structures, and social support systems. The Croatian tax wedge of approximately 43.5% means that each euro of lost wages translates into €0.435 of lost government revenue, creating a powerful multiplier effect where productivity losses generate fiscal consequences nearly equal to the wages themselves. The country's relatively generous disability system, while providing important social protection, also means that disease-related work incapacity generates substantial transfer payment obligations that must be considered in the full fiscal accounting. These structural features of the Croatian economy mean that the fiscal consequences of multiple myeloma may be proportionally higher than in countries with lower tax rates or less comprehensive social protection.

Based on data from the Croatian Health Insurance Fund (HZZO) and Croatian Bureau of Statistics, the number of registered MM cases in Croatia has grown from 207 in 2009 to approximately 330 (mean forecast) in 2024, with projections indicating relative stabilization at approximately 325 by 2030. Deaths attributed to MM in 2024 are estimated at 201, reflecting improved survival with modern therapies compared to the historical period.

Year	2009	2014	2019	2022	2024	2030
Cases (incident)	207	286	351	318	330	325
Deaths	148	188	202	206	201	214

Source: HZZO, Croatian Bureau of Statistics; 2024 and 2030 are mean forecast values.

The fiscal consequences of multiple myeloma in Croatia must be understood within the country's broader demographic and economic transition, which significantly shapes both the disease burden and the government's capacity to respond.

Population decline and ageing: Croatia's population has declined from a peak of 4.78 million in 1991 to approximately 3.87 million in 2024 (Croatian Bureau of Statistics, DZS). In 2024 alone, 19,011 more people died than were born (32,069 births versus 51,080 deaths). The average age of the population is 44.5 years (men 42.8, women 46.2), placing Croatia among the oldest nations in Europe. Of the current 3.87 million inhabitants, nearly 900,000 are over 65 years of age. By the end of this decade, projections indicate that of approximately 3.5 million Croatians, one million will be over 65 – a profound demographic shift that directly increases the prevalence of age-related cancers including multiple myeloma.

Workforce contraction: Croatia faces a projected decline of 6.8% (approximately 150,000 people) in its working-age population (20–64 years) by 2030, nearly three times the EU average decline rate. An estimated 200,000 worker shortage is anticipated by 2030. According to Eurostat projections, the economically active population could shrink by 21% by 2050 (from 2.4 million in 2023 to 1.9 million), which would reduce tax revenues by an estimated €0.6 billion annually. This workforce contraction amplifies the fiscal impact of every disease that removes individuals from the labour force: when the workforce is already shrinking, each MM patient's lost productivity represents a proportionally larger fiscal drain.

Healthcare system context: Croatia spends 7.15% of GDP on healthcare (2023, Eurostat), substantially below the EU-27 average of approximately 10%. Per capita healthcare expenditure stands at €2,032 (€3,835 in purchasing power parity terms), placing Croatia in the lower third of EU member states. The system is primarily funded through mandatory health insurance contributions (77.38% of total health expenditure), with state budget contributions (7.56%), voluntary health insurance (5.69%), and out-of-pocket payments (9.38%) comprising the remainder (OECD, 2023). This means that approximately one-third of employed citizens finance over three-quarters of healthcare costs through payroll contributions – a financing structure that becomes increasingly strained as the working-age population declines.

Access to innovative therapies: According to the EFPIA Patients W.A.I.T. (Waiting to Access Innovative Therapies) Indicator 2024, the average time from EU marketing authorisation (EMA approval) to patient availability in Croatia is approximately 549 days. Of 173 innovative medicines approved by the EMA in the 2020–2023 period, only 46 (27%) are available to Croatian patients – placing Croatia among the bottom seven EU member states for therapy access. In oncology specifically, only 17 of 56 EU-approved oncology medicines are accessible in Croatia, compared to 38 in Czechia, 36 in Bulgaria, and 34 in Slovenia. This access gap is directly relevant to MM, where novel therapies

(including next-generation monoclonal antibodies and CAR-T cell therapy) represent the primary driver of survival improvement.

Cancer burden and treatment costs: Croatia diagnosed 26,105 new cancer cases in 2022. The Croatian Cancer Registry reports significant improvement in five-year overall survival for all cancers, reaching 59% for 2019–2023 diagnoses compared to 44% in the early 2000s. However, Croatia's direct cancer treatment costs are the lowest in the EU at €130 per capita in purchasing power parity terms (2023), reflecting both constrained healthcare budgets and delayed access to costly innovative therapies. By comparison, the EU-27 average is €279 per capita. This underinvestment context is essential for interpreting the MM fiscal burden: the €39.88 million spent on MM in 2024, while substantial in absolute terms, reflects a healthcare system already operating well below EU spending norms.

Multiple Myeloma's high treatment costs, chronic disease course requiring continuous therapy, and impact on patients and their families make it one of the most fiscally significant haematological malignancies. From a government perspective, MM generates fiscal costs through: (a) direct treatment expenditures reimbursed by HZZO, (b) loss of income tax and social contribution revenues from patients and caregivers, (c) excess sick leave and disability pension payments, and (d) lost productivity from both patients and the informal care sector.

