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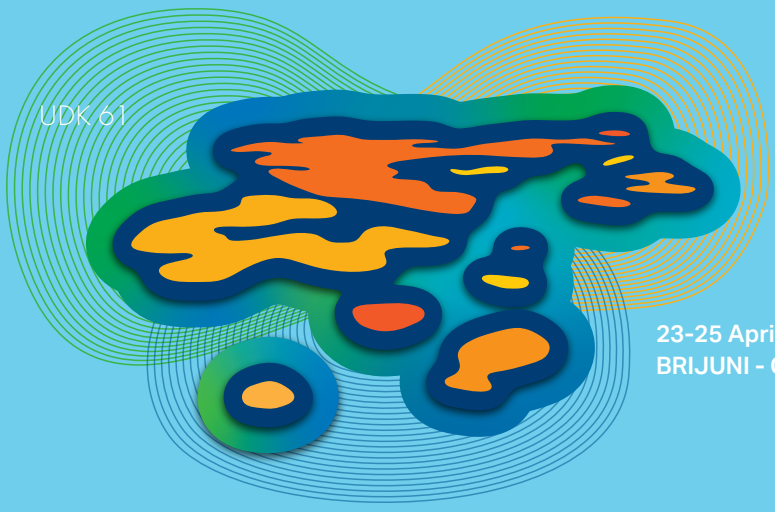

23-25 April, 2026
BRIJUNI - CROATIA

14th ADRIATIC CONGRESS OF PHARMACOECONOMICS AND OUTCOMES RESEARCH with focus on CEE

pharmaca

GLASILO HRVATSKOG DRUŠTVA ZA
KLINIČKU FARMAKOLOGIJU I TERAPIJU

HRVATSKI ČASOPIS ZA FARMAKOTERAPIJU

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Final Programme and Abstracts

from the

14th Adriatic Congress of Pharmacoeconomics and Outomes Research with focus on CEE

Unlocking Economic Growth Through Value driven Investment In Healthcare Innovation In Central And Eastern Europe

23-25 April, Brijuni, Croatia

Guest Editors:

Dinko Vitezić

Viktorija Erdeljić Turk

EDITORIAL

Editorial by the editor-in-chief of Pharmaca

Somehow, it seems to me that I very often write editorials for supplements that are prepared with our Pharmaca, and are dedicated to pharmacotherapy. This time, specifically, to pharmacoeconomics and research on treatment outcomes. The 14th Adriatic Congress, will be held from April 23 to 25, 2026 on the beautiful Brijuni Islands.

There is no need to talk about Brijuni and its long history, from prehistoric times to a fashionable summer resort and one of the summer cultural centers. However, the election for the place of the congress also confirms the importance of the social life of each congress, including this one.

The need for pharmacoeconomic research and analysis today is not surprising to anyone today. It is quite clear, although it has always been so, that in times of accelerated development of drugs (especially innovative ones) with limited resources in healthcare, pharmacoeconomics represents the key tongue on the scale for deciding on the affordability and effectiveness of a new (expensive) drug. Pharmacoeconomic analyses and conclusions are particularly important and should be clear to all clinicians from different health professions. How to ensure equitable access of patients to medical innovations and how to finance them in the long term? How to strengthen the role of patients in decision-making in healthcare policy? Can and should we integrate patient-centered treatment outcomes into the national healthcare planning strategy? - these are just some of the questions that the upcoming congress will try to answer.

At the same time, we must not forget about driving economic growth through value-driven investments in health innovations, which is particularly important for the countries of Central and Eastern Europe. This is also the main professional and scientific topic that will be discussed by many foreign and domestic congress participants. As announced, the organizers will do their best to provide interesting participants from the entire healthcare field, from healthcare professionals, members of the academic community, various associations, regulatory and health service funding bodies, politicians and the pharmaceutical industry.

In the end, as always, I wish success to the Congress, interesting discussions, wise conclusions and their implementation in real (health) life!

Prim. Ksenija Makar-Aušperger, MD, PhD

Editor-in-Chief

FOREWORD

Dear Colleagues and Friends,

It is our distinct honour and pleasure to present this supplement of Pharmaca, which contains the programme and abstracts of the 14th Adriatic Congress of Pharmacoeconomics and Outcomes Research, with a focus on Central and Eastern Europe (CEE). The Congress took place on April 23-25, 2026, at the Conference Centre of Hotel Istra, Brijuni, Croatia. The Congress is organised by the Section for Pharmacoeconomics and Outcomes Research of the Croatian Society of Clinical Pharmacology and Therapeutics, Croatian Medical Association.

This year's Congress is dedicated to the overarching theme:

"Unlocking Economic Growth through Value-Driven Investment in Healthcare Innovation in Central and Eastern Europe."

Over the past decade, the Adriatic Congress has served as a leading regional platform for critical reflection on patient access to innovation, equity in healthcare delivery, and disparities between CEE countries and more developed EU member states. Through rigorous academic exchange and policy dialogue, we have identified structural gaps and systemic barriers that limit timely and equitable access to innovative health technologies.

Building upon this foundation, the 2026 Congress moves decisively from problem identification toward solution-oriented dialogue. The focus is on sustainable, value-driven strategies capable of accelerating access to healthcare innovation while strengthening the long-term financial resilience of healthcare systems across CEE. A growing body of evidence demonstrates that investment in health is not merely a budgetary expenditure, but a driver of economic productivity, social stability, and sustainable growth. Improved patient access to effective and innovative interventions translates into better health outcomes, increased life expectancy, and broader macroeconomic benefits.

The scientific programme of this year's Congress reflects both the maturity and the dynamism of the regional health economics community. We are proud to present 50 scientific presentations, complemented by 6 panel discussions and 2 interactive workshops, fostering in-depth exchange among stakeholders. The Congress has gathered more than 150 participants from 17 countries, representing academia, healthcare professionals, regulatory and payer authorities, policymakers, patient organizations, and the pharmaceutical and health technology industries. Such broad and active engagement confirms the growing relevance of pharmacoeconomics and outcomes research within the CEE region.

Importantly, the regional ecosystem has significantly strengthened in recent years.

Academic institutions, governmental bodies, industry partners, and patient organisations have enhanced their analytical capacity and collaborative readiness. These developments create a unique opportunity to move beyond identifying challenges and toward implementing coordinated, evidence-based solutions tailored to national and regional contexts.

We express our sincere and profound gratitude to our sponsors, whose generous support has made this Congress possible. Their commitment to advancing dialogue, innovation, and responsible investment in healthcare is essential for fostering sustainable progress in our region.

The Croatian Society for Clinical Pharmacology and Therapeutics takes pride in the active involvement of many of its members in the scientific programme. We are pleased that the Society was able to support their participation, thereby strengthening professional development, academic contribution, and regional collaboration.

The abstracts presented in this volume address a broad range of thematic domains, including sustainable financing models for innovation, integration of patient-reported outcomes into decision-making frameworks, implications of the EU Health Technology Assessment Regulation, strategic impact of the European Pharmaceutical Strategy, pharmaceutical pricing and reimbursement policies, comparative effectiveness research, and health-economic evaluations in priority therapeutic areas.

The overarching goal of the Adriatic Congress remains clear: to advance public healthcare policies that maximise societal welfare, strengthen value-based decision-making, and optimize the diffusion of and access to innovative health technologies - enabling patients to achieve their full health and life potential.

We extend our sincere appreciation to all authors, speakers, participants, partners, and supporters whose contributions have shaped this Congress and this Abstract Book. We look forward to continued collaboration in shaping a sustainable, innovative, and equitable healthcare future for Central and Eastern Europe.

Professor Dinko Vitezić, MD, PhD

Congress Chair

President, Section for Pharmacoeconomics and Outcomes Research

Croatian Society for Clinical Pharmacology and Therapeutics

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UNDER THE AUSPICES

Ministry of Health of the Republic of Croatia

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14th Adriatic Congress of Pharmacoeconomics and Outcomes Research with the focus on CEE Countries:

Unlocking economic growth through value-driven investment in healthcare innovation in CEE

Thursday (23 April 2026)

Congress Educational Workshop organized by Syreon Research Institute and European Federation of Pharmaceutical Industries and Associations (EFPIA):
STRENGTHENING THE VOICE OF PATIENTS IN CEE COUNTRIES

09:15 - 12:00 ***(Conference room Verige)***

Faculty: ***Zoltan Kalo, Oana Scarlatescu, Matteo Scarabelli, Réka Pozsár***

Current value frameworks in Central and Eastern European (CEE) countries have limited focus on patient centric value elements and patient representatives are rarely engaged in HTA processes. Significant changes are expected in the implementation of HTA in CEE countries in the forthcoming years. This session provides an overview on why HTA processes matter to patient communities in CEE countries, which have more limited patient access to new health technologies compared to Western European countries. It highlights current barriers, expected challenges, and opportunities for considering patient centric value elements and improved patient involvement in HTA in the CEE region. The voice of CEE patients in the HTA process should be strengthened.

12:00 **Lunch for Pre-congress Workshop participants**

CONGRESS OPENING CEREMONY

(Conference room Kastrum)

13:00 Welcome address by ***Zoltan Kalo***, **Congress Partner**

Welcome address by ***Matteo Scarabelli***, **on behalf of EFPIA**

Welcome address by ***Maciej Niewada***, **on behalf of ISPOR Chapter CEE**

Welcome address by ***Giuseppe Maduri***, **on behalf of EFPIA CEE TF**

Welcome address and Congress opening by ***Dinko Vitezic***, **Congress Chair**

Healthcare investments and outcomes in Central and Eastern Europe

Chairmen: *Herbert Altmann, Dinko Vitezic*

13:30 ***Malina Müller***, Germany: **Healthy returns: A Catalyst for Economic Growth and Resilience**

13:50 ***Arkadi Sharkov***, Bulgaria: **Crossfire Economics: Healthcare Innovation Investment in Central and Eastern Europe**

14:10 ***Slaveyko Djambazov***, Bulgaria: **From Spending to Impact: Rethinking Healthcare Investments in CEE**

14:30 ***Luka Voncina***, Croatia: **Healthcare investment and outcomes in Central and Eastern Europe - country case studies**

14:50 **Panel discussion:**

Healthcare investments and outcomes in Central and Eastern Europe

Moderator: ***Herbert Altmann*** (Germany)

Participants: ***Slaveyko Djambazov*** (Bulgaria), ***Davor Katavic*** (Croatia), ***Giuseppe Maduri*** (Italy), ***Malina Müller*** (Germany), ***Maciej Niewada*** (Poland), ***Arkadi Sharkov*** (Bulgaria), ***Luka Voncina*** (Croatia)

15:40 **Roundtable conclusion**

15:45 **Coffee & Connect**

Critical Reflections and Lessons Learned from the Implementation of the European Union Health Technology Assessment (EU HTA) Regulation

Chairmen: ***Zoltan Kalo, Guenka Petrova***

16:15 ***Matteo Scarabelli***, Belgium: **Update on companies' experience with the JCA.**

16:35 ***Katarina Beravs Bervar***, Slovenia**: Slovenia's Experience in Joint Clinical Assessments (JCA) and the Broader Implementation of the HTA Regulation (HTAR)**

16:55 ***Maciej Niewada***, Poland: **HTA Evolution in Poland: Achievements, Challenges and the Future (personal insights of an eyewitness)**

17:15 ***Viktorija Erdeljic Turk***, Croatia: **Readiness of the Croatian Healthcare System to Integrate Joint Clinical Assessments into Reimbursement Decision-Making for New Medicines**

17:35 **Panel discussion:**

Critical Reflections and Lessons Learned from the Implementation of the European Union Health Technology Assessment (EU HTA) Regulation

Moderator: ***Zoltan Kalo*** (Hungary)

Participants: ***Herbert Altmann*** (Germany), ***Katarina Beravs Bervar*** (Slovenia), ***Viktorija Edreljic Turk*** (Croatia), ***Bertalan Nemeth*** (Hungary), ***Maciej Niewada*** (Poland), ***Guenka Petrova*** (Bulgaria), ***Matteo Scarabelli*** (Belgium)

18:25 **Roundtable conclusion**

18:30 ***Welcome & Networking Reception***

Friday (24 April 2026)

(Conference room Kastrum)

From Evidence to Access: Policy, Value, and Decision-Making in Health Technologies

Chairmen: *Jelena Matuzovic, Goran Bencina*

8:30 *Bertalan Jászkuti*, Hungary: **Strategic decision frameworks and funding strategies of investigational health technologies in the early development phase**

8:45 *Zoltán Kaló*, Hungary: **Principles of selecting cost-effectiveness thresholds in price-taker countries**

9:00 *Guenka Petrova*, Bulgaria: **Shared decision-making including the cost of therapy: lessons learned from Central and Eastern and Western European countries**

9:15 *Natalija Krunic*, Croatia: **Access to innovative medicines as a prerequisite for achieving better treatment outcomes from Croatian Health Insurance Fund perspective**

9:30 *Dalma Hosszú*, *Zoltán Kaló*, Hungary: **Policy recommendations to facilitate drug repurposing in the European Union**

9:45 *Bertalan Németh*, Hungary: **Barriers and facilitators of utilising real-world evidence to support policy decisions in Central and Eastern Europe**

10:00 **Coffee & Connect**

Health-Economic Evaluations and Outcomes Research in Rare Diseases: Access, Equity, and Value

Chairmen: *Dinko Vitezic, Jurij Furst*

10:20 *Patrick Jordan*, Greece: **Orphan Drugs in the Global Spotlight: Trends, Trade-offs, and Tough Choices**

