UDK 61

ISSN 0031-6857

12. JADRANSKI I 8. HRVATSKI KONGRES FARMAKOEKONOMIKE I ISTRAŽIVANJA ISHODA LIJEČENJA

12TH ADRIATIC AND 8TH CROATIAN CONGRESS OF PHARMACOECONOMICS AND OUTCOMES RESEARCH

pharmaca

GLASILO HRVATSKOG DRUŠTVA ZA
KLINIČKU FARMAKOLOGIJU I TERAPIJU

HRVATSKI ČASOPIS ZA FARMAKOTERAPIJU

Pharmaca 2024; 52 Suppl 1

Zagreb, 2024.

12TH ADRIATIC AND 8TH CROATIAN CONGRESS OF PHARMACOECONOMICS AND OUTCOMES RESEARCH

PHARMACA

Final programme and abstracts from the

12TH ADRIATIC AND 8TH CROATIAN CONGRESS OF PHARMACOECONOMICS AND OUTCOMES RESEARCH

18-20 April 2024 Lovran, Croatia

Guest Editor: Dinko Vitezić

PHARMACA Supplement 1 2024

CONTENT:

EDITORIAL

Every year, Pharmaca publishes one or two special supplements linked to professional meetings or congresses, establishing itself as a vital medium for the exchange and dissemination of information. This aspect of our work brings us on the Editorial Board great satisfaction.

This supplement is dedicated to the 12th Adriatic and 8th Croatian Congress of Pharmacoeconomics and Outcomes Research, scheduled to occur in Lovran from April 18-20, 2024. In keeping with tradition, the congress is organized by the Section for Pharmacoeconomics and Outcomes Research of the Croatian Society for Clinical Pharmacology and Therapy, under the auspices of the Croatian Medical Association, every other year in Croatia, with regional congresses held in alternate years. This year, the congress focuses on facilitating access to medicines in Central and Eastern Europe through principles of value and equity. It seeks to explore solutions to numerous challenges related to patient access and the equitable distribution of innovative treatments in the realm of medicine through its presentations and workshops. Congress sessions offer a prime opportunity for collaborative dialogue among all stakeholders involved in addressing key disease areas - including scientists, practitioners, regulators, pharmaceutical industry representatives, and patients.

On behalf of myself and the Editorial Board, I extend our best wishes to all congress participants and organizers for a successful event characterized by enriching discussions, eminent lectures, and most importantly, rewarding interactions.

Ksenija Makar-Aušperger
Editor-In-Chief

FOREWORD

Dear Colleagues,

It is our great pleasure that we have organised the 12th Adriatic and 8th Croatian Congress of Pharmacoeconomics and Outcomes Research with focus on CEE countries in Lovran, Croatia, from April 18-20, 2024. The Congress is organised by the Section for Pharmacoeconomics and Outcomes Research of the Croatian Society of Clinical Pharmacology and Therapeutics, Croatian Medical Association.
The main objective of this year's congress is to intensify and enhance professional and scientific discussions and collaboration between various stakeholders on the following topic:

"VALUE & EQUITY BASED ACCESS TO MEDICINE IN CEE"

After several years during which we had been focusing to problem identification, assessment, and measurement, mostly around patient access and equity rights to innovation, and identifying the gaps to more developed EU countries, the main goal of past few congresses was to focus on finding solutions. This year's congress will try to achieve the same goal.
During our 14 years' journey, the knowledge, capacity, and experience of CEE countries to identify and implement solutions have improved, both at Academia and Government as well as at Health Technology Industry. Additionally, and most importantly, Patient's capacity to be involved and consulted in this process have also significantly improved, so we believe all pre-requisites have now been met to start focusing on the implementation and monitoring of the optimal solutions across priority disease areas, for which we need all relevant stakeholders to be at the same table and working against the same, Patient Outcomes' focused goals.

In addition to the main congress theme, these are the sub-topics of this Congress:

- Access to Innovation, Value, and Equity in Healthcare Decision Making
- Implementation Readiness for Emerging EU Legislation Changes
- Real World Data and Information Systems
- National Patient Access Policy Challenges
- Alternative Pricing Arrangements as an Opportunity for Broader Access to ATMPs
- Developing and Successfully Implementing Health Technology Management (HTM) Processes Following a Drug Reimbursement Decision.

The full congress agenda have other important topics, such as development of healthcare policies, pharmaceutical pricing and reimbursement, comparative efficacy studies, outcomes research, value of health and health interventions, and many others. As introduction to the Congress, we have two pre-congress workshops, the first is in Collaboration with VITAL and ValueDx: Evidence based policy decisions to tackle infectious disease in lower income European countries and the second is Croatian - Slovenian bilateral workshop under the title Monitoring and reporting on treatment outcomes as a backbone of the value based healthcare aspirations. Two important topics will be discussed in the form of round table discussion i.e. Reform of the EU pharmaceutical legislation and The (r)evolution of HTA in CEE/EU. Other important topics includes hot topics such as oncology, orphan medicinal products, obesity and diabetes, etc.

We are glad that in addition to numerous active participants from abroad, we also have a significant number of active participants from Croatia. The presentations of members of the Croatian Society for Clinical Pharmacology and Therapeutics stand out, as well as the presentations of medical students, which were done with mentors. We are proud that the Society made possible all of them to participate in the congress, and this is also the result of the sponsors who supported the

Congress. We are grateful for their support as unrestricted educational grants.

We have to emphasise that our Congress has established itself as the forum (i) to share research and help advance the science of health economics within the Adriatic and CEE region, (ii) to give opportunity for networking and interacting, and (iii) to get involved in debating controversial and complex issues of the health care involving a range of stakeholders. We are proud that during the past 13 years our annual Congress has become a reference point in the field of Pharmacoeconomics and Outcomes Research in our region.

It is important to note that we, as the organisers, will ensure participation of a wide range of stakeholders within the health care: the health care professionals (local, regional and international), members of academia, different associations, regulatory and payer authorities, politicians, and last but not least the pharmaceutical industry.

This Congress is under the auspices of the Croatian Ministry of Health and Faculty of Medicine of the University of Rijeka. The overarching goal of the Congress organiser is to advance public health care policies to maximise societal welfare and optimise diffusion of and access to innovative health care technologies, so that patients can reach their full life and health potential.

With kind regards,

Prof. Dinko Vitezić, MD, PhD

Congress President

President, Section for Pharmacoeconomics and Outcomes Research, Croatian Society for Clinical Pharmacology and Therapeutics CMA

ORGANISING AND SCIENTIFIC COMMITTEE

Congress President
Dinko Vitezić, Croatia

Congress Secretary General
Slobodanka Bolanča, Croatia

Congress Treasury
Viktorija Erdeljić Turk, Croatia

Congress Organizing Committee
Andrej Belančić, Croatia
Tonći Buble, Croatia
Sandra Knežević, Croatia
Marta Kučan Štiglić, Croatia
Ksenija Makar Aušperger, Croatia
Iva Mikulić, Croatia
Suzana Mimica, Croatia
Jasenka Mršić Pelčić, Croatia
Bertalan Nemeth, Hungary
Natalija Podjaveršek Petković, Slovenia
Janos Pitter, Hungary
Luka Vončina, Croatia

Congress Scientific Committee

Pero Draganić, Croatia
Marcin Czech, Poland
Igor Francetić, Croatia
Jurij Furst, Slovenia
Livio Garattini, Italy
Slobodan Janković, Serbia
Zoltan Kalo, Hungary
Robert Likić, Croatia
Iveta Merćep, Croatia
Guenka Petrova, Bulgaria
Tabassome Simon, France
Svetoslav Tsenov, Bulgaria

CONGRESS ORGANISED BY

Section for Pharmacoeconomics and Outcomes Research, Croatian Society for Clinical
Pharmacology and Therapeutics, Croatian Medical Association

UNDER THE AUSPICES

Ministry of Health of the Republic of Croatia
Faculty of Medicine of the University of Rijeka

PROGRAME

THURSDAY (18th April 2024)

10:00 - 14:00

Pre-Congress Workshop in Collaboration with VITAL and ValueDx: Evidence based policy decisions to tackle infectious disease in lower income European countries

Faculty: Janos Pitter, Maarten Postma

11:30 - 13:30

Pre-Congress Croatian - Slovenian Bilateral Workshop (held in local languages)**:**

Monitoring and reporting on treatment outcomes as a backbone of the value based healthcare aspirations

Faculty: Tonci Buble, Jurij Furst, Tea Strbad, Petra Dosenovic Bonca, Dinko Vitezic

CONGRESS OPENING CEREMONY

14:00 Welcome address by Svetoslav Tsenov, Former Congress Co-Chair

Welcome address by Bertalan Nemeth, on behalf of ISPOR CEE Chapter

Welcome address and formal congress opening by Dinko Vitezic, Congress President

Reform of the EU pharmaceutical legislation - a carrot or a stick?