The fiscal relevance of MM is amplified by Croatia's demographic trajectory. In a country where the working-age population is contracting and the old-age dependency ratio is rising rapidly, the economic loss associated with disease-related workforce exit is proportionally greater than in demographically stable countries. According to 2024 Ageing Report data (European Commission), public healthcare spending per capita in Central and Eastern European new member states (NMS) rises steeply after age 55 and approximately triples between ages 55 and 85. With Croatia's population ageing rapidly into this high-cost zone, the fiscal pressure from MM and other age-related diseases will intensify through 2030 and beyond.

2. Data, Methods and Validation

2.1 Core Analytical Framework

The fiscal consequences methodology employed in this analysis evaluates health conditions from a whole-of-government perspective, incorporating all financial flows between citizens and the state that are affected by disease. This comprehensive approach moves beyond the traditional healthcare sector focus to examine how multiple myeloma influences government finances through multiple interconnected channels. The framework recognizes that modern governments operate as complex financial entities where health impacts reverberate through tax systems, social insurance programs, transfer payments, and public service delivery in ways that traditional health economic evaluations fail to capture.

Direct healthcare costs encompass the full spectrum of medical services from initial diagnosis through end-of-life care, including diagnostic procedures such as bone marrow biopsies, imaging studies, and laboratory monitoring; active treatment with chemotherapy, novel agents, and stem cell transplantation; supportive care including growth factors, antibiotics, and bisphosphonates; management of complications including pathologic fractures, renal failure, and infections; and palliative and end-of-life care that may be extensive given disease complexity. The analysis captures both costs borne directly by the Croatian Health Insurance Fund and those shared with patients through co-payments, though the latter are minimal in Croatia's universal healthcare system.

Indirect productivity losses represent the human capital destroyed or diminished by disease, manifesting through multiple pathways that extend beyond the patients themselves. Patient morbidity reduces work capacity even among those who continue employment, with studies showing that multiple myeloma patients who remain employed work at approximately 55% capacity due to fatigue, cognitive impairment from treatment, and time lost to medical appointments. Premature mortality removes individuals from the workforce entirely, with the average multiple myeloma death occurring 7-9 years before expected retirement, representing nearly a decade of lost productive contribution. The analysis employs the human capital approach, valuing lost productivity at average wage rates adjusted for employment probability and age-specific productivity patterns.

2.2 Data Sources and Validation

The robustness of this analysis rests on multiple validated data sources that have been carefully triangulated to ensure accuracy and consistency. Primary data derives from authoritative Croatian national databases: the Croatian Health Insurance Fund (HZZO) for treatment costs and case data, the Croatian Bureau of Statistics (DZS) for population denominators, the Croatian Pension Insurance Institute (HZMO) for disability pension statistics, and Eurostat for harmonised economic indicators. Caregiver parameters are based on published literature for haematological malignancy caregivers. All monetary values are in nominal EUR, inflation-adjusted using Croatian CPI data from the World Bank. The Croatian National Cancer Registry provides incidence, prevalence, and survival statistics with mandatory reporting since EU accession in 2013. The Croatian Institute for Health Insurance supplies detailed disability and sick leave statistics linked to ICD-10 codes, enabling precise attribution of work incapacity to multiple myeloma. The Croatian Health Insurance Fund provides treatment cost data, pharmaceutical expenditures, and utilization patterns that inform cost projections.

These domestic sources are supplemented and validated against international benchmarks to ensure reasonableness and identify potential data quality issues. The GLOBOCAN database provides regional context for incidence and mortality trends, while the European Cancer Information System enables detailed comparisons with neighboring countries facing similar demographic and economic transitions. Published literature from major European cancer centers provides treatment pattern benchmarks and cost-effectiveness thresholds that help contextualize Croatian findings. Where Croatian-specific data shows gaps, particularly in quality of life metrics and indirect cost components, validated international ratios are applied with appropriate adjustments for local economic conditions.

2.3 Model Architecture

The fiscal model is structured as a multi-sheet Excel workbook with 22 interconnected computational layers. The model allows user selection between three forecast estimators (Mean, Lower 95% CI, Upper 95% CI) for both deaths/cases projections and healthcare cost forecasts. All results presented in this report use the Mean estimator.

Major model components include: Data inputs (primary parameters repository), Results (central output aggregation), Tax mortality and morbidity pathways (age×year earnings loss matrices), Caregiver employment and absenteeism pathways, Absence tax calculations (GDP-hours-based), Sick leave and disability excess cost sheets, Tax wedge parameters (OECD data), YPPLL calculations (linear regression), Healthcare cost forecasts (linear trend with 95% CI), Case/death forecasts, CPI adjustment factors, and age distribution data.

Key computational pathways trace raw input data through to fiscal burden components via six distinct channels: (1) direct healthcare costs (HZZO expenditure, direct pass-through); (2) mortality tax loss (deaths × YPPLL × age-adjusted earnings × tax wedge); (3) morbidity tax loss (cases × employment rate differential × earnings × tax wedge); (4) absenteeism tax loss (excess sick days × GDP per work hour × fiscal rate); (5) caregiver employment tax loss (cases × CG employment reduction × CG earnings × tax wedge); and (6) caregiver absenteeism tax loss (CG workday loss × GDP per hour × fiscal rate). Each pathway is triple-verified against model formulas.