10:40 *Sandra Rose*, Austria: **Driving Equity in Rare Disease Treatment: Insights from Central & Eastern Europe**

11:00 *Rok Hren*, Slovenia: **Optimizing Patient Access to Orphan Medicinal Products: Lessons from Central and Eastern Europe**

11:20 *Srecko Marusic*, Croatia: **The Economic Burden and Value of Optimized Care in Rare Bone Diseases: Insights from Adult X-Linked Hypophosphatemia (XLH).**

11:40 *Robert Babela*, Slovakia: **Cardiovascular hospitalisation costs and cost-effectiveness of Transthyretin Stabilizers in the Slovak heatlhcare system: a Markov model analysis.**

12:00 **Panel discussion:**

Health-Economic Evaluations and Outcomes Research in Rare Diseases: Access, Equity, and Value

Moderator: *Patrick Jordan* (Greece)

Participants: *Robert Babela* (Slovakia), *Jurij Furst* (Slovenia), *Rok Hren* (Slovenia), *Srecko Marusic* (Croatia), *Sandra Rose* (Austria), *Tea Strbad* (Croatia), *Dinko Vitezic* (Croatia)

12:30 **Rountable Conclusion**

12:35 **Lunch break**

From Burden to Breakthroughs: Optimizing Cancer Care Through Policy and Personalized Therapies

Chairmen: *Viktorija Erdeljic Turk, Svetoslav Tsenov*

13:15 *Thomas Hofmarcher*, Sweden: **Beating Cancer Inequalities in Croatia: Are we investing enough in cancer care – and does it pay off?**

13:35 *Goran Bencina*, Croatia: **Premature mortality and econmic impact of lung and pancreatic cancer in Central and Eastern Europe, 2010 - 2021**

13:55 *Robert Babela*, Slovakia: **Multiple myeloma as a cross-sectoral fiscal burden in Slovakia: a whole-of-government analysis from 2009 to 2030**

14:15 *Drazen Huic*, Croatia: **Radioligand therapy - a new chapter in personalized cancer care**

14:35 *Réka Pozsár*, Hungary: **Policy approach to optimize multiple myeloma treatment sequencing practices**

14:55 *Dinko Vitezic*, Croatia: **From single agents to regimens: redefining patient access in the era of combination therapies**

15:15 **Panel discussion:**

From Burden to Breakthroughs: Optimizing Cancer Care Through Policy and Personalized Therapies

Moderator: *Svetoslav Tsenov* (Bulgaria)

Participants: *Robert Babela* (Slovakia), *Goran Bencina* (Croatia), *Viktorija Erdeljić Turk* (Croatia), *Thomas Hofmarcher* (Sweden), *Drazen Huic* (Croatia), *Malina Müller* (Germany), *Réka Pozsár* (Hungary), *Dinko Vitezic*, (Croatia)

15:55 **Rountable Conclusion**

16:00 **Coffee & Connect**

Economic and Societal Impact of Vision and Neurological Diseases

Chairmen: *Slaveyko Djambazov, Romana Rupcic*

16:15 *Guenka Petrova*, Bulgaria: **The Economic Burden of AMD and DME: Insights from Cost-of-Illness Studies**

16:35 *Ivica Belina*, Croatia: **Transforming care in AMD and DR: a call-to-action to preserve vision. White paper of patient organizations from CEE Countries**

16:55 *Mojca Urbančič*, Slovenia: **Diabetic retinopathy screening and treatment in Slovenia**

17:15 *Joze Sambt, Gregor Brecl Jakob*, Slovenia: **Lifetime economic and societal impact of multiple sclerosis treatment**

17:35 *Aleksandra Kapedanovska Nestorovska*, North Macedonia: **Implementation of pharmacoeconomic in healthcare - North Macedonian case study cost-effectiveness and reimbursement assessment of siponimod for secondary progressive multiple sclerosis (SPMS)**

17:50 **Panel discussion:**

THE BROADER SOCIETAL VALUE OF SELECTED THERAPEUTIC AREAS IN CEE, FROM OUTCOMES TO INVESTMENTS

Moderator: *Slaveyko Djambazov* (Bulgaria)

Participants: *Ivica Belina* (Croatia), *Aleksandra Kapedanovska Nestorovska* (North Macedonia), *Bertalan Németh* (Hungary), *Guenka Petrova* (Bulgaria), *Igor Rubinic* (Croatia), *Joze Sambt* (Slovenia), *Mojca Urbančič* (Slovenia)

18:20 **Rountable Conclusion**

SHORT PODIUM PRESENTATIONS

Selected topics in the field of health economics and outcomes research

Chairmen: *Aleksandar Knezevic, Suzana Mimica*

18:30 *Kornélia Lovas*, Hungary: **Cost-effectiveness of radiofrequency renal denervation for resistant hypertension in Hungary**

18:35 *Marta Kucan*, Croatia: **25 years of statin use in Croatia: have we reduced cardiovascular mortality?**

18:40 *Slaveyko Djambazov*, Bulgaria: **Societal and economic burden of migraine in Bulgaria**

18:45 *Darija Krzhovska*, North Macedonia: **Perspectives on value based health-care implementation in North Macedonia**

18:50 *Evgenija Mihajoska*, North Macedonia: **Health system challenges in North Macedonia: fragmented data systems, cancer screening gaps, and demographic ageing implications for value-based healthcare**

18:55 *Iva Mikulic*, Croatia: **Assessing the Cost-Effectiveness of Universal HPV Vaccination in Croatia**

20:00 **Congress networking dinner for all registered Congress participants**

Saturday (25 April 2026)

(Conference room KASTRUM)

Educational Workshop organized by ICHOM, The Swedish Institute of Health Economics and the HTA Ltd.:
FROM OUTCOMES TO INVESTMENT: HOW ICHOM SETS STRENGTHEN ECONOMIC EVALUATION AND SOCIAL VALUE ASSESSMENT

Faculty: ***Slaveyko Djambazov, Spencer Connell, Urska Kosir***

08:30 - 10:15

Workshop overview:

As patient-centered health systems increasingly become the norm, health technology assessment (HTA), regulatory decision-making, and investment strategies are evolving in parallel. Recent policy developments, including the European Medicines Agency's 2025 position emphasizing the expanded role of patient-reported outcomes (PROs), highlight the growing expectation that outcomes meaningful to patients must be systematically integrated beyond clinical care and into value assessment, reimbursement, and innovation incentives. This shift sits at the core of Value-Based Healthcare (VBHC).

This interactive, hands-on workshop explores how ICHOM Standard Sets, grounded in robust clinical and outcomes theory, can be translated from concept to real-world implementation, and ultimately used to strengthen economic evaluation, social value assessment, and investment decision-making.

10:15 **Coffee & Connect**

Pharmacoeconomics of Obesity: Burden, Costs, and Value-Based Treatment Choices

Chairmen: ***Natalija Krunic, Bertalan Németh***

10:30 ***Dinko Vitezic***, Croatia: **The Cost of Weight: A Pharmacoeconomic Perspective of Obesity Management**

10:50 ***Slaveyko Djambazov***, Bulgaria: **Obesity in Bulgaria: Health Burden, Economic Impact, and the Need for Integrated Care**

11:10 ***Andrej Belancic***, Croatia: **Cost-effectiveness of pharmacotherapy for weight management: comparative evidence and future directions**

11:25 ***Said Wani***, Oman: **Cost-effectiveness of metabolic bariatric surgeries, incretin-based therapies, and lifestyle modifications for obesity in Oman**

11:40 ***Spencer Connell***, USA: **Standardizing Outcomes in Obesity to Drive Prevention, Value, and Long-Term System Sustainability**

12:00 **Panel discussion:**

Pharmacoeconomics of Obesity: Burden, Costs, and Value-Based Treatment Choices

Moderator: ***Bertalan Németh*** (Hungary)

Participants: ***Ivica Belina*** (Croatia), ***Spencer Connell*** (USA), ***Slaveyko Djambazov*** (Bulgaria), ***Jurij Furst*** (Slovenia), ***Jelena Matuzovic*** (Croatia), ***Dinko Vitezic*** (Croatia), ***Said Wani*** (Oman)

12:25 **Rountable Conclusion**

SHORT PODIUM PRESENTATIONS
Selected topics in the field of health economics and outcomes research

Chairmen: *Suzana Mimica, Sandra Knezevic*

12:30 ***Slaveyko Djambazov***, Bulgaria: **Melanoma Patient Health Literacy, Perceived Care Quality, and Access to Psychosocial Support: A Cross-Sectional Survey from a Bulgarian Patient Community**

12:35 ***Slaveyko Djambazov***, Bulgaria: **Assessment of Health-Related Quality of Life in Patients with Melanoma Using the EQ-5D-5L: A Pilot Observational Study**

12:40 ***Igor Rubinic***, Croatia: **Alternative Pembrolizumab Dosing in Non-Small Cell Lung Cancer: A Pharmacoeconomic Analysis**

12:45 ***Ivana Stevic***, Serbia: **Economic Evaluation of the Treatment of Non-Chemotherapy Drug-Induced Cytopenias**

12:50 ***Sandra Knezevic***, Croatia: **Economic burden and clinical value of bermegane geperpavec in dystrophic epidermolysis bullose: implications for health systems**

12:55 ***Dominik Strikic***, Croatia: **Drug Exists - But Can the Patient Get It? Knowledge of Pharmacoeconomics and Drug Regulation Among Young Physicians in Croatia**

13:00 ***Karolina Majstorović Barać***, Croatia: **Folic acid supplementation as a low-cost adjunctive intervention for negative symptoms in Schizophrenia: a pharmacoeconomic perpective for Central and Eastern Europe**

13:05 ***Marija Kurtov***, Croatia: **From Brain Energy to Budget Savings: Evaluating the Societal Returns of Creatine Supplementation for Depression in Women**

13:10 ***Maja Ilijanić Samošćanec***, Croatia: **Online queries on medication safety during breastfeeding as an indicator of informational uncertainty costs**

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CONGRESS CLOSING AND FAREWELL

(Conference room KASTRUM)

13:15 Closing remarks by ***Slaveyko Djambazov***, **Congress Partner**

Closing remarks and invitation to the next year congress by ***Dinko Vitezic***, **Congress Chair**

13:30 **Farewell snack**

Collaborative Associations' Meeting

14:30 **Feedback from the 14th Adriatic Congress on Pharmacoeconomics and Outcomes Research**

15:30 **Proposal for venue, topics and committees for the 15th Adriatic Congress on Pharmacoeconomics and Outcomes Research**

16:15 **Collaborative regional research opportunities**

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SAŽETCI / ABSTRACTS

Note: The organizers are not responsible for the contents of submitted abstracts

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HEALTHCARE INVESTMENTS AND OUTCOMES IN CENTRAL AND EASTERN EUROPE

CROSSFIRE ECONOMICS: HEALTHCARE INNOVATION INVESTMENT IN CENTRAL AND EASTERN EUROPE

SUBTITLE: THE INTERSECTION OF WAR, TRADE REALIGNMENT, AND EUROPEAN FRAGMENTATION

Arkadi Sharkov[1]

[1]Healthcare economist, Member of the executive board, Brain Health Council Foundation, Sofia, Bulgaria

As supply chains increasingly serve as strategic front lines and trade policy becomes inseparable from foreign policy, Central and Eastern Europe (CEE) confronts a convergence of pressures that would challenge even the most resilient economies. Armed conflict on the eastern border is straining fiscal resources and altering investment priorities. Houthi attacks on Red Sea shipping routes have revealed the fragility of pharmaceutical supply chains that Europe previously considered secure. Ongoing instability in the Middle East continues to disrupt energy markets and logistics corridors. At the same time, the European Union faces internal divisions driven by divergent foreign policy objectives, subsidy disputes, and unresolved questions regarding the allocation of collective security costs. The introduction of sweeping United States tariffs further destabilizes an already vulnerable trading system, making the pursuit of strategic self-reliance not only compelling but essential. Onshoring and friendshoring, defined as the intentional relocation and reorientation of critical industrial capacity toward trusted partners, have shifted from economic jargon to central tenets of national security strategy. For CEE, this period is a unique, time-sensitive opportunity to position itself as the trusted manufacturing and innovation hub for a Europe that now recognizes dependency as vulnerability, and that regional capacity to produce medicines, devices, and health technologies is fundamental to resilience against external coercion.