Chairmen: Dinko Vitezic, Svetoslav Tsenov

14:20 Tomislav Sokol, Croatia: Balancing innovation and affordability: reform of the EU pharmaceutical legislation

14:45 Deyan Denev, Bulgaria: EU pharmaceutical legislation revision: opportunities for innovative therapies

15:10 Marcin Czech, Poland: European pharmaceutical package – implications for central and eastern european health care systems

15:30 Ole Henriksen, Denmark: Implementation readiness for emerging EU legislation change: is there any impact on future patient access to innovation

15:50 Arkadi Sharkov, Bulgaria: GPL in the scope of a political turbulence - the case of Bulgaria

16:10 Livio Garattini, Italy: Pharmaceutical patents and regulatory data protection in Europe: radical reforms?

16:30 Coffee & Connect

17:00 Round table discussion

Reform of the EU pharmaceutical legislation - a carrot or a stick?

Moderator: Slobodanka Bolanca

Panelists: Zoltan Kalo, Arkadi Sharkov, Marcin Czech, Jurij Furst, Ole Henriksen, Herbert Altmann, Livio Garattini, Deyan Denev

17:55 Round table conclusion

Selected topics and trends in health systems and clinical oncology

Chairmen: Slobodan Jankovic, Natalija Podjaversek Petkovic

18:00 Livio Garattini, Italy: Modelling European health systems: a theoretical exercise

18:20 Ksenija Purkovic, Serbia: Partnership for health system sustainability and resilience – building sustainable and resilient health systems

18:40 Peter Harper, UK: Evaluating the lung cancer risk reduction potential of novel tobacco and nicotine containing products - a matter of dose response

19:00 Tea Strbad, Croatia: Very expensive medicines: a challenge for health insurance

19:20 Ivica Belina, Croatia: From testing to targeted treatments alliance (FT3 alliance)

19:45 Welcome & networking reception (hotel reception area)

20:30 Dinner by invitation

FRIDAY (19th April 2024)

Addressing assessment and access issues for orphan medicinal products

Chairmen: Viktorija Erdeljic Turk, Jurij Furst

8:30 Dinko Vitezic, Croatia: Orphan medicinal products: challenges for assessing the value and decision making

8:50 Slobodan Jankovic, Serbia: Cost effectiveness of drugs for rare diseases: an unsolved issue

9:10 Mirjana Bjelos, Croatia: Advancing ophthalmic gene therapy in Croatia: a paradigm of global healthcare innovation

9:30 Svetoslav Tsenov, Bulgaria: Regulatory evolution and support for orphan drugs

9:50 Andrej Belancic, Croatia: Is choosing risdiplam instead of nusinersen in the treatment of type 1 spinal muscular atrophy a cost minimisation opportunity?

10:15 Coffee & Connect

Hot topics in modern medicine - obesity and diabetes

Chairmen: Andrej Belancic, Petra Verzun

10:30 Sanja Klobucar, Croatia: Changing the paradigm of obesity

10:50 Vanesa Benkovic, Croatia: The economic impact of obesity and value of weight loss in Croatia: healthcare resource use associated with obesity related complication and the impact of weight loss on RR.

11:10 Zoltan Kalo, Hungary: Economic value of bariatric surgery in the management of obese type 2 diabetic patients

11:30 Petra Dosenovic Bonca, Slovenia: Direct diabetes-related healthcare expenditures in Slovenia: recent evolution and future projections based on population-level data

11:50 Tarik Catic, Bosnia & Herzegovina: Cost of diabetes in Bosnia and Herzegovina - a cost of illness study

12:15 Lunch break

The (r)evolution of HTA in CEE/EU

Chairmen: Zoltan Kalo, Marcin Czech

13:00 Bertalan Nemeth, Hungary: Transferability considerations for CEE countries on using real-world data and real-world evidence for HTA

13:25 Herbert Altmann, Germany: Evolution of German pricing & reimbursement system and EUHTAR impact

13:50 Slaveyko Djambazov, Bulgaria: From market access to patient impact: maximizing HTA's role in healthcare policy for better outcomes

14:15 Adina Turcu-Stiolica, Romania: Assessing the landscape of health technology assessment in Romania: Preparing for the implementation of the new European HTA regulation

14:35 Said Wani, Oman: HTA implementation roadmap

15:00 Coffee & Connect

15:15 Roisin Adams, Ireland: HTAR: Preparing for a EU HTA system: How ready are we and what do Member States need to do to prepare?

15:40 Matteo Scarabelli, Belgium: A new European access pathway: how the EU JCA can deliver?

16:00 Krisztina Toth, Hungary: The role of patients in (EU)HTA

16:20 Round table discussion

The (r)evolution of HTA in CEE/EU

Moderator: Zoltan Kalo

Panelists: Roisin Adamas, Bertalan Nemeth, Mateo Scarabelli, Slaveyko Djambazov, Krisztina Toth, Dinko Vitezic, Adina Turcu-Stiolica

17:30 Round table: Conclusion

Short podium presentations & networking - selected health economic and policy topics (10')

Chairmen: Robert Likic, Suzana Mimica, Andrej Belancic, Sandra Knezevic

17:45 Slobodan Jankovic, Serbia: Velmanase alfa vs. Bone marrow transplantation in patients with mild to moderate alpha-mannosidosis: comparison of cost utility in Croatia, Serbia and Montenegro

17:55 Elvira Meni Maria Gkrinia, Greece: Orphan medicines for the management of spinal muscular atrophy: pharmacoeconomic evaluations and comments on willingness to pay thresholds

18:05 Sandra Knezevic, Croatia: PGx testing on DPYD variants c.496 and *6 in Croatian oncologic patients – Value for money or not?

18:15 Ivana Cegec, Croatia: Cutting Costs, Not Care: The Case for Subcutaneous HER2 Therapy in Breast Cancer Treatment

18:25 Romano Oguic, Croatia: Cost-effectiveness of prostate cancer (CaP) treatment: Croatian and Central and Eastern European Countries (CEE) perspective

18:35 Suzana Mimica, Croatia: Uptake of biosimilars in oncology in Croatia - national and hospital level

18:45 Hana Kalinic, Croatia: Financial impact of generic therapeutic interchange of abirateron

18:55 Zeljko Jovanovic, Croatia: Patient experiences related to reporting suspected vaccine side effects

19:05 Igor Rubinic, Croatia: The use of large language models in pharmacoeconomics

19:15 Miro Vukovic, Croatia: Assessing the current landscape of health technology assessment knowledge and skills among clinicians in Croatia

Short podium presentations & networking - selected health economic and policy topics (5')

(Healthy pre-dinner refreshments & coffee will be made available to participants during this session)

19:30 Marija Kurtov, Croatia: Cost-effectiveness of using probiotics to enhance checkpoint inhibitor therapy response

19:35 Andro Koren, Croatia: Imatinib and the treatment of CML

19:40 Karolina Majstorovic Barac, Croatia: The cost-effectiveness of vitamin D supplementation in vitamin D deficient population in order to prevent acute respiratory infections

19:45 Lovro Pendic, Croatia: Comparative pharmacoeconomic analysis of eravacycline and colistin in multi-drug resisant infections

19:50 Fran Posavec, Croatia: AI-enhanced detection of adverse drug reactions in multimorbid patients: hypersensitivity pneumonitis case study

19:55 Marin Gobac, Croatia: Standard healthcare versus clinical trial care - overview of benefits through national fund and patients perspective using a model of dyslipidemia

20:00 Melissa Seven, Croatia: A literature review of economic evaluations of rivaroxaban with or without acetylsalicylic acid in stable cardiovascular disease

20:05 Luciana Koren, Croatia: Efficacy of senolytic research in cost control of chronic age-related diseases

20:10 Karlo Petkovic, Croatia: The pharmacoeconomic impact of folate (B9) in enhancing antidepressive activity

20:15 Zdeslav Strika, Croatia: Cost effectivenss and role of AI as a medical assistant

20:20 Art Sefedini, Croatia: Semaglutide versus tirzepatide in the treatment of obesity: a systematic review of economic evaluations

20:30 Congress networking dinner for all registered congress participants

SATURDAY (20th April 2024)

Selected health economic and policy topics

Chairmen: Aleksandar Knezevic, Tea Strbad

8:00 Iveta Mercep, Croatia: Unlocking the cost of mental health: navigating the pharmacoeconomics of psychiatric drugs in Europe

8:15 Jelena Susac, Croatia: Predicting the risk of high healthcare costs for patients with Alzheimer's disease

8:30 Marta Kucan Stiglic, Croatia: Anxiolytics prescribing in Croatia: How to make prescribing patterns more rational