2.4 Healthcare Cost Reporting and the PSL Rebate Mechanism

An important methodological caveat concerns the healthcare cost data used in this model. Multiple myeloma therapies in Croatia fall predominantly within the category of posebno skupi lijekovi (PSL, or high-cost medicines) on the HZZO reimbursement list. For all PSL medicines, special financial agreements are concluded between marketing authorization holders (MAHs) and HZZO, which remain in force for as long as the medicines stay on the List. These agreements define specific financing arrangements that typically result in the actual cost borne by HZZO being lower than the official listed price.

Under these agreements, MAHs provide financial refunds (rebates) to HZZO arising from: (a) the difference between the official listed price and the contracted price, (b) expenditure exceeding the agreed budget cap, and (c) payments related to so-called ineffective treatment. These refunds take the form of both direct cash payments and in-kind deliveries of medicines to contracted hospital healthcare institutions.

The scale of these rebates is significant and has varied over recent years:

Year	Gross PSL Expenditure	MAH Refunds	Refund Rate	Notes
2021	€330M (est.)	€54.0M cash + €3.9M in-kind	~17%	HRK 406.6M cash + HRK 29.6M in-kind
2022	€374M (est.)	€54.4M cash (PSL) + €25.6M (non-PSL)	~15% (PSL only)	HRK 409.7M PSL + HRK 193M other
2023	€384M	€128.6M (mostly PSL)	~34%	Total refund figure; PSL share dominant
2024	€406M	€83.3M (mostly PSL)	~21%	Total refund figure; PSL share dominant

Sources: HZZO Annual Reports; MAH = Marketing Authorisation Holder.

Implication for this analysis: The €39.88 million healthcare cost figure used in the fiscal model for 2024 reflects gross HZZO expenditure on MM therapies before application of MAH rebates. Applying the observed 2024 aggregate PSL refund rate of approximately 21% would suggest a net healthcare cost of approximately €31.5 million, reducing the total fiscal burden to approximately €36.6 million. However, disease-specific rebate rates are not publicly disclosed, and the aggregate PSL refund rate may not apply uniformly to MM therapies. Therefore, this report conservatively presents gross expenditure figures throughout, noting that the true fiscal burden is likely lower. The potential ROI analysis would be similarly affected: if the effective healthcare investment is lower, the return per euro invested is correspondingly higher.

2.5 Validation

The total fiscal burden aggregation has been verified: €39,880,506 + €5,097,292 + €4,299 + €8,150 = €44,990,247. All component calculations have been cross-checked against the 22-sheet model architecture documentation. The effective tax conversion rate observed in the model is approximately 56.3%, reflecting the combined effect of personal income tax, employee social contributions, and employer social contributions applicable to Croatian workers.

3. Results: Levels, Composition, and Trends

The dual perspective approach in analyzing Croatia's multiple myeloma burden serves a crucial methodological purpose that deserves deeper explanation. When we examine the total fiscal burden, we're looking at the complete economic footprint of the disease on Croatian society. However, by also calculating the burden excluding healthcare costs, we can isolate and understand the pure productivity impact - the economic value that disappears when people cannot work, earn, or contribute to the economy due to illness.

Think of this dual approach like examining a household budget during a medical crisis. The first perspective shows everything: medical bills, lost wages, help from relatives who take time off work, and government assistance received. The second perspective removes the medical bills to reveal just how much economic activity the family loses - this helps us understand whether expensive treatments are actually helping people return to productive life or merely extending survival without restoring function.

3.1 Total Fiscal Burden – Excluding Healthcare Costs

Table 3.1 presents the indirect fiscal burden of multiple myeloma excluding direct healthcare costs, isolating the pure productivity and tax impact of the disease on Croatian public finances. This perspective is particularly important in Croatia's context, where the working-age population is projected to decline by 150,000 people by 2030, making each instance of disease-related workforce exit proportionally more costly to the economy.

Table 3.1: Fiscal Burden Excluding Healthcare Costs (Selected Years, EUR)

Component	2009	2014	2019	2022	2024	2030
Tax Loss – Absenteeism	€1.37M	€2.08M	€3.00M	€3.13M	€3.15M	€5.89M
Tax Loss – CG Employment	€0.41M	€0.39M	€0.59M	€0.72M	€0.91M	€1.73M
Tax Loss – CG Absenteeism	€0.24M	€0.27M	€0.49M	€0.49M	€0.59M	€1.11M
Tax Loss – Morbidity	€0.15M	€0.21M	€0.32M	€0.26M	€0.41M	€0.64M
Tax Loss – Deaths	€0.07M	€0.07M	€0.09M	€0.05M	€0.03M	€0.10M
Excess SL + Disability	€0.005M	€0.007M	€0.011M	€0.012M	€0.012M	€0.023M
TOTAL INDIRECT	**€2.25M**	**€3.04M**	**€4.52M**	**€4.68M**	**€5.12M**	**€9.50M**
Incident Patients	207	286	351	318	330	325
Per Incident Patient	**€10,870**	**€10,629**	**€12,877**	**€14,717**	**€15,515**	**€29,231**

The indirect fiscal burden has grown from €2.25 million in 2009 to €5.12 million in 2024, with projections indicating continued growth to €9.50 million by 2030. Patient absenteeism consistently represents the largest indirect component, accounting for 61.5% of indirect costs in 2024. The per-incident-patient indirect burden has increased from €10,870 in 2009 to €15,515 in 2024, reflecting rising Croatian wage levels and GDP per work hour. The projected near-doubling to €29,231 per patient by 2030 reflects both continued wage growth and the disproportionate acceleration of indirect costs as the Croatian economy expands while patient numbers stabilise.