FROM SPENDING TO IMPACT: RETHINKING HEALTHCARE INVESTMENTS IN CEE

OBESITY IN BULGARIA: HEALTH BURDEN, ECONOMIC IMPACT, AND THE NEED FOR INTEGRATED CARE

Veneta Todorova[1], Georgi Slavchev[1], Slaveyko Djambazov[1]

[1]HTA Ltd., Sofia, Bulgaria

Objectives: To assess obesity as a chronic disease in Bulgaria by analyzing its epidemiology, clinical burden, and economic impact, and to identify gaps in current management and opportunities for improved healthcare system response. Methods: A comprehensive literature review and health economic analysis were conducted using national and international data sources. The study evaluates clinical characteristics, epidemiology, and disease burden, alongside a cost-of-illness approach. Direct medical costs (diagnosis, treatment, monitoring, and complications) and indirect costs (productivity loss and disability-adjusted life years, DALYs) were estimated over a one-year time horizon from a societal perspective. Results: Obesity is a chronic, relapsing, multifactorial disease associated with significant metabolic, cardiovascular, respiratory, and oncological comorbidities. It affects approximately 15% of the global population, with increasing prevalence trends also observed in Bulgaria. The disease contributes substantially to reduced quality of life and increased mortality. The total economic burden of obesity in Bulgaria is estimated at €3.32 billion annually, representing approximately 3.2% of the national GDP. Direct healthcare costs account for €342 million (10.3%), with the majority driven by the management of complications (approximately 84% of direct costs). Indirect costs are the dominant component, reaching €3 billion BGN (89.7%), primarily due to productivity losses and premature mortality. Additionally, obesity contributes to approximately 67,700 DALYs annually in Bulgaria, highlighting its significant impact on population health. Despite this burden, the healthcare system remains largely focused on treating complications rather than early diagnosis and long-term disease management. Limited recognition of obesity as a chronic disease further hinders effective care pathways. Conclusion: Obesity represents a major public health and economic challenge in Bulgaria, with substantial direct and indirect costs. Current healthcare approaches are insufficient, emphasizing the need for systemic change. Recognizing obesity as a chronic disease and implementing integrated, value-based care models focused on prevention, early intervention, and long-term management could significantly reduce its burden and improve patient outcomes.

HEALTHCARE INVESTMENT AND OUTCOMES IN CENTRAL AND EASTERN EUROPE: COUNTRY CASE STUDIES OF CROATIA, ROMANIA & SERBIA

Luka Vončina[1,2]

[1]Freyr d.o.o.

[2]Faculty of Health Studies, Rijeka, Croatia

Public health spending relies on both a nation's capacity to pay—its overall wealth—and its willingness to prioritize health within government budgets. Compared to Western Europe, countries like Romania and Serbia, and to a lesser degree Croatia, invest modestly in healthcare per capita. While this underfunding has significant implications for patient access and outcomes, an encouraging upward trend is emerging across Central and Eastern Europe (CEE). Currently, public healthcare investment per capita in the CEE region (excluding Serbia) is growing at a faster rate than in the EU4 countries of Germany, Italy, Spain, and France.

However, the consequences of historically low public spending remain severe. The financial burden frequently shifts to patients, resulting in high out-of-pocket costs and catastrophic health expenditures in Serbia and Romania, though Croatia remains a positive exception. Consequently, all three nations consistently lag behind developed Western countries across key health indicators. These lagging metrics—which include lower life expectancy, higher Disability-Adjusted Life Years (DALYs), and elevated rates of treatable and premature mortality from major non-communicable diseases—correlate directly with their lower public health expenditures.

Too often, the policy debate surrounding healthcare is dominated by cost containment, treating health systems as a resource drain rather than a productive sector. Yet, robust empirical evidence demonstrates that health is a vital component of human capital. Healthy populations fuel economic growth through higher employment rates, reduced absenteeism, and increased workplace productivity. Furthermore, improved longevity incentivizes greater investment in education and higher retirement savings, thereby generating capital for broader economic investment. Health, health systems, and national wealth operate in a mutually reinforcing "virtuous circle." The poorer health outcomes in CEE countries directly mirror their economic underperformance, such as lower GDP per hour worked. Ultimately, stakeholders must recognize that investing in healthcare is a direct investment in GDP growth.

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CRITICAL REFLECTIONS AND LESSONS LEARNED FROM THE IMPLEMENTATION OF THE EUROPEAN UNION HEALTH TECHNOLOGY ASSESS

HTA EVOLUTION IN POLAND: ACHIEVEMENTS, CHALLENGES AND THE FUTURE (PERSONAL INSIGHTS OF AN EYEWITNESS)

Maciej Niewada[1]

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The views expressed in this presentation reflect the author's personal insights and should not be attributed to or associated with any institution with which the author is currently affiliated or has previously been affiliated.

Poland established its health technology assessment infrastructure in 2005, when the Agency for Health Technology Assessment (AOTM) was created by ministerial regulation as an advisory body to the Minister of Health. Gaining full legal entity status in 2009 and later expanding its mandate to include tariff-setting — reflected in its current name, AOTMiT — the Agency has operated under a deliberately lean, advisory model: producing mostly appraisals and issuing recommendations while formal reimbursement decisions remain with the Ministry of Health. Since its inception, AOTMiT has issued about 25 hundreds of reimbursement recommendations across drugs, medical devices and health services, and contributed to costing evaluations of many healthcare services. Its HTA methodological foundation has been revised three times — guidelines first published in 2007, updated in 2009 and again in 2016 — with a fourth update formally launched in November 2025 as part of the Agency's 2026–2028 strategic plan, the first such revision in nearly a decade.

Despite progress, significant challenges remain. Constructing well-informed, locally relevant PICO frameworks is increasingly complex — a difficulty that will resonate when Poland absorbs Joint Clinical Assessments under the EU HTA Regulation. Economic evaluation requires further attention, particularly around the transparency of confidential discount arrangements, the discount rates and the main framework of cost-effectiveness applied. Budget impact analysis calls for a broader scope, while ethical, regulatory, system-level and societal dimensions of appraised technologies remain underaddressed in current practice. Notably, dedicated methodological guidance for medical devices and non-drug interventions is still lacking, and the assessment of drugs for rare diseases continues to raise unresolved questions around evidence standards and value frameworks that existing guidelines have yet to fully tackle.

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READINESS OF THE CROATIAN HEALTHCARE SYSTEM TO INTEGRATE JOINT CLINICAL ASSESSMENTS INTO REIMBURSEMENT DECISION-MAKING FOR NEW MEDICINES

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Objectives: The introduction of Joint Clinical Assessment (JCA) under Regulation (EU) 2021/2282 represents a major shift in the European health technology assessment (HTA) landscape, aiming to harmonise clinical evidence across Member States. While JCA provides a common assessment of relative clinical effectiveness for new oncology medicines and advanced therapy medicinal products, it does not replace national decision-making on pricing and reimbursement. This creates important challenges for countries with less formalised HTA structures, such as Croatia, where the integration of JCA outputs into existing decision-making frameworks remains undefined. This presentation aims to explore the key challenges and prerequisites for integrating JCA into reimbursement decisions in Croatia, with a focus on system readiness and practical implementation. Methods: This presentation is based on a structured review of current European policy developments and literature, complemented by an exploratory stakeholder survey conducted in Croatia. The analysis focuses on key implementation domains, including alignment of timelines between EU and national processes, adaptation of JCA outputs to local clinical practice, availability of data for decision-making, and institutional responsibilities. An anonymous online questionnaire targeting key stakeholders involved in the evaluation and funding of medicines (policy-makers, payers, public health and regulatory bodies, clinicians, and industry) is used to complement the analysis by capturing real-world perceptions of system readiness and implementation barriers. Results: Emerging evidence indicates that JCA will serve as a valuable source of standardised clinical evidence; however, it will not be sufficient to support national reimbursement decisions without additional contextualisation. Key gaps are expected in defining the actual target population, identifying relevant comparators within local clinical pathways, assessing budget impact, and evaluating organisational implications. Furthermore, challenges related to timing misalignment, limited data availability, and constrained institutional capacity are likely to affect the effective integration of JCA into national processes. Preliminary stakeholder insights suggest that the need for structured post-JCA processes will be particularly pronounced for high-cost and high-uncertainty therapies, including oncology medicines, advanced therapies, and treatments for rare diseases.

Conclusion: JCA represents a significant step towards greater harmonisation of clinical evidence in Europe; however, its successful integration into national decision-making will depend on the ability of individual countries to develop complementary frameworks. For Croatia, this implies establishing a pragmatic post-JCA approach that includes systematic national contextualisation, clearly defined institutional roles, and the selective use of real-world data and reassessment mechanisms. Without such adaptations, the potential benefits of JCA may not be fully realised in national reimbursement decision-making.

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FROM EVIDENCE TO ACCESS: POLICY, VALUE, AND DECISION-MAKING IN HEALTH TECHNOLOGIES

STRATEGIC DECISION FRAMEWORKS AND FUNDING STRATEGIES OF INVESTIGATIONAL HEALTH TECHNOLOGIES IN THE EARLY DEVELOPMENT PHASE

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Introduction: Societal need for health innovation remains strong; amongst other factors, age dynamics and citizen expectations continue to force health innovation stakeholders to push for more lab ideas to reach patients' bedside. What keeps changing are some key environmental factors such as continued scarcity of public budgets available for health, low-hanging innovation areas exploited already and key places of innovation shifting towards Academia and Spin-offs. While in the past, key strategic decision tools and related funding resources for health innovation concentrated at small number of large innovators, such knowledge is rather scarce in smaller innovation hubs, especially when it comes to early-phase health innovation, when clinical evidence is rather scarce. Decisions are, however, still needed; whether to continue with an idea (Go/No Go) and if so, how to fund the innovation until it reaches patients.

Areas covered: An overview is provided on a strategic decision framework that may help innovators i) to improve their own assessment tool for the various early-phase ideas all through the development cycle and ii) to adopt the most appropriate funding strategy to each stage of the development. Adopting such framework may increase the likelihood of successfully addressing the two most important dilemmas of any early-phase health innovation idea: will it reach patients and at what price (Monetization or Revenue-generation) and, until then, how can pre-Revenue costs be covered (Funding)?

Expert Opinion: As key top-down trends continue to prevail (driving forces as well as key obstacles), health innovation continues to be shifting towards smaller innovation hubs and large companies are expected to increase their innovation pipelines through turning to such smaller hubs for cooperation. This will only work if smaller hubs can improve their own efficiency in selecting viable early-phase lab ideas internally and then can secure the necessary funding until clinical evidence is more robust and commercial deployment is more visible.

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PRINCIPLES OF SELECTING COST-EFFECTIVENESS THRESHOLDS IN PRICE-TAKER COUNTRIES

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Introduction: Countries with relatively small market size typically lack the bargaining power to influence the prices set by multinational pharmaceutical companies, so they function as price-taker rather than price-maker. For price-taker countries it is essential to assess the value of new medicines at the prices proposed: if the proposed price is higher than the value of the medicine, health care payers must seek price reduction to ensure the efficient use of limited resources. Carefully established cost-effectiveness thresholds (CETs) are essential tools to assess local economic value of new medicines.

Areas covered: An overview is provided on how pharmaceutical price-taker countries may establish or reconsider their CETs. Key aspects of selecting appropriate CETs in price-taker countries include i) the methodology for establishing the main CETs, ii) the selection of factors to modify the baseline CET, if higher spending for one unit of health gain seems justified and iii) the process of using CETs in policy decisions.

Expert Opinion: There is a gap between academic research and real word policy practices in establishing CETs. Many approaches described in scientific articles are not implemented, the majority of countries establish or make changes in their CETs without strong theoretical foundation. In the next years several price-taker countries will introduce or update CETs. Lower-income countries, who linked their CETs to the GDP per capita and whose economy has been growing significantly, may reduce their baseline thresholds. There will be significant pressure on higher-income countries to increase their CETs, who did not adjust their absolute CETs for economic growth and/or inflation in recent years.

SHARED DECISION-MAKING INCLUDING THE COST OF THERAPY: LESSONS LEARNED FROM CENTRAL AND EASTERN AND WESTERN EUROPEAN COUNTRIES

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Introduction: Shared decision making (SDM) in healthcare is a concept that has been practiced in Western European (WE) countries, but it remains relatively new in Central and Eastern European (CEE) ones. Discussing the cost of therapy as part of SDM is also a relatively new topic for all European countries.

Objective: The current study focuses on differences in patients' and healthcare professionals' perceptions regarding SDM, including discussions about the cost of therapy in WE and CEE countries.

Methods: A qualitative, non-interventional study was conducted as a series of focus group discussions in Bulgaria, Hungary, and France. The focus group guideline contained a set of preliminarily formulated questions, consistent across countries, about the potential importance of discussing treatment effectiveness, safety, and costs between patients and their physicians. The focus groups involved both patients and healthcare professionals.

Results: Across all focus groups, participants agreed that SDM is an important component of communication between physicians and patients, but the cost of therapy is rarely included in these discussions. It was also highlighted that discussing this topic was more important for therapies where co-payment exists. For both groups of countries, the information flow is mainly going from physicians to patients rather than in the opposite direction. Nevertheless, patients from WE countries tended to be more open to such discussions, while in CEE countries, a more traditional, physician-led model of

care still tends to prevail. However, many expressed the view that pricing and reimbursement decisions are made by authorities on behalf of society, and therefore, patients should not necessarily be involved. It was also evident that economic considerations influence discussions, particularly when attempting to identify more affordable treatment options.

Conclusions: There is a need for appropriate training for both patients and physicians in SDM, as well as for the establishment of a structured methodological framework to support such discussions.

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ACCESS TO INOVATIVE MEDICINES AS A PREREQUISITE FOR ACHIEVING BETTER TREATMENT OUTCOMES - CHIF PERSPECTIVE

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Introduction: The concepts of supply and demand are fundamental to the functioning of any market, including the pharmaceutical industry. Supply refers to the quantity of products that producers are willing and able to produce and sell at various prices, while demand reflects the quantity that consumers are willing and able to purchase at those prices. In the context of pharmaceuticals, understanding these economic principles is essential. However, supply and demand are not the only interacting forces within the pharmaceutical system. Numerous stakeholders, including the Ministry of Health, Ministry of Finance, national insurance fund, HTA bodies, wholesalers, and hospital management, significantly influence these relationships.