8:45 Zeljko Cabrijan, Croatia: Pharmacoeconomic aspects of treating IBD

9:00 Robert Marcec, Croatia: Impact of biosimilar approval on financial consumption: a simple modelling study estimating cost savings following infliximab biosimilar approval

9:15 Viktorija Erdeljic, Croatia: The cost of dialysis in Croatia: a comprehensive assessment of hemodialysis and periotoneal dialysis costs beyond the payer's perspective

9:30 Dominik Strikic, Croatia: The pharmacist's prescription: a potential cure for Croatia's healthcare overload

9:45 Robert Likic, Croatia: Medical deserts: a growing global concern

10:00 Iva Mikulic, Croatia: Price and potential savings in second-line treatment of patients with active Crohn’s disease and ulcerative colitis in Croatia

10:15 Coffee & Connect

EDUCATIONAL WORKSHOP:

Faculty: Zoltan Kalo

10:30 Principles of transforming the pharmaceutical pricing and reimbursement systems in lower income European countries

Congress Closing and Farewell

13:00 Farewell snacks for workshop participants

Collaborative Associations' Meeting /closed session/

14:30 Feedback from the 12th Adriatic and 8th Croatian Congress on Pharmacoeconomics and Outcomes Research

14:45 Proposal for venue, topics and committees for the 13th Adriatic Congress on Pharmacoeconomics and Outcomes Research

15:15 Collaborative regional research opportunities

ABSTRACTS

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

PRE-CONGRESS WORKSHOP IN COLLABORATION WITH VITAL AND VALUEDX

EVIDENCE BASED POLICY DECISIONS TO TACKLE INFECTIOUS DISEASE IN LOWER INCOME EUROPEAN COUNTRIES

Janos Pitter [1], Maarten Postma [2]

[1] Syreon Research Institute, Budapest, Hungary
[2] University of Groningen, Groningen, Netherlands

In recent years the importance of infectious diseases has been increased especially due to the COVID pandemic and concerns related to antimicrobial resistance. The European Commission has been funding several projects to increase the resilience of European health care systems against infectious diseases. The first part of the workshop provides updates about two European projects funded by the Innovative Medicines Initiative, VITAL (Vaccines and Infectious disease in the Ageing Populations and ValueDx (The value of diagnostics to combat antimicrobial resistance by optimising antibiotic use). The second part of the workshop focuses on a case study of influenza vaccination strategy for elderly patients in Central and Eastern European countries. Barriers to evidence-based health policy decisions on the extension and optimisation of seasonal influenza vaccination programmes include low confidence in locally collected epidemiology data and limited relevance of foreign data due to dissimilar population health status.
Insufficient quality of available data on clinical burden may result in the underuse of health economic evidence in health policy decisions. This workshop will overview the identified barriers related to economic

modelling of optimised seasonal influenza vaccination programmes in lower income European countries, and look for pragmatic solutions and recommendations on how to improve the evidence base of public health policy decisions. Based on the workshop a scientific manuscript on the main conclusions will be prepared.

PRE-CONGRESS WORKSHOP SLOVENIAN BILATERAL WORKSHOP (HELD IN LOCAL LANGUAGES)

MONITORING AND REPORTING ON TREATMENT OUTCOMES AS A BACKBONE OF THE VALUE BASED HEALTHCARE ASPIRATIONS

Tonći Buble[1], Jurij Furst [2], Tea Strbad [3], Petra Došenović Bonča [4], Dinko Vitezić [5, 6]

[1] The Ministry of Health of the Republic of Croatia
[2] The Health Insurance Institute of Slovenia
[3] Croatian Health Insurance Fund, Zagreb, Croatia
[4] School of Economics and Business, University of Ljubljana, Slovenia
[5] University of Rijeka Medical School
[6] University Hospital Centre Rijeka

Value-based healthcare aims to measure health outcomes against the cost of delivering the outcomes. Therefore, tracking and evaluating patient outcomes are the most critical elements of successful value-based health systems. Outcomes have to be measured consistently and comprehensively across all segments of integrated care solutions. The system needs to be supported with appropriate legislative changes to to secure the establishment of the right infrastructure and platforms for capturing and validating patient relevant outcomes. There are multiple benefits that could be successfully achieved by transforming traditional 'service based' healthcare system into value-based healthcare systems, such as: better outcomes for patients, better system efficiency for healthcare providers, better budget planning and stronger cost controls for payers, alignment of prices with meaningful patient outcomes for suppliers and bette+A6r overall health with sustainable healthcare investment.

REFORM OF THE EU PHARMACEUTICAL LEGISLATION - A CARROT OR A STICK?

BALANCING INNOVATION AND AFFORDABILITY: REFORM OF THE EU PHARMACEUTICAL LEGISLATION

Tomislav Sokol [1]

[1] Member of the European Parliament, Brussels, Belgium

The Commission's legislative proposal, adopted on April 26, 2023, marks a significant overhaul of existing pharmaceutical legislation within the EU. This proposal revises and supersedes the current general pharmaceutical regulations (Regulation 726/2004 and Directive 2001/83/EC), as well as regulations pertaining to medicines for children and rare diseases (Regulation 1901/2006 and Regulation 141/2000/EC, respectively). This revision represents the most substantial review of EU pharmaceutical legislation since 2004. Its primary objectives are to stimulate innovation, ensure equitable and timely access to medications, and fortify the security of supply while addressing shortages through targeted measures. Achieving these goals necessitates striking a delicate balance. The reform aims to foster the global competitiveness and innovative capacity of the pharmaceutical sector by incentivizing innovation, prioritizing unmet medical needs, and implementing measures to promote fairness in access and affordability. The reform addresses fundamental challenges. Despite authorization within the EU, medicines often fail to reach patients promptly and evenly across Member States. Critical gaps persist in addressing unmet medical needs, rare diseases, and antimicrobial resistance (AMR). High costs of innovative treatments and medicine shortages remain pressing concerns for patients and healthcare systems alike. Moreover, adapting EU regulations to accommodate digital transformation and emerging

technologies is crucial for maintaining the EU's attractiveness for investment and its leadership in medicine development. In simpler terms, the Directive encompasses all the necessary requisites for authorization, monitoring, labelling, regulatory protection, market placement, and other regulatory procedures for medicines authorized both at the EU and national levels. On the other hand, the Regulation establishes additional specific provisions, particularly for medicines authorized at the EU level, notably innovative treatments such as orphan medicinal products. It delineates rules for the coordinated management of critical shortages and the security of supply for vital medicines. Additionally, it outlines the governance of the European Medicines Agency (EMA) and includes provisions to combat antimicrobial resistance (AMR). The speech will primarily focus on the revised Regulation, since I have been EPP Shadow Rapporteur and I have worked on this legislative proposal for last 9 months.

EU PHARMACEUTICAL LEGISLATION REVISION: OPPORTUNITIES FOR INNOVATIVE THERAPIES

Deyan Denev [1,2], Katja Standke [3]

[1] Co-chair, EFPIA CEE Task Force
[2] CEO, ARPharM Bulgaria
[3] Director, EFPIA Country Liaison

"EU pharmaceutical legislation revision: the opportunities arising for innovative therapies" In April 2023, the European Commission published a proposal for complete revision of the EU pharmaceutical legislation, which was needed considering that this framework was 20-year old and unable to keep pace with the upcoming scientific developments. The genesis of this process dates back to 2016, with the Council conclusions on pharmaceuticals promoted by The Netherlands focusing on access, affordability, availability and competitiveness. But it is with COVID-19 that the world realized the real impact of health on our economy, and the value of innovation, with the first vaccine being approved not even one year after the WHO proclaimed the global pandemic. Europe has been leading in the fight against COVID-19 with over 40% of vaccines being developed in our continent. However, the European medicines approval process is currently one the slowest worldwide, European patients need to wait almost the double than US citizens to see innovative products approved in Europe. The European Medicines Agency uses expedited pathways only in 9% of the cases, the FDA in the US in over 70%. Europe’s research and development base is gradually eroding. At EFPIA we welcomed the package proposed by the Commission last April. Since then, the European Parliament and Health Ministers in the countries are discussing the proposals, but we see it as an opportunity to modernize the regulatory framework and attract innovation in Europe. Some of the Commission proposals are going towards the right direction - streamlining the work of the European Medicines Agency, cutting the approval timelines and

facilitating the use of expedited pathways, regulatory sandboxes, transferable exclusivity vouchers for the development of new antibiotics. Despite these important improvements, there are some concerning elements in the Commission proposal. If adopted, their negative impact will overcome the positive measures just described. In particular this is the reduction of the duration of the regulatory data protection (or orphan market exclusivity) and making the recuperation of the lost years dependent on factors that are outside the control of pharmaceutical industry. EFPIA has provided extensive arguments against these proposals and has tabled alternative solutions. Europe needs to get this revision right as it will regulate the way we authorize, develop and produce medicines in Europe for the next 20 to 30 years. And this matters for patients, for the sustainability of our health systems and for our economies.