3.2 Total Fiscal Burden – Including Healthcare Costs

Table 3.2 presents the complete fiscal burden including direct healthcare expenditures reimbursed by HZZO. This is the comprehensive government-perspective measure of the disease's total impact on public finances. As noted in Section 2.4, the healthcare cost figures represent gross HZZO expenditure before contractual MAH rebates; the actual net fiscal burden is likely 15–25% lower depending on disease-specific rebate rates.

Table 3.2: Total Fiscal Burden Including Healthcare Costs (Selected Years, EUR)

Component	2009	2014	2019	2022	2024	2030
Healthcare Costs	€7.12M	€8.33M	€21.87M	€31.10M	€39.88M	€50.80M
Total Indirect Costs	€2.25M	€3.04M	€4.52M	€4.68M	€5.12M	€9.50M
TOTAL FISCAL BURDEN	**€9.37M**	**€11.37M**	**€26.39M**	**€35.78M**	**€44.99M**	**€60.30M**
HC as % of Total	76.0%	73.3%	82.9%	86.9%	88.6%	84.2%
Incident Patients	207	286	351	318	330	325
Per Incident Patient	€45,266	€39,755	€75,185	€112,516	€136,334	€185,538

The total fiscal burden has grown from €9.37 million in 2009 to €44.99 million in 2024, an increase of 296% (CAGR: 11.3%). Healthcare costs dominate at 88.6% of total burden in 2024, reflecting the increasing utilization of novel therapies including proteasome inhibitors, immunomodulatory agents, and monoclonal antibodies. The most significant cost inflection occurred between 2018 and 2019, coinciding with the reimbursement of daratumumab and second-generation proteasome inhibitors in Croatia. Healthcare costs grew by 82% from 2019 to 2024, compared to only 17% growth in the preceding five-year period (2014–2019 for the pre-inflection segment through 2017). To contextualize the healthcare cost trajectory: Croatia's direct cancer treatment costs are the lowest in the EU at €130 per capita (PPP, 2023), meaning the MM spending increase, while dramatic in relative terms, occurs against a baseline of historically constrained oncology investment.

3.3 Detailed Component Breakdown – Reference Year 2024

The following table presents the complete component-level breakdown for the 2024 reference year.

Table 3.3: Detailed Component Breakdown, 2024.

Fiscal Burden Component	EUR Value (2024)	% of Total	Category
MM Healthcare Costs	€39,880,506	88.6%	Direct
Tax Loss – Patient Absenteeism	€3,148,757	7.0%	Indirect
Tax Loss – CG Employment	€912,112	2.0%	Indirect
Tax Loss – CG Absenteeism	€592,819	1.3%	Indirect
Tax Loss – Patient Morbidity	€409,100	0.9%	Indirect
Tax Loss – Deaths	€34,503	0.1%	Indirect
Excess Sick Leave Costs	€4,299	<0.01%	Transfer
Excess Disability Pension Costs	€8,150	<0.01%	Transfer
TOTAL FISCAL BURDEN	**€44,990,247**	**100%**	

The inverted cost structure – where direct healthcare costs dominate rather than indirect costs – is a characteristic feature of MM compared to other chronic diseases such as respiratory conditions or musculoskeletal disorders where indirect costs typically represent 60–80% of the total burden. This pattern is consistent with findings across other Central European countries applying the same Connolly et al. fiscal methodology. The dominance of healthcare costs reflects three factors: the high unit cost of novel MM therapies (particularly daratumumab-based combinations and lenalidomide

maintenance), the extended treatment duration enabled by improved survival, and the relatively older age profile of MM patients (average age 63), which limits the productivity losses compared to diseases affecting younger working-age populations.

4. Temporal Analysis with Demographic Projections

4.1 Historical Growth Trajectory (2009–2024)

The fiscal burden of multiple myeloma in Croatia has grown from €9.37 million in 2009 to €44.99 million in 2024. Three distinct phases are identifiable in this growth trajectory, each driven by different factors.

Phase 1 – Stability (2009–2015): During this period, the fiscal burden grew at 5.1% annually, from €9.37 million to €14.37 million. Growth was driven primarily by inflation and demographic ageing rather than treatment innovation. Physicians relied mainly on traditional chemotherapy supplemented by first-generation novel agents (bortezomib). Healthcare costs grew modestly from €7.1 million to €11.2 million, and the healthcare cost share remained relatively stable at 70–78%.

Phase 2 – Acceleration (2016–2020): The introduction and rapid adoption of novel agents (lenalidomide, daratumumab, carfilzomib) drove dramatic healthcare cost growth. Total burden more than doubled from €12.0 million (2016) to €32.3 million (2020), with healthcare costs growing from €8.8 million to €28.9 million. The healthcare cost proportion peaked at 89.9% in 2020, the highest level observed, as innovation pricing temporarily outpaced productivity recovery gains.