Context: As in many other countries, the Croatian Health Insurance Fund (CHIF) plays a central role in bridging the gap between supply and demand by providing resources while balancing patients' unmet needs with the availability of medicines. CHIF operates within clear fiscal limitations; however, this does not prevent continuous efforts to improve cost tracking, measure the value generated by funded medicines, and reallocate resources more efficiently. The aim is not only to increase spending but to spend smarter, align health budgets with national and patient priorities, improve managerial capacity, and ensure value for money.

Results: In recent decades, innovative medicines have significantly improved survival rates and quality of life, while also altering the natural history of many diseases. However, reimbursement decisions alone are not sufficient. Achieving and monitoring treatment outcomes is essential for the sustainability of the healthcare system. Outcome-based reimbursement models have the potential to reduce financial risk for payers by linking costs to real clinical value, although their implementation remains challenging due to multiple barriers. CHIF is therefore transitioning towards simpler forms of confidential agreements with marketing authorization holders (MAHs), such as price-volume agreements, utilization caps, and agreements covering initial treatment periods. Monitoring outcomes requires investments in healthcare digitalisation, and CHIF is currently at an early stage of implementing IT systems designed to collect real-world data on treatment outcomes, particularly in oncology and immunotherapy.

Conclusion: Improving the availability and quality of outcome data will enable more rational treatment decisions and a stronger focus on effective therapies. This, in turn, may generate savings that can be reinvested in access to innovative medicines, ultimately contributing to better patient outcomes and a more sustainable healthcare system.

POLICY RECOMMENDATIONS TO FACILITATE DRUG REPURPOSING IN THE EUROPEAN UNION

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Drug repurposing (DR), the identification and translation of new therapeutic use for existing medicines, offers an alternative pathway to de novo drug development, with the potential to provide faster and more affordable treatment options and improve patient access. However, its implementation remains limited by a fragmented and complex ecosystem, including regulatory hurdles, challenges in the business case for DR, and a lack of coordinated policy support.

Within the REMEDi4ALL Horizon Europe project, policy research identified and prioritised policy barriers to DR and explored facilitating mechanisms to address them. Using a multi method approach across sequential steps, including systematic literature review, stakeholder engagement and prioritisation through a policy survey, and qualitative interviews for validation, 33 barriers were identified and assessed in terms of their importance and actionability. In parallel, over 700 facilitating mechanisms were collected from literature, alongside existing policy frameworks, and successful reference cases, then categorised as push and pull incentives. Following stakeholder validation, these mechanisms were consolidated into a Catalogue of Actions (CoA) comprising 10 push and 9 pull mechanism categories. The CoA provides a structured collection of facilitating mechanisms and serves as a basis for aligning these mechanisms with identified policy barriers.

This work is the basis for the ongoing and continuous development of policy recommendations within REMEDi4ALL, with particular attention to the transferability of proposed approaches across Member States and considerations of sustainability and equity within the European Union and beyond.

BARRIERS AND FACILITATORS OF UTILISING REAL-WORLD EVIDENCE TO SUPPORT POLICY DECISIONS IN CENTRAL AND EASTERN EUROPE

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Objectives. We aimed to identify drivers and solutions to overcome the barriers of the effective use of real-world data (RWD) and real-world evidence (RWE) in Central and Eastern Europe.

Methods. Firstly, a targeted literature review (TLR) was followed by an experts' workshop aiming to refine and complement the identification of current barriers and drivers. Next, we performed a gap analysis on the barriers based on their importance and actionability. The scores of importance and actionability for each barrier were determined through a questionnaire completed by the experts. Finally, a second experts' workshop was held to develop recommendations to overcome the most important actionable barriers and to collect case studies of RWD/RWE utilization.

Results. A total of 22 publications were included in the data extraction phase of the TLR. After the first experts' workshop, 16 barriers and 9 drivers were identified. At the second workshop nine solutions were proposed in 4 main intervention areas. In addition, 13 case studies were provided from the four countries, where RWD/RWE was used effectively.

Conclusions. The effective use of RWD/RWE in health-policy decision making still faces several barriers in Czechia, Hungary, Poland, and Slovakia. This research highlighted the most important barriers and collected recommendations by key experts on how to improve the utilization of RWD/RWE.

OPTIMIZING PATIENT ACCESS TO ORPHAN MEDICINAL PRODUCTS: LESSONS FROM CENTRAL AND EASTERN EUROPE

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This study highlights key implementation strategies for improving patient access to orphan medicinal products (OMPs) in Central and Eastern Europe, drawing on detailed case studies from Czechia and Poland. The introduction of dedicated OMP-specific health technology assessment (HTA) pathways emerges as a critical success factor. In Czechia, a structured multi-criteria decision analysis (MCDA) framework enables a comprehensive assessment of clinical, economic, and societal value within a transparent, multi-stakeholder process featuring defined timelines and binding recommendations. In Poland, an alternative pathway (TLI/TLK) complements the standard cost-effectiveness-based approach by facilitating early identification and prioritization of high-value therapies, supported by a dedicated funding mechanism. Both approaches have contributed to increased reimbursement rates of EMA-approved OMPs, indicating the importance of flexible and tailored HTA methodologies.

The study also emphasizes the role of patient inclusion in decision-making as a key enabler of equitable access. The Czech model represents an advanced example of patient empowerment, combining early-stage involvement, through the submission of patient-reported outcomes, with formal voting rights in reimbursement decisions. This approach is supported by a structured, multi-year development process (the “5Ds”: Diagnose, Define, Design, Develop, Deploy), encompassing the establishment of patient organizations, governance frameworks, and targeted education programs. The resulting system helps minimize challenges such as tokenism and strengthens the legitimacy and relevance of HTA decision-making.

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CARDIOVASCULAR HOSPITALIZATION COSTS AND COST-EFFECTIVENESS OF TRANSTHYRETIN STABILIZERS IN THE SLOVAK HEALTHCARE SYSTEM: A MARKOV MODEL ANALYSIS

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Objectives: Transthyretin amyloid cardiomyopathy (ATTR-CM) is a progressive disease in which cardiovascular-related hospitalizations account for 87–93% of direct medical costs. This study quantifies the hospitalization-related economic consequences of acoramidis and tafamidis treatment from the Slovak public-payer perspective and evaluates their cost-effectiveness using Slovak-specific reimbursement data.

Methods: A cohort-based, four-state Markov model with monthly cycles and half-cycle correction was developed. The analysis was conducted from the Slovak public-payer perspective. The base-case used a 12-month time horizon, while an extended 6.5-year scenario was derived from National Amyloidosis Centre staging-based survival projections. Clinical inputs were sourced from two pivotal randomized trials: ATTRibute-CM (acoramidis vs. placebo: 0.22 vs. 0.45 cardiovascular hospitalizations per patient-year) and ATTR-ACT (tafamidis vs. placebo: 0.48 vs. 0.70 events per patient-year). The unit cost per cardiovascular admission was €3,462.94, based on the Slovak NIHO HTA appraisal dossier (Beyonttra, ZHL175). Health state utilities were 0.80 (alive without hospitalization) and 0.56 (hospitalized), derived from the Nordic PROACT ATTR-CM study. A 5% annual discount rate was applied in accordance with MoH Decree No. 422/2011. Incremental cost-effectiveness ratios (ICERs) were calculated.

Results: In the 12-month base case, acoramidis generated hospitalization cost savings of €2,550 per patient, while tafamidis saved €1,905 per patient compared with standard therapy. In the 6.5-year extended analysis, acoramidis produced total hospitalization costs of €9,719 versus €21,916 for standard care (savings: €12,196), while generating 4.82 versus 4.04 QALYs (0.78 QALYs gained), resulting in a dominant ICER of −€15,720.22/QALY. Tafamidis generated costs of €16,371 versus €15,933 for standard care (incremental cost: €437), producing 3.45 versus 2.48 QALYs (0.97 QALYs gained), with an ICER of €450.23/QALY, which is well below conventional European willingness-to-pay thresholds of €20,000–50,000/QALY.

Conclusion: Both transthyretin stabilizers reduce cardiovascular hospitalizations and demonstrate favorable cost-effectiveness from the Slovak public-payer perspective when assessed through the hospitalization cost lens. Acoramidis showed a dominant economic profile, while tafamidis demonstrated highly favorable cost-effectiveness. These hospitalization-driven savings partially offset drug acquisition costs. Establishing a national Slovak ATTR-CM registry is essential to validate these projections and support evidence-based reimbursement decisions.

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FROM BURDEN TO BREAKTHROUGHS: OPTIMIZING CANCER CARE THROUGH POLICY AND PERSONALIZED THERAPIES

PREMATURE MORTALITY AND ECONOMIC IMPACT OF LUNG AND PANCREATIC CANCER IN CENTRAL AND EASTERN EUROPE, 2010-2021

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Background: Cancer-related premature mortality imposes substantial economic losses through reduced productivity. Lung and pancreatic cancers remain among the leading causes of years of life lost (YLL) in Central and Eastern Europe (CEE), yet their indirect economic impact has been insufficiently quantified. This study quantifies years of life lost (YLL) and the associated productivity costs in nine CEE countries between 2010 and 2021.

Methods: YLL data were drawn from the WHO Global Burden of Disease database for Bulgaria, Croatia, Czech Republic, Hungary, Poland, Romania, Serbia, Slovakia, and Slovenia. Productivity costs for individuals dying before the age of 65 were estimated using the human capital approach (HCA), by multiplying years of productive life lost by country-specific average full-time adjusted salary, adjusted for labor force participation.

Results: YLL attributable to lung cancer declined substantially across the CEE region, decreasing from 1,694,868 to 1,472,743 between 2010 and 2021. In contrast, YLL from pancreatic cancer increased across most CEE countries over the same period, rising from 375,802 to 395,652. Lung cancer remained dominant, accounting for 82% of total YLL in both years. Total productivity costs attributable to working-age lung cancer mortality declined from €7.39 billion to €4.90 billion, while pancreatic cancer productivity costs remained relatively stable at approximately €1.51–1.40 billion. Poland, Hungary, and Romania accounted for the largest absolute burden.

Conclusions: Despite meaningful reductions in lung cancer YLL between 2010 and 2021, both cancers continue to impose a substantial and persistent economic burden across the CEE region. The relatively stable pancreatic cancer burden, in contrast to improvements in lung cancer, highlights an emerging policy priority. Targeted interventions in early detection and equitable access to therapy remain essential

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RADIOLIGAND THERAPY - A NEW CHAPTER IN PERSONALIZED CANCER CARE

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Theranostics, or theragnostics, is a technique increasingly used in personalised medicine. In nuclear medicine, one radioactive drug is used to identify and a second radioactive drug is used to treat cancerous tumours (most often thyroid cancer, prostate cancer, and neuroendocrine tumours). Put simply, theranostics combines radionuclide imaging and radiation therapy to target specific biological pathways.

The term "theranostic" is a combination of two words: therapeutic and diagnostic. It refers to a combination of diagnosis and treatment that also allows for ongoing medical assessment of a patient.

Theranostics originated in the field of nuclear medicine; the iodine isotope 131 for the diagnostic study and treatment of thyroid cancer was one of its earliest applications. Nuclear medicine encompasses various substances (for example, prostate-specific membrane antigen (PSMA), somatostatin receptors, and certain blood cell antigens), either alone or in combination, that can be used for diagnostic imaging and targeted therapy. By using these mechanisms, theranostics enables the localisation of pathological tissues through imaging and the targeted destruction of these tissues using high doses of radiation (beta and alpha rays).

The introduction of radioligand therapy presents a significant challenge for healthcare systems regarding diagnosis, patient referral to multidisciplinary teams, RLT facilities in nuclear medicine departments, therapy costs, and radioactive waste management. Many European countries are currently seeking the best solutions for their patients.

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POLICY APPROACH TO OPTIMIZE MULTIPLE MYELOMA TREATMENT SEQUENCING PRACTICES

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Introduction: Advances in therapy have turned multiple myeloma (MM) into a manageable chronic disease, but have also made treatment sequencing increasingly complex. In current practice, new therapies are often introduced in later stages of the disease, although there is limited evidence that this approach leads to the best long-term outcomes. This highlights the importance of better understanding the factors that shape these decisions and identifying ways to support more evidence-informed sequencing.

Areas covered: The presentation draws on insights from a multi-stakeholder discussion involving patient and industry representatives, clinicians, and HTA experts. Several drivers of current practice were identified, including constraints on clinical development pathways, limitations in guideline development, methodological challenges in HTA, financial pressures, and the high disease burden in advanced stages. Potential strategies to optimise sequencing were also discussed, such as enhancing evidence generation, applying whole-disease models, strengthening patient involvement, and expanding evaluation frameworks.

Expert opinion: Uncertainty remains a key factor influencing treatment sequencing decisions in MM, underscoring the need for more robust, comprehensive evidence. As the number of available therapies continues to grow, sequencing decisions are expected to become even more complex, requiring stronger international collaboration and coordinated efforts to support optimal use of treatments.

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FROM SINGLE AGENTS TO REGIMENS: REDEFINING PATIENT ACCESS IN THE ERA OF COMBINATION THERAPIES

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Combination therapies have become a cornerstone of modern oncology, reflecting the biological complexity and adaptability of cancer. By targeting multiple pathways simultaneously, combination regimens enhance efficacy, delay resistance, and improve survival compared with monotherapy. Over the past decade, the proportion of oncology clinical trials investigating combination therapies has increased substantially, while monotherapy trials have declined from approximately 70% to less than 30% of active studies. Several landmark trials have demonstrated meaningful overall survival gains, often exceeding one year, across diverse malignancies.