EUROPEAN PHARMACEUTICAL PACKAGE – IMPLICATIONS FOR CENTRAL AND EASTERN EUROPEAN HEALTH CARE SYSTEMS

Marcin Czech [1]

[1] Department of Pharmacoeconomics, Institute of Mother and Child, Warsaw, Poland

The European Pharmaceutical Package (EPP) represents a comprehensive framework aimed at harmonizing pharmaceutical regulations across the European Union (EU). This package consists of various directives and regulations designed to streamline processes related to the development, authorization, manufacturing, distribution, and monitoring of pharmaceutical products within the EU member states. While the EPP primarily targets EU countries, including countries from Central Europe, its implications extend beyond the union's borders, particularly to the countries of Central and Eastern Europe (CEE).

For CEE countries, the EPP presents both opportunities and challenges. On one hand, alignment with EU pharmaceutical standards enhances the quality, safety, and efficacy of medicines available in these countries. Accession to the EPP facilitates the adoption of Good Manufacturing Practices (GMP), Good Distribution Practices (GDP), and Good Clinical Practices (GCP), which are essential for ensuring the integrity of pharmaceutical products throughout the supply chain. Moreover, participation in the EU's centralized marketing authorization procedures expedites the approval process for new drugs, potentially accelerating patients' access to innovative treatments.

However, the implementation of EPP regulations can pose significant challenges for CEE countries. Compliance with EU standards often requires substantial investments in infrastructure, technology, and human resources, which may strain the limited resources of these

countries' healthcare systems. Furthermore, stringent regulatory requirements may create barriers for domestic pharmaceutical industries, hindering their competitiveness in the EU market. CEE countries also face difficulties in aligning their healthcare policies and reimbursement systems with EU standards, potentially leading to disparities in access to medicines and healthcare services among EU member states.

Moreover, while the EPP aims to harmonize pharmaceutical regulations across the EU, variations in implementation and interpretation among member states can result in regulatory complexities and inconsistencies, impacting CEE countries' ability to navigate the regulatory landscape effectively.

In conclusion, the European Pharmaceutical Package has profound implications for Eastern and Central European countries, shaping their pharmaceutical landscapes and influencing access to medicines, healthcare policies, and industry competitiveness. As some of these countries strive to align with EU standards, they must navigate the challenges posed by regulatory harmonization while capitalizing on the opportunities for enhancing pharmaceutical quality and market access at affordable prices within their healthcare systems. Collaborative efforts between EU institutions and CEE countries are essential to address these challenges and ensure that the benefits of the EPP are realized equitably across the European pharmaceutical market.

IMPLEMENTATION READINESS FOR EMERGING EU LEGISLATION CHANGE: IS THERE ANY IMPACT ON FUTURE PATIENT ACCESS TO INNOVATION

Ole Henriksen [1]

[1] Nordic Health Care Group, Copenhagen, Capital Region, Denmark

Based on reactions to the recently published European Commission (EC) first draft Implementing Regulation on the Joint Clinical Assessment (JCA) to assess if JCA will have impact on future access to innovation. On 5th March 2024 the first draft Implementing Regulation was published, setting out detailed procedural rules for the JCAs that will apply from 12th January 2025. The regulation established that the JCA process starts on the date of central marketing authorization application, that an EU joint scope of the JCA should be finalized 20 days after CHMP list of questions, that companies should submit the JCA dossier within 90 days of receiving a request and that the endorsed JCA should be available maximum 30 days after marketing authorization by EC. This very speedy process should be viewed in connection to the faster EMA timelines in the revised EU Pharmaceutical regulation of 180 days in the normal procedure and 150 days for accelerated review. The regulation furthermore adopted the German AMNOG dossier template and thereby ensuring that benefit assessment systems like Germany and France can use JCA directly in their existing HTA processes. The Heads of HTA agencies (HAG), comprising 32 agencies in the EEA, commented on the implementation regulation about the time pressures put upon them in the condensed process on JCA. The Swedish HTA agency (TLV) has in its lates annual report flagged up that it has been spending substantial resources on JCA and sees no benefit to its operations. Simulations of the scoping process where national standard of care and guidelines has been

assessed have demonstrated that PICOs will probably be double digit per product putting companies under pressure to deliver data in 90 days.The Joint Clinical Assessments are being implemented from 2025-2030. They have the potential to speed up access to innovative medicines in some parts of the European Economic Area where they apply. They specifically could benefit larger member states already running systems using benefit assessments and small member states not operating HTA systems. In smaller member states with HTA systems, but where few innovative medicines are assessed every year and in member stares having systems based on cost effectiveness, Joint Clinical Assessments could delay access to new innovative medicines.

PHARMACEUTICAL PATENTS IN EUROPE: RADICAL REFORMS?

Livio Garattini [1]

[1] Department of Health Policy, Institute for Pharmacological Research Mario Negri IRCCS, Milan, Italy.

Differently from pharmaceutical regulation, patent regulation is part of commercial law, thus lies outside public legislation. Patents are still national in the EU, so valid only in the countries where the patentee applies for them. Patent claims can be filed through either the domestic patent offices or the European Patent Office (EPO). Once a patent is granted by EPO, the patentee can choose to exploit it in all or a limited basket of countries. Still, in response to the perceived inadequacy of the current market protection period offered by pharmaceutical patents compared to other industries, it is possible to extend the original patent for up to five years through one supplementary protection certificate (SPC). In general, pharmaceutical patents stem from tight collaboration between scientists and attorneys. The main task of attorneys is to convince examiners that the applications fulfill the legal requirements for patentability. Afterwards, another expected result is to extend patent life as long as possible through secondary patents, eventually generating an 'invention cascade'.A radically different European scenario based on three key points can be depicted to (re)establish a more acceptable trade-off between public and private interests. First, the major change should concern the present management of pharmaceutical patents through EPO and the parallel network of domestic offices. EPO is a big organization totally out of control from the public health viewpoint and entirely funded by patent fees, whereas the domestic offices can just play a merely administrative role. It is time to make the EU partly responsible and financially accountable for pharmaceutical patents by introducing a specific agency. The second major issue is the excess of discretion by pharmaceutical companies in

filing patents. Accordingly, primary patents could be restricted to substances with one declared indication, then secondary patents should be granted only to very different therapeutic indications from the first one. The third issue is the shorter duration of market exclusivity on drugs compared to other goods at present. A sound move to re-align such duration could be to guarantee a market exclusivity of 15 years only to compounds that start a clinical trial within 5 years from the granting date. Afterwards, the warranted duration could be progressively reduced reflecting the delay in trialing, i.e. 14 years for drugs starting the first trial during the sixth year after the granting date and so on. At the same time, the SPC tool and the extra regulations on exclusivity should be cancelled.

SELECTED TOPICS AND TRENDS IN HEALTH SYSTEMS AND CLINICAL ONCOLOGY

MODELLING EUROPEAN HEALTH SYSTEMS: A THEORETICAL EXERCISE

Livio Garattini [1]

[1] Department of Health Policy, Institute for Pharmacological Research Mario Negri IRCCS, Milan, Italy.

The health system has always been a highly debated subject in politics, open to ideologies in every nation. Here, we try to put order in the endless debate on health care from the policy point of view. Health economics teaches us that the positive effects induced by competition in free markets cannot be expected in health care by definition, since health is a classic example of market failure from both demand and supply. Once market competition is ruled out, the most reasonable concepts to reference for managing a health system are funding and provision. The most logical criterion to apply for funding a health system is universal coverage through general taxation. Being able to spread the total risks on the whole population, the State is the best insurer to cover the illness risks of its citizens. Health care provision is offered by a mix of public and private bodies in most European countries. While it is pretty obvious to opt for a public health system for funding, the choice between public and private sector for providing health care is less straightforward. Integrated care (IC) is the modern approach that better supports the choice in favour of the public sector for health care provision. In fact, the existence of multiple (public and/or private) providers strongly discourages integration, since any player is obviously orientated to follow its own financial interests in the long run. Therefore,

IC is certainly favoured by a (necessarily public) single employer. If a public NHS should be recommended as a blueprint for any European country, however the experience of the existing NHSs in Europe has undeniably raised the concerns of political influence and administrative bureaucracy as the major issues to tackle. Democracy necessarily entails the potential impact of political governments on health through policies and laws that can be influenced by dominant ideologies. So, alternate governments of opposite parties can inject inconsistent changes in the health systems. Bureaucracy is associated with unnecessary administrative activities, which mainly penalize health professionals who work hard for patients and do not fully respect bureaucratic rules. The negative effects of the most serious motivation-killing threats of public systems on our virtual NHS could be constrained by introducing clear-cut rules of the game. In particular, safeguard clauses to restrict the meddling by politicians on the matter of health policy and the introduction of a national school for mandatorily educating the NHS potential managers should help to constrain the negative influences.