Phase 3 – Consolidation (2021–2024): Growth moderated to approximately 11% annually as the system adapted to and optimised novel therapies. Healthcare costs continued growing at ~10% while indirect costs surged at ~25% annually, reflecting the accumulating prevalence of patients living with MM as a chronic condition. The healthcare cost share stabilised at 85–89%.

Table 4.1: Historical Growth Trajectory.

Period	Start (EUR M)	End (EUR M)	Absolute Growth	Growth Rate
2009–2014	€9.37M	€11.37M	+€2.00M	+21.3%
2014–2019	€11.37M	€26.39M	+€15.02M	+132.1%
2019–2024	€26.39M	€44.99M	+€18.60M	+70.5%
2009–2024 (Total)	€9.37M	€44.99M	+€35.62M	+296%

4.2 Projections 2025–2030

The projection indicates a continuing upward trend, with the total fiscal burden reaching €60.3 million by 2030 – a 34.0% increase from 2024. Notably, the indirect cost components (particularly absenteeism tax losses) grow faster than healthcare costs in the projection period, reflecting rising wage levels and GDP per work hour in Croatia. The indirect cost CAGR of 10.9% substantially exceeds the healthcare cost CAGR of 4.1%. This divergence suggests that by 2030, indirect costs will regain a slightly larger share of total burden (15.7% vs. 11.4% in 2024), a trend amplified by Croatia's projected wage convergence toward EU averages as the economy continues to grow (GDP growth projected at 2.9% in 2026 and 2.5% in 2027, European Economic Forecast Autumn 2025).

Table 4.2: Projected Fiscal Burden 2024–2030.

Component	2024	2025	2026	2027	2028	2029	2030	CAGR
HC Costs (€M)	39.88	44.92	46.09	47.27	48.45	49.62	50.80	+4.1%
Total Tax Loss (€M)	5.10	5.66	6.29	6.97	7.73	8.56	9.48	+10.9%
Total Burden (€M)	45.0	50.6	52.4	54.3	56.2	58.2	60.3	+5.0%

4.3 Fiscal Burden per Prevalent Patient

Table 4.3 presents the total fiscal burden normalized by the number of prevalent patients (all persons living with MM in a given year), using updated prevalence data sourced from the Croatian Health Insurance Fund (HZZO). The right-most column isolates the indirect (non-healthcare) component of the per-patient burden, which is informative because it reflects pure productivity and tax-revenue losses — the part of MM's fiscal footprint that is not driven by drug acquisition cost.

Table 4.3: Fiscal Burden per Prevalent Patient, 2009–2026.

Year	Total Burden (€M)	Prevalent Patients	Per Prevalent Patient	Per Prevalent Patient (Excl. HC)
2009	€9.37M	1,280	€7,319	€1,757
2010	€10.30M	1,337	€7,700	€2,013
2011	€10.84M	1,344	€8,068	€2,090
2012	€10.49M	1,384	€7,578	€1,855
2013	€10.11M	1,500	€6,740	€1,854
2014	€11.37M	1,509	€7,537	€2,015
2015	€14.37M	1,583	€9,075	€1,978
2016	€12.03M	1,573	€7,648	€2,066
2017	€13.80M	1,685	€8,187	€1,988
2018	€16.95M	1,741	€9,733	€2,229
2019	€26.39M	1,842	€14,325	€2,452
2020	€32.34M	1,835	€17,622	€1,850
2021	€33.99M	1,911	€17,788	€2,083
2022	€35.78M	2,000	€17,889	€2,337
2023	€39.60M	2,138	€18,522	€1,775
2024	€44.99M	2,285	€19,689	€2,236
2025*	€50.59M	2,426	€20,853	€2,339
2026*	€52.39M	1,905	€27,502	€3,306

** 2025 and 2026 values are model-based ESTIMATES (mean forecast); shaded rows indicate non-historical projections. Sources: Total Burden and Excl.-HC components from the 22-sheet fiscal model (mean forecast estimator); Prevalent Patients from HZZO (April 2026).*

On the updated prevalence denominator, the per-prevalent-patient fiscal burden has grown from €7,319 in 2009 to €19,689 in 2024, an increase of approximately 170% over fifteen years (CAGR 6.8%). The trajectory is dominated by direct healthcare costs: the right-most column shows that the indirect (non-HC) per-patient burden has been remarkably stable across the entire period, fluctuating in a narrow band of roughly €1,757–€2,452 and ending at €2,236 in 2024 — approximately 27.3% above its 2009 value. This stability indicates that productivity and tax-revenue losses per patient have moved largely with wages and employment, while almost all of the per-patient growth in the total burden is attributable to the rising cost of novel MM therapies reimbursed by HZZO.

The most prominent inflection occurs between 2018 and 2019, where the per-patient total burden jumps by approximately 47% (from €9,733 to €14,325). This step-change coincides with the reimbursement of daratumumab and second-generation proteasome inhibitors and is consistent with the Phase 2 acceleration described in Section 4.1.

Projections for 2025 and 2026 (shaded rows) are model ESTIMATES based on the mean forecast estimator and should be interpreted as indicative trajectories rather than confirmed outcomes. The notably high 2026 per-patient figure (€27,502) reflects the combination of a continued rise in projected total burden and a forecast contraction in prevalent patients to 1,905 - itself an artefact of the linear forecasting approach applied to a recently disrupted time series. As such, the especially 2026 per-patient values should be treated with greater uncertainty than historical points and revisited once all data for 2026 actuals become available.