Despite clear clinical benefits, combination therapies face significant access barriers. In Europe, oncology combinations take on average 193 days longer to become available to patients compared with oncology therapies overall. The primary challenges are economic and structural rather than scientific. Additive pricing, where each component is priced independently, often results in high cumulative costs and unfavourable cost-effectiveness ratios. Cross-company pricing misalignment can create negotiation deadlocks, while difficulties in value attribution complicate health technology assessment (HTA). Additional barriers include regulatory, HTA evidence misalignment, high budget impact, uncertainty regarding sequential versus concurrent use, complexities in managed entry agreements, patent lifecycle asymmetry, and international reference pricing constraints.

Current HTA frameworks, whether based on therapeutic added value or QALY assessment, struggle to evaluate multi-component regimens effectively. No European country has fully resolved pricing and reimbursement challenges for oncology combinations.

Ensuring sustainable patient access requires coordinated pricing mechanisms, early alignment between regulators and HTA bodies, outcome-based agreements, and policy reform. The future of oncology access depends on shifting from drug-by-drug evaluation toward value-based assessment of entire treatment strategies.

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ECONOMIC AND SOCIETAL IMPACT OF VISION AND NEUROLOGICAL DISEASES

DIABETIC RETINOPATHY SCREENING AND TREATMENT IN SLOVENIA

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Background: Diabetic retinopathy (DR) is a leading cause of preventable blindness and poses a substantial clinical and socioeconomic burden. This study aims to present the current status and performance of the Slovenian National Diabetic Retinopathy Screening Program (SNDRSP), evaluate its economic relevance, and identify key barriers to participation, while also highlighting treatment availability and outcomes.

Methods: A descriptive analysis of the national screening program was conducted using coverage data from 2022–2024, clinical performance indicators, and published evidence on cost-effectiveness and screening strategies. Barriers to participation were identified based on clinical experience and literature findings.

Results: Screening coverage in Slovenia remains suboptimal, reaching 21.3% in 2022, 23.3% in 2023, and 22.8% in 2024. Despite this, the program demonstrates good clinical performance, with DR detected in 29.1% of screened individuals and sight-threatening DR (STDR) in 0.89%. However, low participation limits the overall public health impact and cost-effectiveness of the program. Barriers to participation are multifactorial and include limited awareness, psychological factors, logistical and financial constraints, and systemic challenges such as regional disparities, organizational variability, and limited resources. From an economic perspective, DR screening is considered cost-effective, reducing both direct and indirect costs, while risk-based screening intervals may further optimize resource use. All major treatment options for DR and diabetic macular edema (DME) are available in Slovenia. Intravitreal therapies for DME provide significant clinical and economic benefits by improving vision, quality of life, and work capacity, with outcomes comparable to international data.

Conclusion: Although the Slovenian DR screening program shows good clinical performance, its full clinical and economic potential is limited by low participation. Increasing coverage through targeted organizational, educational, and behavioral interventions is essential to improve both effectiveness and sustainability.

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TRANSFORMING CARE IN AMD AND DR: A CALL-TO-ACTION TO PRESERVE VISION - WHITE PAPER OF PATIENT ORGANIZATIONS FORM CEE COUNTRIES

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Across Central and East Europe (CEE), preventable vision loss caused by age-related macular degeneration (AMD) and diabetic retinopathy (DR) continues to rise, with profound personal and healthcare system costs. Despite the growing prevalence and economic impact of these conditions, the European Union has not established a comprehensive framework to address eye health, leaving vision care overlooked in national ageing strategies and health agendas.

This White Paper, developed in collaboration with stakeholders across Bulgaria, Croatia, Estonia, Greece, Hungary, Latvia, Lithuania, North Macedonia, Poland, Romania, Serbia and Slovakia and International Agency for the Prevention of Blindness (IAPB). sets out to change this trajectory.

Five main goals:

- Promotion of early detection of retinal diseases associated with age through national screening and referral systems
- Standardisation of care across countries by defining best practices and clinical pathways
- Increasing access to innovative diagnostics and treatment
- Raising awareness among patients and healthcare professionals
- Support rehabilitation and long-term patient engagement in care

The demographic pressures of ageing populations and the rising incidence of cardiometabolic diseases make immediate action both urgent and achievable. By implementing the recommendations outlined in this White Paper, CEE countries can significantly reduce preventable blindness, support healthy ageing, and close the current equity gap with Western Europe. Governments must seize this opportunity to prioritise vision health, ensuring that no patient is left behind.

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THE ECONOMIC BURDEN OF AMD AND DME: INSIGHTS FROM COST-OF-ILLNESS STUDIES

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Background: Visual impairment is not only a clinical issue but also a significant macroeconomic burden, leading to substantial productivity losses for patients. This presentation provides a brief review of cost-of-illness studies and the activities of the ISPOR Bulgaria chapter in this field, aiming to raise awareness of the societal and individual economic burden of visual impairment.

Results: According to a recent analysis by the WIFOR Institute, the socioeconomic burden of neovascular age-related macular degeneration (nAMD) and diabetic macular edema (DME) in 12 Central and Eastern European (CEE) countries is projected to increase from €7.1 billion to €18.6 billion over the next decade. A study by Retina International highlights the substantial cost of illness (COI) of AMD in Bulgaria, estimated at €450 million. The major components of the COI are not direct or indirect medical costs but productivity losses, such as early withdrawal from the workforce, and well-being costs, including depression, anxiety, and social isolation, which together account for the majority of the societal burden. The concept of the “cost of passive behaviour” is particularly relevant, as every untreated patient represents a permanent economic loss. A recent study conducted by the ISPOR Bulgaria chapter and the Department of Ophthalmology at the Medical University of Sofia demonstrated the cost-benefit of diabetic retinopathy screening.

Conclusion: ISPOR Bulgaria activities contribute to raising awareness and emphasize the need for proactive approaches to early detection of visual health problems. Investment in eye health should be viewed not as a cost, but as a strategic investment in improved population health and a more productive economy.

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LIFETIME ECONOMIC AND SOCIETAL IMPACT OF MULTIPLE SCLEROSIS TREATMENT

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Background: Population ageing is projected to increase public sector spending, particularly on pensions, health care, and long-term care. Consequently, governments must allocate resources efficiently to avoid excessive crowding out of other expenditure categories such as social transfers, education, and productivity-enhancing investments. In addition, overall economic sustainability, in terms of total production relative to total consumption, will be increasingly challenged. Certain health interventions can generate substantial economic and social returns by preventing higher future costs, thereby helping to mitigate pressure on long-term sustainability.

Methods: Multiple sclerosis (MS) is used as a case study to illustrate the compounding value of early, high-efficacy intervention. A lifetime Markov model is being developed to assess the societal return on investment (SROI) of disease-modifying treatments for MS. The model captures a comprehensive range of benefits, including reductions in absenteeism and presenteeism, delayed disability retirement, increased full-time employment, higher household productivity, decreased need for informal care, lower out-of-pocket expenses, and reduced intangible costs.

Results: Early and effective intervention in MS has the potential to slow disease progression, delay disability, and generate significant societal benefits. By addressing both direct and indirect costs, such interventions can substantially reduce the long-term economic burden associated with the disease and contribute to improved workforce participation and productivity.

Conclusion: Limiting investment decisions to short-term and narrowly defined perspectives leads to avoidable losses and unsustainable future costs. A shift towards comprehensive societal evaluation is essential, as it enables more effective strategic resource allocation and supports long-term economic and social sustainability.

Pharmaca 2026;56 (supl 1): 1-88

SHORT PODIUM PRESENTATIONS

Selected topics in the field of health economics and outcomes research

COST-EFFECTIVENESS OF RADIOFREQUENCY RENAL DENERVATION FOR RESISTANT HYPERTENSION IN HUNGARY

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Introduction: Radiofrequency renal denervation (RF RDN) is a guideline-recommended adjunct treatment option for patients with resistant hypertension, a population with a high cardiovascular risk burden. This analysis evaluated the cost-effectiveness of RF RDN in Hungary using contemporary clinical trial and real-world registry data.

Methods: A decision-analytic Markov model, including health states of stroke, myocardial infarction (MI), angina pectoris/coronary heart disease (AP/CHD), heart failure (HF), and all-cause death (ACD), was utilized to project strategy-specific costs and quality-adjusted life-years over a lifetime horizon. Transition probabilities were informed by multivariate risk equations and calibrated to reflect a resistant hypertension population. The base-case cohort and effect size were sourced from the GSR DEFINE study, with extensive sensitivity analyses performed. Costs and utilities were derived from fee schedules and published literature and discounted at an annual rate of 3.7%. The primary outcome was the incremental cost-effectiveness ratio (ICER), and cost-effectiveness was evaluated against a one-time GDP per capita threshold.

Results: At ten years, RF RDN was associated with meaningful reductions in clinical events, with resulting relative risks (RR) of 0.68 for stroke, 0.83 for MI, 0.86 for AP/CHD, 0.50 for HF, and 0.92 for ACD. Over a lifetime horizon, RF RDN resulted in increased costs and QALYs of HUF 2,922,939 and 0.57, respectively, leading to a base-case ICER of HUF 5,089,776 per QALY gained, which is well below the Hungarian willingness-to-pay threshold. RF RDN remained cost-effective across all explored scenarios.

Conclusion: RF RDN is a cost-effective treatment option for patients with resistant hypertension in Hungary, with ICER values below the national one-time GDP per capita willingness-to-pay threshold of HUF 7,878,170. These findings support the value of RF RDN as an adjunctive treatment for patients with uncontrolled hypertension despite optimal medical therapy.

Declaration of funding: This work received support from Medtronic.

TRANSFUSION DEPENDENCE AND OVERALL SURVIVAL - NEW INSIGHTS AND EMERGING DILEMMAS

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Objectives: Over the past 25 years, lipid-lowering therapy in Croatia has evolved from limited use to widespread implementation, with statins becoming a key intervention in dyslipidemia management. This study aims to assess long-term trends in statin utilization and examine whether increased use is accompanied by changes in cardiovascular mortality at the population level, with a focus on pharmacoeconomic implications.

Methods: A population-based observational analysis was conducted using national pharmaceutical consumption data from 2000 to 2023. Drug utilization was expressed as defined daily doses per 1000 inhabitants per day (DDD/1000). Trends in statin use, prescribing patterns, and costs per DDD were analyzed. Mortality data for diseases of the circulatory system (ICD I00–I99) were obtained from national health statistics.

Results: Total lipid-lowering drug utilization increased more than 30-fold, from 4.91 DDD/1000 in 2000 to 152.56 DDD/1000 in 2023, with statins accounting for the majority of this growth. High-potency statins, particularly atorvastatin and rosuvastatin, became dominant over time. At the same time, the average cost per DDD of statins decreased substantially, driven by generic availability and pricing policies, improving treatment affordability. From a pharmacoeconomic perspective, this reflects a marked increase in treatment volume accompanied by improved cost-efficiency. Despite fluctuations in total expenditure, expanded access to therapy was achieved without proportional cost escalation. During the same period, cardiovascular mortality declined notably. The number of deaths due to diseases of the circulatory system decreased from 26,712 in 2000 to 19,937 in 2023, while their proportion among total deaths decreased from 53.16% to 38.80%.

Conclusion: Over the past 25 years, Croatia has experienced a substantial increase in statin utilization alongside a significant reduction in cardiovascular mortality. This period is characterized by improved accessibility, broader implementation of guideline-based therapy, and declining treatment costs. These findings highlight the importance of sustained investment in lipid-lowering strategies and support the continued role of statins as a cost-effective approach to cardiovascular prevention at the population level.

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SOCIETAL AND ECONOMIC BURDEN OF MIGRAINE IN BULGARIA

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Background: Migraine is a prevalent neurological disorder associated with substantial disability and reduced work productivity, particularly among working-age populations. Despite its impact, the economic burden of migraine and the value of modern preventive therapies have not been comprehensively assessed in Bulgaria.

Methods: This study evaluated the economic burden of migraine in Bulgaria and estimated the return on investment (ROI) of migraine pharmacotherapy. A cost-of-illness analysis was conducted from both payer and societal perspectives using a one-year time horizon and a bottom-up approach combining patient-reported, literature-based, and national statistical data. Direct costs included pharmacotherapy and healthcare services, while indirect costs captured productivity losses. An additional ROI analysis assessed long-term economic value over a 10-year horizon.

Results: An estimated 341,634 working individuals in Bulgaria were affected by migraine. The total annual economic burden was €3.33 billion, with indirect costs accounting for approximately 88%. Over a 10-year period, pharmacotherapy yielded 4.90 QALYs per patient and a ROI of 4004%, equivalent to €40 returned per €1 invested.

Conclusion: Migraine imposes a substantial economic burden in Bulgaria, largely driven by productivity losses. Effective migraine pharmacotherapy provides meaningful health benefits and represents a high-value societal investment, supporting the inclusion of economic value considerations in reimbursement decision-making.

PERSPECTIVES ON VALUE-BASED HEALTHCARE IMPLEMENTATION IN NORTH MACDONIA

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Objectives: To evaluate the implementation potential of Value-Based Healthcare (VBHC) in North Macedonia and identify key policy, organizational, financing, and digital challenges relevant to efficiency, equity, and long-term sustainability.

Methods: A two-step narrative review was undertaken. Evidence on VBHC implementation in selected European countries was retrieved from PubMed, Scopus, and Web of Science and supplemented with case studies and EU health policy handbooks. The North Macedonian context was assessed using official reports and policy documents from international and national institutions. The collected evidence was analyzed according to key VBHC domains, including financing, payment models, digital infrastructure, outcome measurement, and governance.