PARTNERSHIP FOR HEALTH SYSTEM SUSTAINABILITY AND RESILIENCE - BUILDING SUSTAINABLE AND RESILIENT HEALTH SYSTEMS

Ksenija Purković [1]

[1] AstraZeneca, Cluster Director Balkans, Belgrade, Serbia

Globally, health systems are struggling with comparable challenges. Issues related to workforce shortages and staff burn out, increased service demand due to ageing and growing populations and increases in non-communicable diseases (NCDs), alongside economic pressures and climate disasters, have overstretched systems in crisis leaving them vulnerable and ill-equipped to respond to future needs. While it is impossible to prevent all issues, maximum efforts should be taken to ensure that health systems are able to continually deliver their services over the long-term, whilst also being able to better prepare for, adapt to, learn, and recover from shocks and accumulated stresses. Innovation in the healthcare sector, its digitization, and implementation of solutions which support disease prevention and early intervention, can all provide opportunities to accelerate progress in transforming health systems and future proof them from the challenges faced. The Partnership for Health System Sustainability and Resilience (PHSSR) is a non-profit, multi-sector, global collaboration with a unified goal of building more sustainable and resilient health systems. To support this goal, the PHSSR is active in over 30 countries, and has published 26 reports to date on its commissioned independent research, providing evidence-based recommendations on health system strengthening.

EVALUATING THE LUNG CANCER RISK REDUCTION POTENTIAL OF NOVEL TOBACCO AND NICOTINE CONTAINING PRODUCTS - A MATTER OF DOSE RESPONSE

Peter Harper [1]

[1] Leaders in Oncology Care, London, UK

Smoking is one of the most important risk factors for lung cancer and therefore, for any smoker, quitting is the best approach. However, many smokers do not quit, even in the face of serious disease. Doctors and public health authorities have begun to examine the role novel tobacco products (NTPs) can play in reducing the negative impact of smoking on health.While the availability of epidemiological data and trends may vary by disease, the impact that these products may have in reducing the incidence of smoking-related cancer will take decades to fully understand. In the absence of long-term disease data, an interim approach is needed to understand the risk reduction potential of these new products relative to cigarettes. For cancer, epidemiology shows us that the lower the exposure to carcinogens, the lower the risk of cancer. Given that both industry and independent studies have confirmed that these NTPs contain fewer toxicants and lower levels of the carcinogens found in cigarette smoke, we need to better understand how this translates to the risk of developing cancer. Because we know that the key mechanisms that drive the development and invasiveness of cancer are: (1) the amount of genetic damage and (2) the level of inflammation, we can qualitatively understand the cancer risk potential of these products relative to cigarettes while the epidemiological data are still being generated.To reduce the risk of smoking-related cancer, the best option is to stop smoking. But for those who don’t we need to look at the data emerging on the risk reduction potential of NTPs. Using data from the HTP recently authorized by the US FDA to illustrate this approach there is a reasonable indication that smokers who don’t quit smoking

would be able to reduce their risk of smoking-related cancers such as lung cancer if they switch to products such as HTPs with a demonstrated lower carcinogen exposure.

DISCLOSURE: Dr Peter Harper provides scientific consulting services to Philip Morris International on the topic of tobacco harm reduction.

VERY EXPENSIVE MEDICINES: A CHALLENGE FOR HEALTH INSURANCE

Tea Strbad [1]

[1] Assistant Director, Croatian Health Insurance Fund, Zagreb, Croatia

The Croatian Health Insurance Fund (CHIF) primary list of medicines contains specific medicines for the treatment of serious and rare diseases. These medicines are fully available to insured persons and fully covered by CHIF specific fund if they are used in accordance with the criteria specified in the list of medicines. The fund for very expensive medicines (VEM) has been in existence since 2005. The VEMs List includes mainly medicines for the treatment of rare diseases and innovative medicines that have a targeted effect and are intended for use in a small number of patients. CHIF monitors the consumption of VEMs, adjusts treatment costs according to indication, and uses other models to keep the increase in costs within the limits of predictable costs. Considering that financial resources are not unlimited, the CHIF have special financial contracts with pharmaceutical companies for an individual medicine.With the aim of providing patients treatment in accordance with professional guidelines and to available funds, a new system is created for more intensive and systematic outcomes monitoring. This system means that during the financial negotiations the CHIF will use a model based on monitoring the outcomes of VEMs which gives the possibility for the return of the cost of ineffective therapy. Outcomes results monitoring is simple in case of curable diseases, such as chronic hepatitis C. If this is not the case the outcomes will, certainly be monitored and compared with the results that we have from clinical trials and real-world evidence data.This process of outcomes monitoring and analysing the effectiveness of the administered medicine is a demanding procedure. Initial data on the patient’s status (clinical status, laboratory and other diagnostic test

results), data on the disease itself and the stage at which the treatment was started are recorded, as well as the course of the disease and findings during treatment, which are used to monitor the effect of a specific medicine at each re-evaluation and the final outcomes results. Further, important outcomes data connected to institutions/hospitals will be collected as well. In conclusion, these outcomes approach is established through the legal framework changes, amendments to the Law on Compulsory Health Insurance, and finally will lead to more rational use of VEMs for the benefit of the patients i.e. will give the financial means to introduce some new therapies.

ADDRESSING ASSESSMENT AND ACCESS ISSUES FOR ORPHAN MEDICINAL PRODUCTS

ORPHAN MEDICINAL PRODUCTS: CHALLENGES FOR ASSESSING THE VALUE AND DECISION MAKING

Dinko Vitezić [1,2,3]

[1] University of Rijeka Medical School
[2] University Hospital Centre Rijeka
[3] COMP member of EMA

In the EU, 6-8 % of the population (27 to 36 million people of the EU) is affected by rare diseases. EU definition for a rare disease is the one that affects less than 5 in 10000 of the general population. European Medicines Agency (EMA) and the EMA's Committee for Orphan Medicinal Products (COMP) are responsible for reviewing applications from sponsors for orphan designation. Orphan medicinal products (OMPs) benefit from the incentives and the result of this approach is that from 2000 to 2023 the COMP discussed 4393 applications with 2890 positive opinions, 1284 applications withdrawn, 39 EC refusals, 2871 EC designations, 244 designated OMPs with the EU marketing authorisations and 50 extensions of indication. After the medicine approval, the next important step for availability and access of orphan drugs to patients is depending to decisions on reimbursement from HTA organisations, and/or national payers (financial possibilities of health insurance). During the process of developing the recommendation HTA will evaluate, besides others, for specific orphan drug, their relative effectiveness (RE) which usually include a clinical assessment i.e. the benefit of the new medicine to comparators already available in the same indication. Because the average price of ODs is several times higher than for non-orphan it is important to set the criteria for assessing the value of new ODs. These criteria need to include

disease-specific factors (i.e. incidence or prevalence, aetiology, pathogenesis, clinical severity etc.), analysis of costs to manufacturer and benefits to patient. A general method for establishing a reasonable price need to include adjusted cost-effectiveness thresholds which includes incremental cost-effectiveness ratio (ICER). This is important for availability and access of ODs to patients (a value-based pricing policy, etc.), because the rising of budget impact of ODs is a challenge for public insurance.

COST EFFECTIVENESS OF DRUGS FOR RARE DISEASES: AN UNSOLVED ISSUE

Slobodan Janković [1], Ivana Stević [2]

[1] University of Kragujevac, Faculty of Medical Science, Kragujevac, Serbia
[2] University of Belgrade, Pharmacy Faculty, Belgrade, Serbia

Due to their exorbitant costs, many medications for rare diseases have incremental cost/effectiveness ratios (ICERs) that are far higher than the acceptable cost/effectiveness threshold for reimbursement, raising concerns about their accessibility. This article's goal was to examine the modifications that need be made to the techniques used to analyze the cost-effectiveness of medications for rare diseases. Methods: To obtain a more accurate estimate of the ICER threshold—a crucial piece of information for decision-makers—this paper presents a narrative assessment of techniques for modifying the cost/effectiveness analysis of medications for uncommon diseases. The findings indicate that various adjustments should be made to the inputs used in cost/effectiveness analyses of medications for rare diseases. These adjustments include adjusting discount rates, eliminating costs unrelated to treatment, precisely estimating utilities, determining the local C/E threshold, and negotiating drug prices until the C/E threshold is not exceeded. Further research of methods for adjusting inputs in pharmaco-economical studies of therapies for rare diseases will help to eliminate many uncertainties and determine the real-world cost/effectiveness of medications for such diseases, which will have a sustainable impact on pricing. In summary, the modifications will allow for the true cost/effectiveness of medicines for rare diseases to be considered, allowing for evidence-based and fully transparent reimbursement choices.