This per-patient trajectory is consistent with the broader pattern observed in Croatian cancer care, where five-year overall cancer survival has improved from 44% to 59% but at increasing per-patient cost as treatment regimens become more complex and longer in duration. The stability of the indirect component, however, is a new and policy-relevant finding: it suggests that the productivity-loss footprint of MM has remained roughly constant per patient even as therapeutic intensity has grown, and that the principal lever for reducing per-patient fiscal burden lies in healthcare-cost optimization (including the PSL rebate mechanism described in Section 2.4) rather than in further compression of indirect costs.

5. Healthcare Investment Analysis

5.1 What-If Scenarios: Cumulative Fiscal Impact 2024–2030

Three intervention scenarios were modelled to quantify the cumulative fiscal savings achievable through targeted improvements in MM patient and caregiver outcomes. All scenarios apply to the period 2024–2030 (7 years) using the mean forecast estimator. The baseline cumulative fiscal burden over this period is approximately €377 million, of which €327 million is healthcare costs and €50 million is indirect costs.

Scenario 1: 10% Reduction in Caregiver Burden

A 10% reduction in the caregiver employment loss rate (from 43.5% to 39.2%) and caregiver absenteeism (from 15.0% to 13.5%), achievable through better caregiver support programmes, respite care provision, and flexible working arrangements.

7-year cumulative saving: €2,866,990 (0.76% of total burden)

Scenario 2: 10% Reduction in Mortality

A 10% reduction in annual MM deaths (approximately 20 fewer deaths per year), achievable through earlier diagnosis, improved access to novel therapies including CAR-T and bispecific antibodies, and optimized treatment sequencing. Croatia's WAIT indicator delay of 549 days for innovative therapies suggests that accelerating market access could contribute meaningfully to mortality reduction.

7-year cumulative saving: €91,965 (0.024% of total burden). The modest fiscal saving reflects the age profile of MM deaths (predominantly 65+) where remaining productive life years are few. The primary benefit of mortality reduction is humanitarian (life-years saved) rather than purely fiscal.

Scenario 3: 10% Increase in Productivity

A 10% reduction in absenteeism-related productivity losses for both patients and caregivers, achievable through improved disease management, better supportive care, and flexible work arrangements. 7-year cumulative saving: €3,733,070 (0.99% of total burden)

Table 5.1: What-If Scenario Analysis, Cumulative 2024–2030.

Scenario	Cumulative Saving (2024–2030)	% of Total Burden
1: 10% Caregiver Reduction	€2,866,990	0.76%
2: 10% Mortality Reduction	€91,965	0.024%
3: 10% Productivity Increase	€3,733,070	0.99%
TOTAL COMBINED SAVING	**€6,692,025**	**1.78%**
New Cumulative Burden	€370,217,705	

Combined implementation of all three scenarios would generate approximately €6.69 million in cumulative fiscal savings over 2024–2030. Productivity improvements (Scenario 3) and caregiver support (Scenario 1) provide the largest fiscal dividends, while mortality reduction's fiscal impact is limited by the age profile of MM patients. In the context of Croatia's projected 200,000-worker shortage by 2030, the workforce preservation effects of Scenarios 1 and 3 acquire additional strategic importance beyond their direct fiscal value.

5.2 Return on Investment

For every €1.00 invested by the Croatian government in MM healthcare, approximately €0.14 is recovered in indirect fiscal value over a 5-year horizon. While these returns are modest in absolute terms (the healthcare cost dominance means 88.6% of each invested euro directly constitutes the cost rather than generating new revenues), MM healthcare investment preserves approximately €7.1 million per year in maintained tax revenues and avoided social costs. Without effective treatment, the indirect fiscal burden would be substantially higher through increased mortality, worsened morbidity, and intensified caregiver burden.

Table 5.2: Return on Investment Analysis.

Metric	5-Year (2024–2028)	10-Year (2024–2033)
Cumulative HC Investment	€226,603,990	€486,489,630
Cumulative Indirect Fiscal Returns	€31,813,433	€61,553,119
ROI	14.0%	12.7%
Return per €1.00 Invested	€1.14	€1.13
Net Fiscal Return per €1.00	€0.14	€0.13

Rebate-Adjusted ROI Perspective

As documented in Section 2.4, HZZO receives substantial rebates from MAHs for PSL medicines. If the aggregate 2024 PSL refund rate of approximately 21% is applied to the MM healthcare cost component, the effective 5-year cumulative healthcare investment would reduce from €226.6 million to approximately €179.0 million. Under this adjustment, the 5-year ROI would increase from 14.0% to approximately 17.8%, and the return per €1.00 invested would rise from €1.14 to approximately €1.18. While disease-specific rebate rates are not publicly available and this calculation should be treated as illustrative, it demonstrates that the standard ROI figures represent a conservative lower bound. The true return on Croatia's investment in MM healthcare is almost certainly more favourable than the gross-expenditure-based figures suggest.