Results: Experiences from Spain, the Netherlands, and Germany show that progress toward VBHC is supported by systematic outcome measurement, integrated multidisciplinary care pathways, and payment approaches that move beyond activity-based reimbursement toward value-oriented incentives. Experiences from Bulgaria and Slovenia suggest that even health systems with structural limitations can advance toward VBHC when reforms strengthen care coordination, expand digital integration, and progressively align financing with measurable outcomes. In North Macedonia, the transition remains constrained by low public financing, high out-of-pocket payments, underutilization of primary care, fragmented service delivery, incomplete data integration, and limited use of routine health information for outcome monitoring and strategic decision-making. In 2021, total health expenditure accounted for 8.5% of GDP, while public funding covered only 54.5% of overall health spending. Out-of-pocket payments reached 41.7%, compared with 15.0% in the EU, highlighting a substantial financial burden on households and reduced equity in access. At the same time, several elements relevant to VBHC are already in place, including the DRG payment system introduced in 2009, the national “My Appointment” platform integrating health data from public healthcare institutions, and conditional budgets for 29 public institutions, which increased from €11.72 million in 2019 to €56.9 million in 2024. These findings indicate that North Macedonia has established initial operational foundations for VBHC; however, their current use remains too fragmented to generate consistent value-based performance at the system level.

Conclusion: Evidence from other European countries demonstrates that progress toward VBHC is achievable even in structurally constrained health systems. In North Macedonia, the priority is to better integrate existing elements into a more efficient and value-oriented model of care. This requires stronger public investment, interoperable digital systems, standardized outcomes, and payment reform linked to measurable value. From a pharmacoeconomic perspective, these reforms improve allocative efficiency, reduce patient financial burden, and support long-term system sustainability.

HEALTH SYSTEM CHALLENGES IN NORTH MACEDONIA: FRAGMENTED DATA SYSTEMS, CANCER SCREENING GAPS, AND DEMOGRAPHIC AGEING-IMPLICATIONS FOR VALUE-BASED HEALTHCARE

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Background: Value-based healthcare (VBHC) focuses on maximizing patient-relevant health outcomes relative to resource use and is increasingly recognized as a key framework for improving health system performance. Previous research evaluating VBHC readiness in North Macedonia has identified key structural gaps, including fragmented data systems and limited outcome measurement. Demographic ageing, together with low coverage of preventive and cancer screening programs, further highlights constraints in achieving more value-oriented healthcare. This study aims to assess the implications of recent national data on cancer screening programs and population ageing in North Macedonia within the context of VBHC implementation.

Methods: A qualitative analysis of national screening reports on cervical and breast cancer in North Macedonia, aligned with recent demographic data, was conducted to assess gaps between healthcare activities and outcomes and their implications for health policy and system performance.

Results: The findings highlight the absence of a stable, long-term cancer screening framework, as well as a lack of integrated patient care pathways and outcome registries. Low screening coverage (0.8%–5.4% for breast cancer and 10.3%–15.5% for cervical cancer), together with the fact that 80% of patients initiate treatment at later disease stages, indicates that current screening programs fail to achieve their intended outcomes. From a VBHC perspective, these findings, along with fragmented data systems that hinder patient tracking, reflect an inability to link resource use to patient-relevant health outcomes, thereby limiting performance assessment and system efficiency. At the same time, demographic projections indicate a pronounced ageing trend, with the proportion of individuals aged over 65 years expected to exceed 34% by 2055, while the population aged over 80 years is projected to increase more than sixfold compared to 2024. The working-age population is expected to decline by nearly half a million, further intensifying pressure on public finances. These trends will have a particularly significant impact in small-population countries such as North Macedonia (total population 1,836,713), where health spending remains below 8% of GDP and high out-of-pocket payments (41.7%) impose a substantial financial burden on households, limiting access to timely and equitable healthcare services. This underscores the need for timely and well-organized screening programs with clearly defined outcomes, as without a shift toward outcome-based policies, rising healthcare spending

may lead to inefficient resource use, limited health gains, and increased fiscal pressure.

Conclusion: The findings align with previous research and highlight the need to transition toward value-oriented health policies and strengthen preventive and screening programs to improve health outcomes and population health.

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ASSESSING THE COST-EFFECTIVENESS OF UNIVERSAL HPV VACCINATION IN CROATIA

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Background: Human papillomavirus (HPV) vaccination is an effective strategy for the prevention of cervical cancer. In Croatia, HPV vaccination is currently available free of charge for both girls and boys; however, it is not mandatory. Mandatory vaccination for both sexes in the 8th grade of primary school is planned from 2027. The World Health Organization has defined a global strategy for cervical cancer elimination based on the 90–70–90 targets: 90% vaccination coverage, 70% screening coverage, and 90% treatment of cervical disease. However, implementation may be limited in settings with reduced access to preventive services. In Croatia, cervical cancer prevention is partly constrained by limited availability of primary gynecological care. Previous modelling studies, including the PRIME study, have demonstrated that HPV vaccination of girls is cost-effective for cervical cancer prevention in Croatia, while the cost-effectiveness of sex-neutral vaccination using updated data remains uncertain.

Objective: To estimate the cost-effectiveness of sex-neutral HPV vaccination (girls and boys) for cervical cancer prevention in Croatia using updated epidemiological and economic data, based on an extrapolation of the PRIME modelling approach.

Methods: A simplified static lifetime cohort cost-effectiveness model was developed from the healthcare payer perspective. The analysis compared sex-neutral HPV vaccination with no vaccination. The vaccinated cohort included girls and boys with 90% coverage, using a two-dose 9-valent vaccine (EUR 118.09 per dose). Contemporary Croatian epidemiological inputs were applied, including a cumulative lifetime risk of cervical cancer of 1.0% and a mortality-to-incidence ratio of 0.45. Outcomes were expressed as disability-adjusted life years (DALYs) averted, with a 3% annual discount rate. Treatment costs were based on Croatian data and adjusted using GDP-based multipliers. Herd-effect scenarios of 2%, 5%, and 10% were explored.

Results: In the base-case scenario (5% herd effect), sex-neutral vaccination was estimated to prevent approximately 158 cervical cancer cases and 71 deaths, corresponding to 387 DALYs averted. Total vaccination costs were EUR 7.88 million, with treatment cost savings of EUR 1.21 million, resulting in a net cost of EUR 6.66 million. The incremental cost-effectiveness ratio (ICER) was EUR 17,216 per DALY averted. Sensitivity analyses yielded ICERs between EUR 16,291 and EUR 17,815 per DALY averted.

Conclusion: Using updated Croatian data and extrapolating the PRIME model, sex-neutral HPV vaccination appears cost-effective for cervical cancer prevention. However, the model did not include vaccine adverse event costs or additional benefits related to other HPV-associated malignancies, which may further improve cost-effectiveness.

PHARMACOECONOMICS OF OBESITY: BURDEN, COSTS, AND VALUE-BASED TREATMENT CHOICES

THE COST OF WEIGHT: A PHARMACOECONOMIC PERSPECTIVE OF OBESITY MANAGEMENT

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Obesity is a chronic, multifactorial disease defined by excessive adiposity and associated with increased risk of noncommunicable diseases, including cardiovascular disease, type 2 diabetes, obstructive sleep apnea, and multiple malignancies. According to the World Health Organization, in 2022 more than 2.5 billion adults were overweight, including 890 million living with obesity, with life expectancy reduced by an average of three years or more in affected individuals. The increasing prevalence of obesity represents a major public health challenge and a substantial, escalating economic burden for healthcare systems worldwide.

Pharmacoeconomic analyses consistently demonstrate that obesity-related complications (ORCs) generate significant direct medical costs, while indirect costs, such as productivity loss, disability, and premature mortality, often exceed direct expenditures over the long term. According to data from European populations show that, under no-intervention scenarios, both the prevalence of ORCs and associated treatment costs rise markedly over time. Higher body mass index (BMI) categories are associated with progressively greater per-person healthcare expenditures. Comparable findings across multiple countries confirm that obesity imposes a sustained and measurable financial strain on national health budgets.

Weight reduction provides clinically meaningful and economically relevant benefits. Simulation models indicate that sustained weight loss of 5-20% can prevent a substantial number of incident ORCs in representative cohorts, translating into significant annual cost savings. Modest sustained weight loss has been associated with approximately 58% reduction in type 2 diabetes incidence and around 20% reduction in major cardiovascular events in large outcome trials. Over 5-10-year horizons, effective obesity management reduces healthcare utilization and long-term expenditures. These data support the concept that treating obesity is not merely a healthcare cost, but a strategic investment in population health. Despite recommendations from international clinical guidelines, most eligible individuals remain untreated. Prescription rates for obesity management medications are low. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) demonstrate substantial efficacy in weight reduction. However, economic

evaluations suggest that at current prices they are generally not cost-effective for obesity treatment in people without diabetes compared with alternative interventions. Their value improves when targeted to high-risk populations and when evaluated over longer time horizons exceeding 10 years. Health technology assessment bodies therefore recommend restricted and criteria-based use, combined with lifestyle modification and structured follow-up.

In conclusion, obesity imposes a major and growing economic burden on healthcare systems and society. Early, individualized, and guideline-based intervention incorporating pharmacoeconomic principles is essential for optimal resource allocation. Targeted use of effective therapies, aligned with national healthcare priorities and financial capacities, can reduce long-term clinical and economic consequences of obesity.

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OBESITY IN BULGARIA: HEALTH BURDEN, ECONOMIC IMPACT, AND THE NEED FOR INTEGRATED CARE

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Objectives: To assess obesity as a chronic disease in Bulgaria by analyzing its epidemiology, clinical burden, and economic impact, and to identify gaps in current management and opportunities for improved healthcare system response.

Methods: A comprehensive literature review and health economic analysis were conducted using national and international data sources. The study evaluates clinical characteristics, epidemiology, and disease burden, alongside a cost-of-illness approach. Direct medical costs (diagnosis, treatment, monitoring, and complications) and indirect costs (productivity loss and disability-adjusted life years, DALYs) were estimated over a one-year time horizon from a societal perspective.

Results: Obesity is a chronic, relapsing, multifactorial disease associated with significant metabolic, cardiovascular, respiratory, and oncological comorbidities. It affects approximately 15% of the global population, with increasing prevalence trends also observed in Bulgaria. The disease contributes substantially to reduced quality of life and increased mortality. The total economic burden of obesity in Bulgaria is estimated at €3.32 billion annually, representing approximately 3.2% of the national GDP. Direct healthcare costs account for €342 million (10.3%), with the majority driven by the management of complications (approximately 84% of direct costs). Indirect costs are the dominant component, reaching €3 billion BGN (89.7%), primarily due to productivity losses and premature mortality. Additionally, obesity contributes to approximately 67,700 DALYs annually in Bulgaria, highlighting its significant impact on population health. Despite this burden, the healthcare system remains largely focused on treating complications rather than early diagnosis and long-term disease management. Limited recognition of obesity as a chronic disease further hinders effective care pathways.

Conclusion: Obesity represents a major public health and economic challenge in Bulgaria, with substantial direct and indirect costs. Current healthcare approaches are insufficient, emphasizing the need for systemic change. Recognizing obesity as a chronic disease and implementing integrated, value-based care models focused on prevention, early intervention, and long-term management could significantly reduce its burden and improve patient outcomes.

COST-EFFECTIVENESS OF PHARMACOTHERAPY FOR WEIGHT MANAGEMENT: COMPARATIVE EVIDENCE AND FUTURE DIRECTIONS

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Background: The expanding therapeutic landscape for obesity has heightened the importance of economic evaluation in both clinical and policy decision-making. This presentation provides a structured overview of cost-effectiveness considerations in obesity pharmacotherapy.

Methods: First, a systematic review of the literature will be presented, encompassing all available cost-effectiveness and cost-utility analyses of pharmacological treatments for non-syndromic obesity, including comparative assessments across interventions. Second, pharmacotherapy for syndromic obesity will be addressed, with a particular focus on rare disease contexts. This section will include a systematic overview of full economic evaluations of setmelanotide, presented as an example of a targeted therapeutic approach within a distinct clinical and economic framework. Third, the presentation will introduce the European Association for the Study of Obesity (EASO) framework for the pharmacological treatment of obesity and its complications, highlighting its role as an algorithm for treatment selection and outcome optimization. Finally, key considerations for future pharmacoeconomic study designs will be discussed, including the integration of additional outcome measures, the incorporation of real-world evidence, and general principles for their implementation.

Conclusion: Together, these elements provide a comprehensive and structured overview of current evidence and methodological considerations relevant to the economic evaluation of obesity pharmacotherapy.

COST-EFFECTIVENESS OF METABOLIC BARIATRIC SURGERIES, INCRETIN-BASED THERAPIES, AND LIFESTYLE MODIFICATIONS FOR OBESITY IN OMAN

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Introduction:
Obesity is a growing clinical and economic burden in Oman, contributing to cardiometabolic diseases and putting more pressure on limited healthcare resources. Comparative evidence on the cost-effectiveness of bariatric surgery, pharmacotherapy, and lifestyle changes is essential to guide policy decisions.