ADVANCING OPHTHALMIC GENE THERAPY IN CROATIA: A PARADIGM OF GLOBAL HEALTHCARE INNOVATION

Mladen Bušić [1,2], Mirjana Bjeloš [1,2], Damir Bosnar [1,2], Borna Šarić [1], Biljana Kuzmanović Elabjer [1,2], Jurica Predović [1,2], Ana Ćurić [1,2], Benedict Rak [1]

[1] University Eye Department, Faculty of Medicine, Josip Juraj Strossmayer University of Osijek, University Hospital “Sveti Duh”, Zagreb, Croatia
[2] Faculty of Dental Medicine and Health Osijek, Josip Juraj Strossmayer University of Osijek, Croatia.

The University Eye Department, University Hospital "Sveti Duh", Zagreb, Croatia (UEDSD) stands as an exemplar of healthcare innovation, with a legacy tracing back to 1804. Recent decade has witnessed UEDSD's ascent as a frontrunner in ophthalmic care, pioneering advancements that redefine eye treatment paradigms. Rooted in a commitment to excellence and armed with cutting-edge technology, UEDSD has established itself as a regional and global leader in ophthalmic gene therapy.The modern era of UEDSD commenced in 2009, marked by visionary initiatives aimed at augmenting patient care and pushing medical boundaries. Notably, UEDSD embarked on a mission to combat amblyopia, the most prevalent, yet preventable, eye disease in children, through innovative screening protocol. This endeavor laid the groundwork for the National Preventive Program of Early Amblyopia Detection in 2015, garnering recognition as the Ministry of Health's Reference Center for Pediatric Ophthalmology and Strabismus. Additionally, UEDSD attained the WHO Collaborating Center designation for Child Eye Care in 2019. Evolving into a multidisciplinary powerhouse, UEDSD boasts expertise in all six eye disease subspecialties, delivering exceptional care aided

by state-of-the-art technology. In 2017, a monumental achievement was realized with the FDA's approval of voretigene neparvovec, the world's inaugural gene therapy for progressive blinding retinopathy – RPE65 inherited retinal dystrophy (IRD). Anticipating EMA approval in 2018, Croatia's Ministry of Health and Croatian Health Insurance Fund recognized the significance of the therapy, positioning the drug as a fully reimbursed, exclusively available for the treatment at the UEDSD, in January 2020. Overcoming logistical hurdles such as specialized storage requirements and intricate surgical protocols, in July 2020 UEDSD swiftly emerged as the sixth national center worldwide to administer voretigene neparvovec, ushering in a new era of personalized medicine. Despite the rarity of RPE65-IRD, with the estimated prevalence of 1:200000 individuals, UEDSD remained resolute in its mission to provide transformative care. The extreme scarce of genetic testing facilities in Croatia prompted the development of pioneering clinical screening protocols, facilitating timely diagnoses and garnering global recognition. Amidst the COVID-19 challenges, UEDSD upheld its commitment to compassionate care and scientific advancement. This groundbreaking treatment was delivered to 32 patients (59 eyes), with a notable representation of 11 Croatian nationals. It has garnered international recognition for several notable accomplishments, including the UEDSD designation as the world's largest cross-border treatment center. Additionally, it has gained acclaim for successfully treating the world's oldest patient and facilitating the simultaneous treatment of four patients in a single day. What sets this achievement apart is not only its profound impact on patient care but also the economic implications. While the drug costs are quite substantial, the treatment procedure itself comes at a remarkably reduced rate in comparison to neighbouring EU centres, showcasing UEDSD's dedication to accessible and affordable healthcare solutions. The surgical team of experts has not only embraced but also advanced the techniques for administering voretigen neparvovec. This thorough dedication to innovation has earned UEDSD the esteemed designation of the Ministry of Health's Reference Centre

for Inherited Retinal Dystrophies in 2022. UEDSD's impact transcends borders, serving as a beacon of healthcare excellence and fostering international collaborations. As the largest cross-border center for ophthalmic gene therapy, UEDSD attracts top talents and accelerates scientific progress, ensuring equitable treatment access worldwide. Croatia's emergence as a regional healthcare innovation hub, propelled by UEDSD's pioneering efforts, catalyzes economic growth and societal advancement.UEDSD's journey epitomizes the transformative potential of ophthalmic gene therapy, heralding improved patient outcomes and advancing scientific frontiers. Guided by visionary leadership and unwavering dedication, UEDSD continues to shape a brighter, healthier future for all through its trailblazing contributions to medical care and science.

IS CHOOSING RISDIPLAM INSTEAD OF NUSINERSEN IN THE TREATMENT OF TYPE 1 SPINAL MUSCULAR ATROPHY A COST-MINIMIZATION OPPORTUNITY?

Andrej Belančić [1,2], Tea Strbad [3], Dinko Vitezić [1,2]

[1] Department of Clinical Pharmacology, Clinical Hospital Centre Rijeka, Croatia
[2] Department of Basic and Clinical Pharmacology with Toxicology, Faculty of Medicine, University of Rijeka, Croatia
[3] Croatian Health Insurance Fund, Zagreb, Croatia

Nowadays, after the discovery of new disease-modifying drugs (DMDs) on top of nusinersen (as a pioneer option with the intrathecal route of administration), especially due to the availability of options with peroral (risdiplam) and intravenous applications (onasemnogene abeparvovec-xioi), patients with spinal muscular atrophy (SMA) can switch treatments due to personal or clinical reasons. Indirect comparisons support risdiplam as a superior alternative to nusinersen in type 1 SMA. In addition, our pioneer RWE study comparing effectiveness and safety of risdiplam versus nusinersen in a "switch cohort" demonstrated its non-inferiority in type 1 SMA (+1.0 in CHOP INTEND in favour of risdiplam; p = 0.067). Under clinical equivalence hypothesis we aimed to develop a Croatian budget impact analysis comparing the costs of risdiplam and nusinersen in the treatment of type 1 SMA. The highest permitted wholesale price of risdiplam (Evrysdi) per 0.75 mg/mL bottle is €5,679.63, while for nusinersen (Spinraza) 12 mg the price is €70,353.83 for a bottle of 5 mL. Taking into account the maximum daily dosage of risdiplam (5 mg), one would need 30.5 times the price of the bottle per year, which accumulates to an annual cost of €173,228.715. Similarly with nusinersen (12 mg per administration), one would need six applications in the first year, and three applications in each following year, which accumulates to annual cost of €422,122.98, and

€211,061.49, respectively. One could overall save €248,894.265 and €400,225.365 per patient, if we apply the Croatian 1 yr. and 5 yr. time horizon models into calculations, respectively. Overall, bearing in mind the total number of patients with type 1 SMA in Croatia as per Croatian Health Insurance Fund database (N=18; up to 2023), one could save up to €4,480,096.77 in one year and €7,204,056.57 in five year period in case of choosing risdiplam instead of nusinersen. To deduce, such pharmacoeconomic projections based on longer-term prospective outcome (re)evaluations for orphan medicines may potentially result in modification of the national health insurance fund's DMD administration criteria and reimbursement guidelines and a shift of the accompanied financial resources.

HOT TOPICS IN MODERN MEDICINE - OBESITY AND DIABETES

CHANGING THE PARADIGM OF OBESITY

Sanja Klobučar [1,2]

[1] Clinical Hospital Centre Rijeka, Department of Endocrinology, Diabetes and Metabolic Diseases
[2] Medical Faculty, University of Rijeka, Croatia

Obesity is a chronic metabolic disease characterized by abnormal and excessive adipose tissue accumulation in the body accompanied by a whole series of complications that reduce not only the quality of life but also the life expectancy. Over the past 40 years, the number of people living with obesity has almost tripled. The epidemic proportions of obesity are confirmed by the current estimates of the World Health Organization claiming that more than 650 million adults worldwide have obesity and almost two billion have overweight. If current trends prevail the majority of the global population will be living with either overweight or obesity by 2035. Worryingly, childhood obesity is rising particularly fast and rates are expected to double within 12 years time unless significant action is taken. The World Obesity Federation predicts that the global economic impact of overweight and obesity will reach $4.32 trillion annually by 2035 representing nearly 3% of global GDP, which is comparable with the impact of COVID-19 in 2020. Obviously, obesity is a global crisis, with profound social, economic, and health implications for individuals and their communities. What these facts highlight is the need for a sense of urgency for the development of comprehensive national obesity action plans around the world to prevent and treat obesity and support people affected by the disease. Although changing the narrative around obesity may not be easy and will take time, only by

recognising obesity as a complex relapsing disease can governments and healthcare services adequately prioritise and fund its effective prevention and treatment and reduce the burden on individuals as well as society.