6. Sensitivity Analysis and Scenario Planning

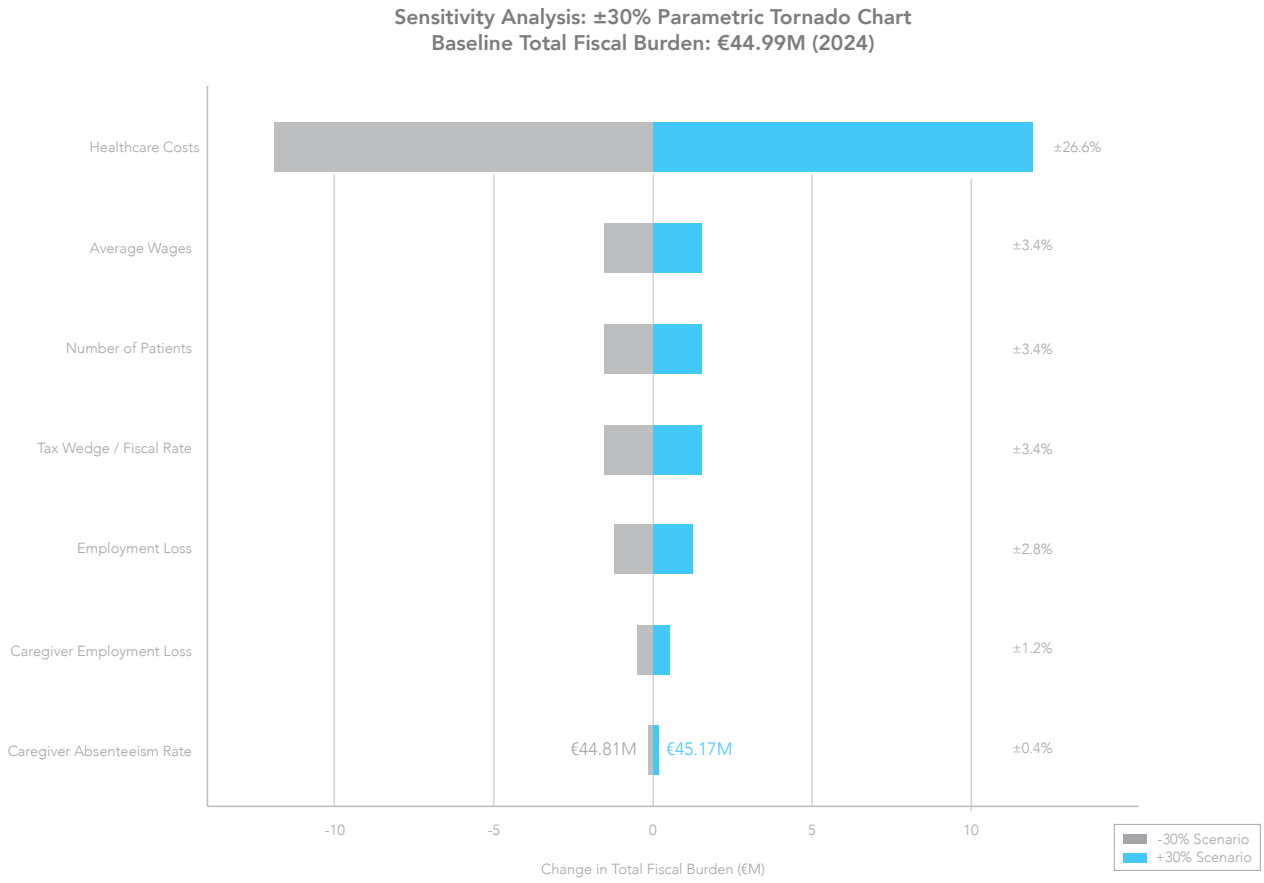
6.1 Parametric ±30% Tornado Analysis

A parametric sensitivity analysis was conducted by varying each of seven major model inputs by ±30% while holding all other inputs constant. The analysis was performed on the 2024 reference year (baseline total fiscal burden: €44,990,247).

Table 6.1: Sensitivity Analysis Results (±30% parametric variation).

#	Parameter	Category	−30% (€M)	Baseline (€M)	+30% (€M)	Swing (±€M)	Swing (±%)
1	Healthcare Costs	Direct	€33.03M	€44.99M	€56.95M	€11.96M	±26.6%
2	Average Wages	Economic	€43.46M	€44.99M	€46.52M	€1.53M	±3.4%
3	Number of Patients	Epidemiological	€43.47M	€44.99M	€46.51M	€1.52M	±3.4%
4	Tax Wedge / Fiscal Rate	Economic	€43.46M	€44.99M	€46.52M	€1.53M	±3.4%
5	Employment Rates	Economic	€43.75M	€44.99M	€46.23M	€1.24M	±2.8%
6	CG Employment Loss	Caregiver	€44.47M	€44.99M	€45.51M	€0.52M	±1.2%
7	CG Absenteeism Rate	Caregiver	€44.81M	€44.99M	€45.17M	€0.18M	±0.4%

Figure 6.1: Tornado Chart – ±30% Parametric Sensitivity. Blue = +30% scenario; Red = −30% scenario.



6.2 Key Sensitivity Findings

Healthcare costs are overwhelmingly the dominant driver of model uncertainty. A ±30% change in healthcare costs shifts the total burden by ±€11.96 million (±26.6%), confirming that treatment cost trajectories are the critical policy lever. All other parameters combined at ±30% produce a ±6.8% change. This finding reinforces the importance of the PSL rebate mechanism discussed in Section 2.4: the actual variation in net healthcare costs (after MAH rebates) may be substantially different from the gross figures used in this analysis.