Methods:
A whole-disease, patient-level simulation model of obesity was developed from the perspective of the Oman Ministry of Health. A synthetic cohort of adults with obesity was simulated over a lifetime horizon using 6-month cycles and a 3% discount rate. Interventions included laparoscopic sleeve gastrectomy (LSG), laparoscopic Roux-en-Y gastric bypass (LRYGB), one-anastomosis gastric bypass (OAGB), semaglutide 2.4mg weekly, tirzepatide 5mg weekly, lifestyle intervention, and no treatment. Outcomes assessed included costs, quality-adjusted life-years (QALYs), and the payback period.

Results:
No intervention had the highest costs (OMR 77,467) and lowest outcomes (15.43 QALYs). All interventions were dominant, improving outcomes while reducing costs. LRYGB showed the greatest benefit (+2.76 QALYs; −OMR 20,395), followed by OAGB and LSG. Tirzepatide and semaglutide also provided gains, with smaller improvements for lifestyle intervention. Break-even for healthcare costs occurred earliest with surgery (4–6 years), followed by pharmacotherapy (13–15 years) and lifestyle intervention (18–19 years).

Conclusion:
All interventions improved outcomes and reduced long-term costs. Bariatric surgery offers the highest value and the fastest return on investment, supporting its priority along with targeted use of other therapies.

SHORT PODIUM PRESENTATIONS

MELANOMA PATIENT HEALTH LITERACY, PERCEIVED CARE QUALITY, AND ACCESS TO PSYCHOSOCIAL SUPPORT: A CROSS-SECTIONAL SURVEY FROM A BULGARIAN PATIENT COMMUNITY

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Background: Patient health literacy and access to psychosocial support are increasingly recognized as determinants of cancer care quality and patient-centered outcomes. In melanoma, the psychological burden is substantial, yet data on patient knowledge and perceived care experience from Central and Eastern European settings remain scarce. This study assessed melanoma-specific health literacy, patient-perceived care quality, and access to psychological support among individuals attending the annual Melanoma Patient Day in Bulgaria.

Methods: A cross-sectional survey was administered in 2025 to attendees of the Melanoma Patient Day in Bulgaria. Forty-four individuals participated (34 diagnosed with melanoma; 26 female; mean age 57.5 years; range 16–87). The questionnaire comprised six melanoma knowledge items (definition, warning signs, prevention, importance of self-examination, biopsy confirmation, and treatment modalities) scored as correct or incorrect, and four patient-experience items capturing: (1) treatment impact on daily life, (2) perceived support from the medical team, (3) health information adequacy, and (4) access to psychological care. Descriptive statistics were applied, and experience items were analysed in the diagnosed subgroup (n=34).

Results: Knowledge levels were generally high for prevention (93.2% correct) and procedural recognition, with 86.4% correctly identifying self-examination as important and 88.6% confirming biopsy as the diagnostic standard. Comprehensive knowledge of all warning signs was reported by 68.2% of respondents, while full recognition of the melanoma definition was achieved by 70.5%. Treatment modality awareness was the weakest knowledge domain, with only 59.1% identifying all available options. Among diagnosed patients, treatment had a moderate-to-extreme impact on daily life in 56.2% of cases, while 43.8% reported little or no impact. Perceived physician support was strong, with 84.4% feeling fully supported by their medical team. Health information adequacy was high, as 96.9% felt well or very well informed about their disease and treatment. Access to psychological support was more limited: 51.6% reported having access, 45.2% had no access or were uncertain, and 3.2% indicated no perceived need.

Conclusions: Bulgarian melanoma patients demonstrated high prevention literacy and strong perceived physician support. However, treatment burden affected daily life in over half of diagnosed patients, and nearly one in two lacked or was uncertain about access to psychological support. These findings complement EQ-5D-5L data from the same cohort, where anxiety and depression were the most affected domains, together indicating a clear unmet need for structured psychosocial care integration in melanoma patient pathways in Bulgaria.

ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH MELANOMA USING THE EQ-5D-5L: A PILOT OBSERVATIONAL STUDY

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Background: Melanoma significantly affects patient-reported outcomes across physical, psychological, and social dimensions. However, real-world evidence on health-related quality of life (HRQoL) from Bulgarian clinical settings is limited. This pilot study evaluates HRQoL in patients with melanoma using the EQ-5D-5L and compares the findings with published Bulgarian population norms.

Methods: This observational pilot study analyzed anonymously collected EQ-5D-5L questionnaires from patients participating annually in the “Melanoma Patient Community in Bulgaria” event. Data were collected in 2024 and 2025 from an overlapping cohort of patients assessed in both years. The EQ-5D-5L includes five domains (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and a visual analogue scale (EQ VAS). Utility values were calculated using the Polish EQ-5D-5L value set, consistent with Bulgarian norm studies. Due to the small sample size, analyses were descriptive. Results are presented as the proportion of patients reporting no problems (level 1), while EQ-5D index and EQ VAS scores are reported as means with 95% confidence intervals (CI). Population norms (n=1005) served as reference.

Results: EQ-5D index data were available for 38 patients in both years, while EQ VAS data were available for 38 patients in 2024 and 37 in 2025. Anxiety and depression represented the most affected domain, with only 42.11% (2024) and 39.47% (2025) reporting no problems, compared with 65.47% in the general population. Pain and discomfort were the next most impacted domain, although results were similar to population norms. Mobility, usual activities, and self-care were largely preserved, with over 78% of patients reporting no issues. Mean EQ-5D index values were 0.959 (95% CI 0.943–0.975) in 2024 and 0.954 (95% CI 0.933–0.975) in 2025, slightly exceeding population norms (0.942). In contrast, mean EQ VAS declined from 0.82 in 2024 to 0.75 (95% CI 0.702–0.798) in 2025, falling below the population average (0.78). The proportion of patients reporting perfect health was notably lower than in the general population.

Conclusions: Anxiety and depression represent the most substantial and persistent burden among melanoma patients. Despite relatively high utility scores, self-perceived health declined over time. These findings likely reflect selection bias, instrument ceiling effects, and demographic differences. Larger, longitudinal studies are needed to better understand HRQoL and address unmet psychological needs in melanoma care.

ALTERNATIVE PEMBROLIZUMAB DOSING IN NON-SMALL CELL LUNG CANCER: A PHARMACOECONOMIC ANALYSIS

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Objectives: Pembrolizumab is among the most costly oncology drugs, posing a significant financial burden on healthcare systems. Fixed dosing may lead to drug wastage, particularly in patients with lower body weight. This study aimed to evaluate the potential cost savings associated with implementing a weight-banded pembrolizumab dosing strategy in patients with advanced non–small cell lung cancer (NSCLC) at a tertiary academic hospital.

Methods: A retrospective pharmacoeconomic analysis was conducted using 2024 pembrolizumab utilization data from the Clinical Hospital Centre Rijeka, Croatia. Adult patients with advanced non-oncogene-addicted NSCLC receiving pembrolizumab 200 mg every three weeks were included. Cost modeling compared current fixed dosing with a simulated weight-banded strategy (<65 kg, 65–90 kg, ≥ 90 kg) from an institutional payer perspective.

Results: Ninety-six patients received pembrolizumab during 2024. Implementation of a weight-banded dosing approach reduced pembrolizumab utilization by approximately 25% at the institutional level, corresponding to annual cost savings exceeding €1.1 million.

Conclusion: Weight-banded pembrolizumab dosing represents a pragmatic and evidence-based strategy to improve efficiency and sustainability in oncology drug spending without compromising treatment quality. These findings support the integration of individualized dosing approaches into institutional protocols and national reimbursement frameworks as part of value-based oncology care.

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ECONOMIC EVALUATION OF THE TREATMENT OF NON-CHEMOTHERAPY DRUG-INDUCED CYTOPENIAS

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Background: Cytopenia is a disorder in which the number of blood cells is reduced. Drug-induced cytopenias (DIC) occur with high frequency in patients treated with chemotherapeutics; however, in practice, they also occur with high frequency with non-chemotherapy drugs.

Objectives: The aim was to conduct pharmacoeconomic evaluations of the treatment of severe non-chemotherapy DIC (anemia, leucopenia, and thrombocytopenia).

Methods: Pharmacoeconomic studies were conducted — a Cost-Effectiveness Analysis (CEA) and a Cost-Utility Analysis (CUA) — from the perspective of the Republic Health Insurance Fund of Serbia. For each type of cytopenia, a separate decision tree model was developed with a lifetime time horizon. The strategies compared were Standard of Care (SoC) versus filgrastim, darbepoetin-alfa, and fondaparinux for off-label treatment of non-chemotherapy drug-induced leucopenia, anemia, and thrombocytopenia, respectively. A Monte Carlo simulation was performed on 1,000 virtual patients, and the robustness of the results was assessed using a one-way sensitivity analysis. For all comparisons, ICER (Incremental Cost-Effectiveness Ratio) and ICUR (Incremental Cost-Utility Ratio), along with NMB (Net Monetary Benefit), were calculated, with results expressed as average values across 1,000 patients with a 99% CI.

Results: Across all three cytopenia types, the pharmacoeconomic evaluation showed that alternative treatments were dominant compared to SoC. In the case of leucopenia (filgrastim versus SoC), ICER was –674,759 ± 96,559 RSD; ICUR: –3,286,657 ± 385,296 RSD, with positive NMB. In the case of anemia (darbepoetin-alfa versus SoC), ICER was –38,427 ± 4,418 RSD; ICUR was –826,046 ± 170,964 RSD, with positive NMB. Treatment of severe thrombocytopenia with fondaparinux versus SoC was cost-effective, with ICER: –2,740,681 ± 350,771 RSD and ICUR: –2,849,280 ± 350,387 RSD, with a positive NMB in both analyses. One-way sensitivity analysis showed that NMB remains positive even with ±50% variations in the input parameters.

Conclusion: Pharmacoeconomic evaluations showed that off-label use of filgrastim, darbepoetin-alfa, and fondaparinux is cost-effective compared to SoC for treatment of non-chemotherapy DIC. These findings suggest that reimbursement of these drugs may represent both a clinically beneficial and economically justified approach in the management of severe DIC.

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ECONOMIC BURDEN AND CLINICAL VALUE OF BEREMAGENE GEPERPAVEC IN DYSTROPHIC EPIDERMOLYSIS BULLOSA: IMPLICATIONS FOR HEALTH SYSTEMS

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Objectives: Dystrophic epidermolysis bullosa (DEB) is a rare, severe genetic disorder caused by mutations in the COL7A1 gene, resulting in type VII collagen deficiency and extreme skin fragility. Beremagene geperpavec (B-VEC, Vyjuvek) is the first topical gene therapy targeting the underlying genetic defect. This narrative review aims to evaluate its clinical benefit alongside its economic impact, with particular focus on budgetary implications, regulatory differences, and long-term sustainability within healthcare systems.

Methods: A structured narrative review was conducted using data from pivotal clinical trials (GEM-1/2 and GEM-3), regulatory assessments (FDA, EMA), and health economic reports. Cost estimates were derived from publicly available pricing data, dosing frequency, and administration settings across US and EU frameworks. Budget impact and long-term cost projections were analysed, accounting for differences in eligibility criteria and delivery models.

Results: Beremagene geperpavec is a replication-defective HSV-1 vector delivering the COL7A1 gene to keratinocytes and fibroblasts, enabling local production of type VII collagen and restoration of anchoring fibrils. In the GEM-3 trial, complete wound closure at six months was achieved in 67% of treated wounds compared with 22% in the placebo group. The therapy demonstrated a favourable safety profile, with predominantly mild adverse events and minimal systemic exposure following topical administration. Despite these clinical benefits, B-VEC is associated with a substantial economic burden. The list price per vial is approximately $24,250, corresponding to an estimated annual maintenance cost of $631,000 per patient. In the United States, projected expenditure is estimated at $268 million in the first year and $805 million over three years, with lifetime treatment costs reaching $15–17 million per patient. European budget impact analyses indicate similarly significant financial implications, with estimates of approximately €20.5 million for defined patient cohorts. Regulatory and organisational differences further influence cost structures. While administration in the

United States requires healthcare professionals, the EU framework permits application by trained patients or caregivers, potentially reducing service-related costs. However, the requirement for repeated, potentially lifelong administration due to the non-integrating nature of the vector raises important concerns regarding long-term affordability and resource allocation.

Conclusion: Beremagene geperpavec represents a paradigm shift in the management of DEB, offering clinically meaningful benefits through a disease-modifying mechanism. However, its high cost and need for sustained administration pose significant challenges for healthcare systems. Robust cost-effectiveness evaluations, innovative reimbursement models, and careful patient selection will be essential to ensure equitable and sustainable access to this transformative therapy.

THE DRUG EXISTS — BUT CAN THE PATIENT GET IT? KNOWLEDGE OF PHARMACOECONOMICS AND DRUG REGULATION AMONG YOUNG PHYSICIANS IN CROATIA

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Background: Advances in modern pharmacotherapy have increased the availability of innovative treatments; however, patient access is often limited by pharmacoeconomic considerations and regulatory frameworks. Despite their growing importance in clinical decision-making, these topics remain insufficiently represented in medical education. This study aimed to assess knowledge and attitudes regarding pharmacoeconomics and drug regulation among young physicians and medical students in Croatia.

Methods: A cross-sectional, questionnaire-based study was conducted among medical students and early-career physicians in Croatia. The survey included six sections: demographic data, prior education, knowledge of pharmacoeconomic concepts (e.g., QALY, ICER, HTA), understanding of the national regulatory framework, clinical practice scenarios, and personal attitudes. Knowledge was assessed using true/false/“I don’t know” statements, while attitudes were evaluated on a 5-point Likert scale. Participants were instructed to respond based on their existing knowledge without using external resources.