THE ECONOMIC IMPACT OF OBESITY AND VALUE OF WEIGHT LOSS IN CROATIA: HEALTHCARE RESOURCE USE ASSOCIATED WITH OBESITY RELATED COMPLICATION AND THE IMPACT OF WEIGHT LOSS ON RR

Vanesa Benković [1]

[1] Novo Nordisk Hrvatska, Zagreb, Hrvatska

Croatia holds an unpopular first place as a top European country by obesity (64% vs 54% EU average). Overweight and obesity are associated with a myriad of comorbid diseases which produce health and economic burden to individuals, society and health care systems. Until now there was no local evidence on the economic and clinical burden as well as implications of value of weight loss. A micro-costing, bottom up, payer perspective approach was taken to estimate direct and indirect costs associated with 10 selected obesity related complications (ORCs). The ORCs were selected by literature review, review of local clinical guidelines and validated by local steering committee. To validate costing and resources use data structured for the study, related clinicians were interviewed for each of the complications. We have performed costing according to publicly available tarifs. Overall cost per patient and per ORC was used to populate the VWL using local obesity epidemiology from EHIS project data. The data on RR VWL tool were taken from UK CPRD data model and scaled to Croatian population demographics. Final data including costing per each ORCs, RR changes with the share of weight loss and costing implications were validated again by steering committee. Diabetes T2, heart failure, CKD and dyslipidemia were the costliest ORCs with annual burden from 1434€ to 2191€ / year per patient. Most of the costs were driven by hospitalizations, transplantations, and dialysis. Osteoarthritis, asthma, sleep apnea and hypertension were the least costly ORC from 315€ to 614€ / year. These may be partly explained that part of these is managed at primary care level and also

due to inability to better estimate the whole universe of rehabilitation costs (for osteoarthritis) and the share in all hospitalizations. As for risk reductions there was a significant RR decrease due to weight loss in sleep apnea (48,5%) and DT2 (28.8%) at 10% of weight loss. Further weight loss incurs deeper difference in RR for complications. Overall, 10 year saving potential goes from 776 m€ for 10% weight loss up to 1bn€. This is the first study in the region to simultaneously calculate the costs of ORCs and at the same time estimate RR reduction and implications of weight loss, addressing the gap in evidence needed to frame strategy for tackling obesity epidemic. In context of Croatian Parliamentary resolution on obesity, the results of the study will bring to light actual numbers which will support the making of framework, concrete action plan as well as developing sustainable health policy.

ECONOMIC VALUE OF BARIATRIC SURGERY IN THE MANAGEMENT OF OBESE TYPE 2 DIABETIC PATIENTS

Zoltán Kaló [1,2], Gábor Kovács [1]

[1] Center for Health Technology Assessment, Semmelweis University, Budapest, Hungary
[2] Syreon Research Institute, Budapest, Hungary

The favourable effects of bariatric surgeries on body weight reduction and glucose control have been demonstrated in several studies. The aim of our analysis was to demonstrate the cost-effectiveness of bariatric surgeries in obese patients with type 2 diabetes in Hungary compared to conventional diabetes treatments based on economic modelling of published clinical trial results. We adapted a simulation diabetes model for sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB) procedures to conventional care of diabetes. The results were provided separately for three BMI categories. Both surgery types were dominant to conventional diabetes care, they saved 17 064 to 24 384 Euro public payer expenditures and resulted in improved health outcomes (1.36-1.50 quality-adjusted life years gain [QALY]) in the three BMI categories. Bariatric surgeries extended the life expectancy and the disease-free survival times of all the investigated diabetes complications. All the scenario analyses confirmed the robustness of the base-case analysis, such that bariatric surgeries remained dominant compared to conventional diabetes treatments. The results of this cost-effectiveness analysis highlight the importance of bariatric surgeries as alternatives to conventional diabetes treatments in the obese population. Despite the fact that in a disease area with public health priority bariatric surgeries generate health gain and result in significant savings in health care costs, they are accessible only to a selected wealthy patient group in the private health care sector mainly

because healthcare policy-makers focus innovative pharmaceuticals, such as GLP1 agonists.

COST OF DIABETES IN BOSNIA AND HERZEGOVINA - A COST OF ILLNESS STUDY

Tarik Čatić [1,2], Nikolina Kovač [1], Anna Maria Zaremba [3], Miodrag Bogdanović [4]

[1] Novo Nordisk Pharma doo, Sarajevo, Bosnia and Herzegovina
[2] Sarajevo School of Science and Technology, Sarajevo, Bosnia and Herzegovina
[3] NN Pharma Sp.z.o.o, Warsaw, Poland
[4] Novo Nordisk Pharma doo, Belgrade, Serbia

Diabetes melitus (DM) is pandemic chronic metabolic disease with global prevalence around 8.8%, and from year to year shows a tendency to grow estimating 571 million diagnosed patients worldwide. Prevalence among adults in Bosnia in Herzegovina (B&H) is approximated to be 12,2% meaning 309 thousand affected. The economic burden induced by all types of diabetes and their complications has reached 1.8% of gross domestic product (GDP) globally; in the region of Europe this percentage is slightly lower (1.4%), but varies from country to country, being higher in countries with lower GDP per capita. Study aim was to investigate the economic burden of diabetes in B&H, including the costs of diagnosing and treating diabetes and its complications. The study was designed as a top-down cost-of-illness study, based on prevalence, analyzing direct and indirect costs of DM and complications caused by DM. Both direct and indirect costs were included in the study, while intangible costs were omitted. Direct medical costs comprise emergency department visits, hospital inpatient care, laboratory and other medical tests, medications to treat diabetes and its complications, and physician's office visits. All costs (prices)

were verified with the Central-Eastern Europe (CEE) benchmark. Indirect costs included costs incurred by increased absenteeism, reduced productivity while at work for the employed population, inability to work due to disease-related disability, and lost productive capacity due to premature death. All costs were expressed at annual level. With a current population of 3,2 mil inhabitants and 9.0% prevalence of DM, there are 301.636 patients with diabetes in B&H. Assuming a treatment rate of 84.9%, in total 256.017 patients will generate healthcare costs. About 0.86% of them, or 2.215 DM patients per year, are newly treated, while the rest are receiving continuous care from year to year. Structured data about annual healthcare utilization and costs are shown in Table 1. The costs of medication used for treatment of DM, complications costs , costs of medical devices (glucose measuring instruments, accessories and test stripes) and indirect costs due to productivity loss are shown in the Table 2. Maximum share of total DM management costs have medication and treatment of complications. Detailed distribution of specific cost types is shown in Figure 1. Economic burden data may be used to assess the value of programs and policies implemented to prevent and treat these conditions. Total costs of DM per patient in B&H are within the range of costs in other CEE countries, reflecting significant economic burden, but also determination of healthcare payers in B&H to provide optimal management of DM in congruence with contemporary clinical guidelines.

THE (R)EVOLUTION OF HTA IN CEE/EU

TRANSFERABILITY CONSIDERATIONS FOR CEE COUNTRIES ON USING REAL-WORLD DATA AND REAL-WORLD EVIDENCE FOR HTA

Bertalan Németh [1]

[1] Syreon Research Institute, Budapest, Hungary

Real-world data and real-world evidence (RWE) are becoming more important for healthcare decision making and health technology assessment. In the European Commission funded HTx – Next Generation Health Tehcnology assessment project we aimed to propose solutions to overcome barriers preventing Central and Eastern European (CEE) countries from using RWE generated in Western Europe. To achieve this, following a scoping review and a webinar, the most important barriers were selected through a survey. A workshop was held with CEE experts to discuss proposed solutions. This was further augmented by another workshop discussing the feasibility of the solutions in various scenarios. Based on survey results, we selected the nine most important barriers. Multiple solutions were proposed, for example, the improvement of knowledge on RWD/RWE across various stakeholder groups, the need for a European consensus, and building trust in using RWE. Through collaboration with regional stakeholders, we proposed a list of solutions to overcome barriers on transferring RWE from Western Europe to CEE countries. The aspect of applicability was also strongly considered.

EVOLUTION OF GERMAN PRICING & REIMBURSEMENT SYSTEM AND EU HTAR IMPACT

Herbert Altmann [1]

[1] Herbert Altmann, VP pan-Europe Market Access and Healthcare Consulting at PharmaLex/Cencora, Munich, Germany

“What impact can we expect from the latest AMNOG reforms in Germany and how will this process be impacted by the EU HTA-R?