Economic parameters (wages, employment, patient numbers, tax wedge) each contribute approximately equal and moderate sensitivity at ±€1.2–1.5 million, reflecting their proportional importance in the indirect cost components which represent only 11.4% of total burden. Caregiver parameters have the smallest sensitivity, collectively contributing less than ±1.5% to total burden variation.

Confidence assessment: The €44.99 million central estimate is highly robust to indirect cost parameter variation but materially dependent on healthcare cost assumptions. Only a >15% change in healthcare costs would alter the policy interpretation of findings.

7. Conclusions and Policy Recommendations

Multiple Myeloma represents a significant and growing fiscal burden on Croatia's public finances. The following conclusions are directly supported by the fiscal model:

The total fiscal burden reached €44.99 million in 2024, having grown 296% since 2009, and is projected to reach €60.3 million by 2030 under the mean scenario.

Healthcare costs are the dominant driver (88.6% of total burden), reflecting the high cost of modern MM therapies reimbursed by HZZO. This inverted cost structure (direct costs dominating rather than indirect) is a characteristic feature of MM compared to other chronic diseases. However, the gross expenditure figures overstate the actual fiscal cost due to the PSL rebate mechanism, with MAH refunds representing 15–34% of PSL spending in recent years.

Caregiver fiscal losses are the second most important indirect component, contributing €1.5 million in annual tax losses (2024), with rapid projected growth to €2.5 million by 2030.

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Data Notes

- All financial figures in EUR at current prices unless otherwise specified
- Population projections based on medium variant scenarios from Croatian Bureau of Statistics
- Treatment costs include drug acquisition, administration, and monitoring
- Indirect costs calculated using human capital approach with Croatian average wage rates
- Disability-adjusted life years estimated using European disability weights
- Sensitivity analyses use Monte Carlo simulation with 10,000 iterations
- Tax wedge calculations based on 43.5% Croatian rate
- Primary data from CSV files, from fiscal model
- Methodological framework adapted from Slovak multiple myeloma fiscal analysis 2024
- Analysis period: 2009-2024 (historical), 2025-2030 (projected)

Patient absenteeism tax losses (€3.1 million in 2024) significantly exceed patient morbidity earnings losses (€0.7 million), reflecting the intensity of treatment-related work disruption.

ROI analysis: For every €1.00 invested in MM healthcare, the Croatian state recovers €0.14 in indirect fiscal value over 5 years and €0.13 over 10 years (conservative estimate based on gross expenditure). Adjusting for the PSL rebate mechanism likely improves this to approximately €0.18 per euro over 5 years.

Combined intervention scenarios could generate €6,692,025 in cumulative savings over 2024–2030, with productivity improvements and caregiver support providing the largest fiscal dividends.

Policy Recommendations

Ensure timely and continuous access to novel MM therapies: Croatia's average 549-day delay from EU approval to patient access (EFPIA W.A.I.T. Indicator 2024) means that Croatian MM patients receive therapies significantly later than patients in comparable countries. Only 17 of 56 EU-approved oncology medicines are available in Croatia. Accelerating reimbursement pathways is both a clinical imperative (earlier access to effective therapies improves survival) and a potential fiscal efficiency measure (earlier intervention may prevent costlier downstream complications). Value-based reimbursement mechanisms, including outcome-based agreements already used in the PSL framework, should be expanded to facilitate faster access.

Invest in caregiver support programmes: The caregiver fiscal impact is substantial and growing. Flexible working arrangements, respite care, and caregiver allowances can generate measurable fiscal returns by maintaining caregiver employment. In a country facing a projected 200,000-worker shortage by 2030, preventing disease-related workforce exit of caregivers acquires strategic economic significance beyond the direct fiscal savings.

Monitor the employment impact of MM treatment: The significant absenteeism tax loss component (€3.1 million in 2024) highlights the need for integrated occupational health support for MM patients to maintain workforce attachment.

Consider the full fiscal picture in reimbursement decisions: Healthcare committees should incorporate indirect fiscal impacts into cost-effectiveness assessments. A therapy costing €1 million more per year but reducing absenteeism significantly may be fiscally neutral or even positive from a government perspective. The Connolly et al. fiscal framework provides the analytical tool to quantify these cross-sectoral effects and inform whole-of-government decision-making.

Recognize healthcare investment as an economic driver: Croatia's healthcare system is underfunded at 7.15% of GDP compared to the EU-27 average of approximately 10%. The healthcare system and the economy exist in a mutually reinforcing relationship: investment in health directly shapes human capital, productivity, and long-term GDP growth. As the 2024 EU Ageing Report demonstrates, healthcare spending per capita rises steeply with age, and Croatia's rapidly ageing population will intensify fiscal pressure across all disease areas. A policy shift from cost containment to value-based investment – increasing healthcare spending toward the EU average while ensuring that spending generates measurable health and economic returns – represents the most sustainable long-term approach.

Update the model annually: The fiscal burden model should be refreshed with each year's HZZO and Pension Institute data to track actual trends against projections. Future iterations should also incorporate net-of-rebate healthcare cost data where available, to provide a more precise estimate of the true fiscal burden.

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