Results: Preliminary findings indicate substantial gaps in knowledge of key pharmacoeconomic concepts, particularly regarding the interpretation of QALY, DALY, and ICER. Misconceptions were also observed in understanding drug approval, reimbursement processes, and pricing regulation in Croatia. A considerable proportion of respondents reported no prior formal education in these areas. Despite this, most participants recognized the importance of pharmacoeconomics and regulatory knowledge in clinical practice and expressed a strong interest in further education. Attitudes toward the role of drug cost in prescribing decisions varied.

Conclusions: Young physicians in Croatia demonstrate limited knowledge of pharmacoeconomics and drug regulation despite acknowledging their clinical relevance. Targeted educational interventions are needed to support rational prescribing and improve patient access to therapies.

FOLIC ACID SUPPLEMENTATION AS A LOW- COST ADJUNCTIVE INTERVENTION FOR NEGATIVE SYMPTOMS IN SCHIZOPHRENIA: A PHARMACOECONOMIC PERSPECTIVE FOR CENTRAL AND EASTERN EUROPE

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Background and rationale: Schizophrenia is a chronic psychiatric illness affecting up to 1% of the population, characterised by positive, negative and cognitive symptoms. Schizophrenia imposes a disproportionate economic burden on Central and Eastern European health systems. In Croatia, data from the Croatian Institute of Public Health (2024) show that schizophrenia accounts for 13.9% of all psychiatric hospitalisations and 26.7% of all psychiatric in-patient bed days, making it the single leading diagnosis by hospital resource consumption. This pattern is consistent with wider CEE trends and reflects the unmet therapeutic need created by antipsychotic drugs, which effectively control positive symptoms but leave negative symptoms (flat affect, social withdrawal, avolition) and cognitive deficits largely untreated. The absence of approved pharmacological options for negative symptoms perpetuates chronicity, long-term hospitalisation dependency, and associated costs.

Evidence base: Growing evidence implicates folic acid deficiency as a modifiable risk factor in schizophrenia, supported by epidemiological, biochemical and gene association research. An inverse relationship between serum folate concentrations and negative symptom severity has been documented, while positive symptoms show no such association. A 2018 systematic review and meta-analysis found that adjunctive folic acid or methylfolate added to antipsychotic therapy produced improvement in negative symptoms, with an acceptable tolerability profile, though effect sizes were small and larger confirmatory studies were recommended. A randomised multicentre trial further demonstrated that response is amplified in patients carrying functional variants in folate-pathway genes (FOLH1, MTHFR), pointing toward a pharmacogenomically informed, precision medicine approach that could improve cost-effectiveness by targeting supplementation to those most likely to benefit.

Pharmacoeconomic implications: Folic acid is a low-cost, widely available intervention with a well-established safety profile. Targeted screening for folate deficiency and adjunctive supplementation in eligible patients with schizophrenia may offer a favourable value proposition: modest direct drug costs offset against potential reductions in hospi-

talisation frequency and duration, which represent the dominant cost driver in this condition. Incorporation of FOLH1/MTHFR genotyping into prescribing pathways would add an upfront cost but could improve the benefit-cost ratio by concentrating the intervention in the subgroup with the greatest expected response. Budget impact modelling in the CEE context, where schizophrenia-related bed-day utilisation is high, could plausibly demonstrate meaningful system-level savings even at modest effect sizes.

Conclusions: Folic acid supplementation represents an inexpensive, tolerable, and evidence-supported adjunctive strategy addressing the largest unmet need in schizophrenia management. In CEE health systems characterised by high schizophrenia-related inpatient burden, a value-driven evaluation of routine folate screening and targeted supplementation, potentially informed by pharmacogenomic stratification, is warranted. Prospective pharmacoeconomic studies and budget impact analyses in the CEE setting are needed to quantify the potential for system-level efficiency gains.

FROM BRAIN ENERGY TO BUDGET SAVINGS: EVALUATING THE SOCIETAL RETURNS OF CREATINE SUPPLEMENTATION FOR DEPRESSION IN WOMEN

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Objectives: Creatine is an endogenous amino acid derivative that serves as a rapid energy buffer, utilising the creatine kinase system to rephosphorylate adenosine triphosphate (ATP) from adenosine diphosphate (ADP) during periods of high metabolic demand. In women, supplementation is particularly relevant due to lower endogenous stores and hormonal fluctuations affecting brain energy homeostasis. Beyond physical performance, creatine exhibits neuroprotective properties that may mitigate cognitive and mood-related effects associated with estrogen decline. Recent data from the Croatian Institute of Public Health (HZJZ) indicate that mental disorders account for 6% of all hospitalisations in Croatia and nearly one-fifth of total hospital days, imposing a substantial burden on the national healthcare system. Depression alone represents 10.6% of these psychiatric admissions, with women hospitalised at twice the rate of men. Given that reduced brain phosphocreatine levels correlate with symptom severity, low-cost creatine monohydrate supplementation may represent a viable intervention to restore cerebral energy metabolism. This approach has the potential to improve treatment response and reduce the proportion of treatment-resistant cases, as demonstrated by Lyoo et al. (2012), who reported that creatine augmentation significantly accelerated recovery and doubled remission rates compared to standard selective serotonin reuptake inhibitor (SSRI) therapy.

Methods: Based on clinical efficacy data from the 8-week trial by Lyoo et al. (2012), a cost-effectiveness analysis was conducted to compare SSRI monotherapy with 5 g/day creatine monohydrate augmentation. The evaluation adopted a societal perspective, incorporating a weekly cost of €150 per patient (including productivity loss and healthcare overhead) alongside fixed medication costs. Due to the short 8-week timeframe, which precluded the use of long-term outcomes such as QALYs, total costs were calculated using the mean number of patients per interval based on a mathematical model developed with AI assistance.

Results: The total 8-week societal costs were €108,682 for the control group and €92,384 for the creatine group, representing a net saving of €16,298 per 100 patients. The creatine intervention improved treatment efficiency, reducing the cost per successful remission by 57.5% (from €4,180 to €1,776). These results are limited by simplified economic assumptions for the Croatian context and reliance on short-term clinical data from a specific study population.

Conclusion: Incorporating low-cost creatine supplementation alongside standard antidepressant therapy may represent a cost-effective strategy to reduce the societal and healthcare burden of depression by accelerating clinical recovery. While these findings are promising, they are based on short-term data and simplified assumptions; therefore, larger randomized trials and long-term economic evaluations are needed to confirm clinical efficacy and validate sustained cost-effectiveness.

ONLINE QUERIES ON MEDICATION SAFETY DURING BREASTFEEDING AS AN INDICATOR OF INFORMATIONAL UNCERTAINTY COSTS

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Background: Breastfeeding is associated with substantial health benefits and reduced overall healthcare costs. Nevertheless, pharmacotherapy during lactation is frequently characterized by inconsistent or insufficiently accessible safety information, which may influence both clinical decision-making and patient behaviour. In the context of health information seeking in digital environments, online queries may serve as measurable indicators of unmet informational needs within formal healthcare systems.

Methods: A retrospective analysis was performed on 238 posts (2022–2025) from a closed online breastfeeding support group, containing a total of 263 individual queries related to medications, diagnostic procedures, or vaccines. Posts in which lactating women sought advice regarding the safety of pharmacotherapy or diagnostic procedures during breastfeeding were included. Analysis was performed at the level of individual queries, as single posts could contain multiple therapeutic entities. Queries were categorized by therapeutic class or type of procedure, and the results were interpreted within a conceptual pharmacoeconomic cost-pathway framework related to informational uncertainty.

Results: Of the 263 individual queries, the most frequently represented categories were antibiotics (22%), antipyretics/analgesics (11.8%), antihistamines (8.7%), diagnostic procedures (8.7%), and anesthetics (local and general; 7.6%). The recurrent predominance of routine and widely used therapies across the four-year period suggests sustained informational uncertainty in high-frequency clinical areas. These patterns indicate the presence of a “cost of informational uncertainty,” defined as an indirect economic burden arising from additional consultations, therapeutic substitutions, delayed treatment, or potential breastfeeding discontinuation. Previous studies have shown that insufficient or conflicting information on medication safety during breastfeeding increases anxiety and uncertainty, while heightened risk perception is associated with medication avoidance and suboptimal treatment decisions. These dynamics may translate into downstream clinical and economic consequences, including additional consultations, therapeutic changes, or delayed treatment. In addition, health policy documents highlight persistent gaps in the availability and consistency of information on medication use during pregnancy and breastfeeding, representing a barrier to optimal clinical decision-making and patient counselling. The stability of these pat-

terns over time suggests that this phenomenon reflects a recurring informational gap in clinically relevant situations rather than random digital activity.

Conclusion: Online queries from breastfeeding women regarding medication safety identify therapeutic areas with a potentially increased risk of downstream pharmacoeconomic burden. Systematic monitoring of such patterns, combined with targeted improvements in the availability of standardized, evidence-based lactation-specific information, may represent a low-cost intervention with the potential to significantly improve healthcare efficiency and resource utilization.

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Kombinaciju **IO+PARPi** u prvoj liniji liječenja uznapredovalog/rekurentnog **pMMR** (non-dMMR) raka endometrija[1,*]

Kombinaciju **CP+IO** u prvoj liniji liječenja uznapredovalog/rekurentnog **dMMR** raka endometrija[1]

*navedena kao jedna od opcija
CP, karboplatin/paklitaksel; IO, imunoonkološki lijek; PARP, poli (ADP-ribozil)polimeraza; pMMR, adekvatan mehanizam popravka pogrešno sparenih baza; dMMR, nedostatak mehanizma popravka pogrešno sparenih baza.
Referenca: 1. Concin N, et al. Lancet Oncol 2025;26: e423–e435 (including supplementary appendix)

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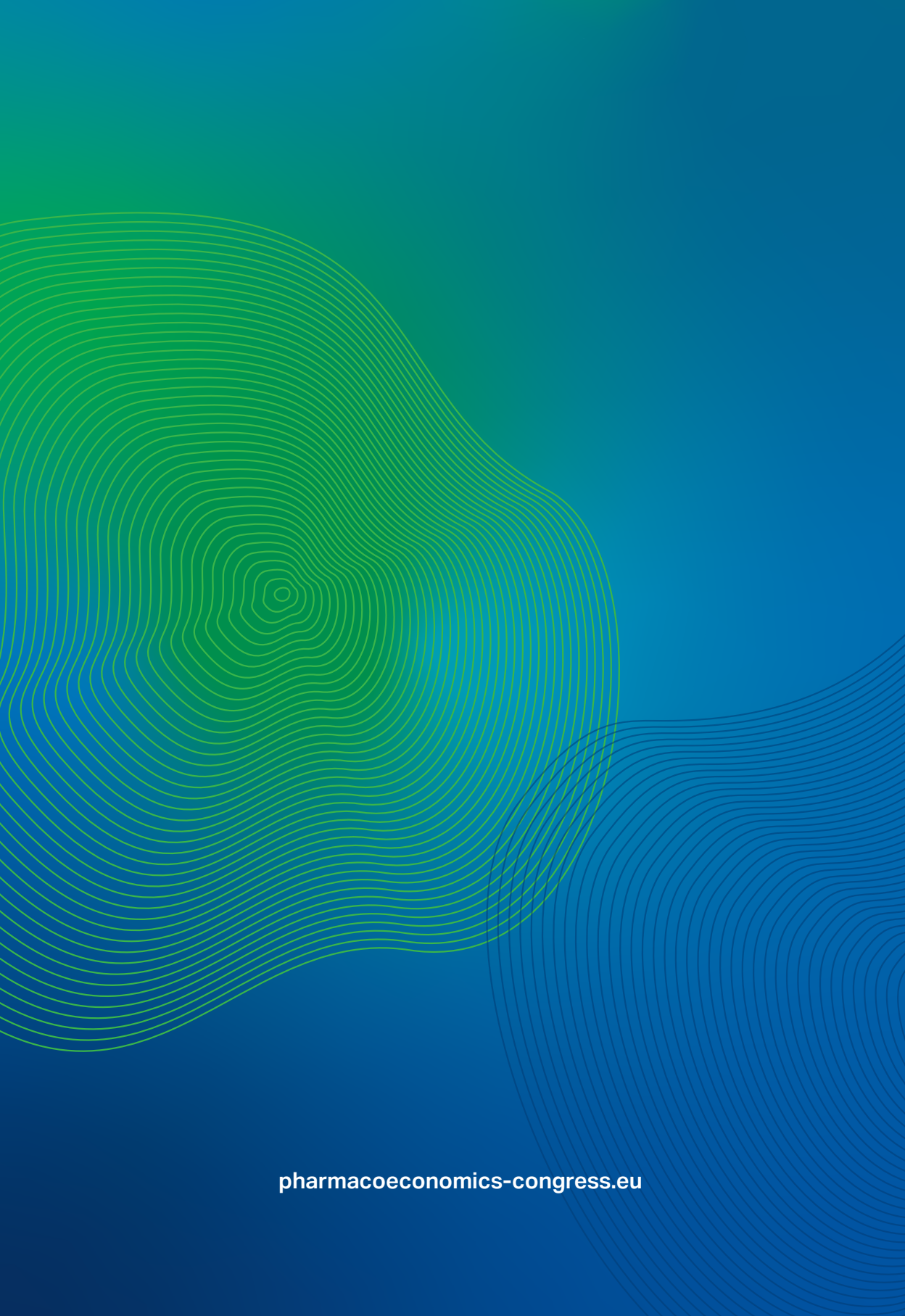
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