In 2021, the AMNOG procedure celebrated its tenth anniversary and since implementation in 2011 was getting more and more attention internationally. Where do we stand today, what has been achieved so far and how should the path of clinical benefit assessment in Germany continue? From G-BA perspective the AMNOG system has largely proven its worth, but manufacturers still see room for improvement, particularly as the AMNOG requirements are increasing, which makes the overall process more demanding and bureaucratic. Recently, some important cost containment changes have been made, like applying the negotiated reimbursement prices retroactively from the 7th month (instead of the 13th month) or reducing the threshold for Orphan Drugs to €30mio (instead of €50mio before). German G-BA and IQWiG are very much working on such local system topics, but at the same time have been heavily involved in supporting the structuring of the EU HTA-R and the development of the JCA (Joint Clinical Assessment) and the JSC (Joint Scientific Consultation) processes. In Jan 2025, in less than nine months from now, this new EU HTA-R will be implemented for Oncology products and ATMPs. This regulation will address the challenges posed by individual country-specific clinical assessments, which often result in different conclusions from different country authorities. Its main objective is to establish a more efficient, transparent, and less bureaucratic single approach for health technology assessments, while enhancing equal access to innovative

medicines and technologies for all patients across the EU. At the same time, the economic impact (e.g. Pricing & Reimbursement decisions) will remain within the responsibility of individual member states. The last few years German authorities took a leading role in shaping this new centralized HTA assessment process, which resulted in EUnetHTA21 suggestions, quite similar to the German AMNOG dossier requirements. Recently the European Commission has published the draft of the first implementing act in which majority of the suggested procedure got confirmed. At the same time, it has been announced that other acts will be delayed by three to six months, raising questions about the feasibility of Health Care System stakeholders being ready for January 2025 start date. While there is still quite some uncertainty about how different member states will incorporate this new regulation, G-BA already confirmed, that they are well prepared to implement and drive JCA as well as JSC implementation."

FROM MARKET ACCESS TO PATIENT IMPACT: MAXIMIZING HTA'S ROLE IN HEALTHCARE POLICY FOR BETTER OUTCOMES

Slaveyko Djambazov [1], Georgi Slavchev [1], Adriana Dacheva [1]

[1] HTA Ltd. Sofia, Bulgaria

From Market Access to Patient Impact: Maximizing HTA's Role in Healthcare Policy for Better Outcomes Since 2015, Bulgaria has seen a significant evolution in Health Technology Assessment (HTA), crucial for healthcare technologies' market access—extending beyond medicinal products and devices. This advancement is marked by the synergy between the National Council for Pricing and Reimbursement (NCPR) and the National Health Insurance Fund (NHIF). The period witnessed a surge in scholarly outputs, the inception of numerous training programs, and the launch of a master's program in HTA at the Medical University in Sofia. HTA's adoption transcended the facilitation of market access for medicinal products, leading to the reimbursement of novel treatments for newly listed diagnoses by the NHIF. Starting in 2020, medical devices underwent HTA assessments at the NHIF, which transitioned to the NCPR by 2024. There's a growing trend in conducting HTA analyses from a societal perspective, increasingly engaging decision-makers. Implementing the Cancer Beating Plan, HTA supported the initiation of screening programs for major cancers – colorectal, breast and cervical. Notably, a pay-for-performance (P4P) pilot in diabetes management was completed early in 2024, highlighting HTA's pivotal role in improving healthcare outcomes and resource allocation efficiency. Future strategies include the introduction of bundle payment programs for orthopedic arthritis – hip and knee replacement, advancing value-based purchasing of medical devices, enhancing outcome measurements – clinical and patient-related, and bolstering patient participation. These efforts aim to embed HTA more deeply in healthcare decisions, aligning payments with value and patient outcomes. Bulgaria's experience identifies critical success factors for

HTA: increased health technology funding, active industry stakeholder participation, and broad implementation strategies. However, challenges like potential implementation failures and an overreliance on short-term financial indicators persist. Bulgaria's HTA journey underscores the importance of a comprehensive approach to decision science, incorporating economic, clinical, and societal outcomes. This narrative offers valuable lessons for other countries aiming to optimize their healthcare systems through strategic HTA application.

ASSESSING THE LANDSCAPE OF HEALTH TECHNOLOGY ASSESSMENT IN ROMANIA: PREPARING FOR THE IMPLEMENTATION OF THE NEW EUROPEAN HTA REGULATION

Adina Turcu-Stiolica [1], Iulia-Alexandra[1] Paliu, Marina-Daniela Dimulescu [1], Mihaela-Simona Naidin [1]

[1] University of Medicine and Pharmacy of Craiova, Romania

Romania has established its own Health Technology Assessment (HTA) system since 2014. However, this system is predicated on a scorecard approach, utilizing a classification that does not incorporate local data but instead relies on predefined models derived from clinical and economic considerations in other countries, namely France, Germany, and the United Kingdom. Nevertheless, this framework is subject to certain limitations, notably its dependence on a scorecard system predominantly sourced from models established abroad, which often overlook Romania's unique local data and contextual factors. Our objective was to evaluate the number of HTA dossiers submitted between 2019 and 2021, specifically focusing on orphan drugs or biologics. To achieve this, we conducted a systematic review of HTA reports available on the website of the Romanian National Agency of Medicines and Medical Devices for each month spanning the aforementioned period. A concise summary of the assessed technologies reveals consistent evaluation numbers: 103 in 2019, 106 in 2020, and 141 in 2021. The evaluations encompassed various innovative healthcare technologies benefiting Romanian patients, with an increasing focus on biologic drugs: from 4 (3.9%) in 2019, to 20 (18.9%) in 2020, and 34 (24.1%) in 2021. Conversely, evaluations of orphan drugs showed a declining trend: from 34 (33%) in 2019, to 27 (25.5%) in 2020, and 22 (15.6%) in 2021. Notably, the number of orphan medicines in Europe rose from 95 in 2017 to 133 by 2021 (Orphanet, 2021). Our study underscores variability in access to reimbursed orphan drugs over the three years: positive reimbursement approval rates were 58.8% in 2019, 63% in 2020, and 45.5% in 2021,

while conditional reimbursement rates were 35.3% in 2019, 33.3% in 2020, and 54.5% in 2021. Reimbursement decisions for pharmaceuticals in Romania have been demonstrated to adhere to transparency standards as outlined in Romanian HTA legislation, but the HTA landscape in Romania stands at the brink of significant transformation with the forthcoming enactment of the new European HTA regulation. This regulation is anticipated to introduce standardized procedures and methodologies for conducting HTA across European Union member states, including Romania. The harmonization with European standards is poised to present numerous challenges, necessitating capacity building, resource allocation, and adaptation to novel methodologies and requirements. Nevertheless, the anticipated implementation of the new European HTA regulation represents a pivotal opportunity for Romania to enhance and refine healthcare decision-making processes within the country.

HTA IMPLEMENTATION ROADMAP: IMPLEMENTATION OF HEALTH TECHNOLOGY ASSESSMENT IN DEVELOPING COUNTRIES WITH RELATIVELY SMALL MARKET POTENTIAL: THE CASE OF OMAN

Said Wani [1,2], Zoltán Kaló [1,3]

[1] Center for Health Technology Assessment, Semmelweis University, Budapest, Hungary
[2] Ministry of Health, Muscat, Sultanate of Oman
[3] Syreon Research Institute, Budapest, Hungary

Health technologies are advancing rapidly and becoming more expensive, posing a challenge for financing healthcare systems. This is especially true for countries with limited population size, as pharmaceutical companies offer less discount to health care payers with less market potential. Health technology assessment (HTA) improves the efficiency of resource allocation by facilitating evidence-informed decisions on the value of health technologies and increases the negotiation power of health care payers. The presentation summarizes steps made in Sultanate of Oman to implement HTA.

THE PAST: The first step of HTA implementation started in Oman with capacity building activities 10 years ago, with special focus on tailor-made short course by international HTA experts. Initial plans for integration of HTA to health policy decisions were made by the Ministry of Health with the support of WHO regional office before 2020, however, the COVID-19 pandemic and the related economic recession slowed down the process. In 2022 the HTA implementation has been revitalized with structured health economic training program for key stakeholder groups. In 2023 a detailed HTA roadmap with an action plan to reach objectives in the short- and long-term was published by the Ministry of Health. In March 2024 HTA methodological guidelines

were prepared with special focus on decision thresholds for economic evaluation.

THE FUTURE: In the next period pilot HTA projects for special technologies in public health priority areas will be implemented. In 2025 legal and regulatory framework for HTA will be prepared, and different scenarios for HTA institutionalization will be concluded. The technology appraisal process will be supported by a transparent critical appraisal checklist.

Based on the Omani experiences, integration of HTA to health policy decisions can be accelerated by strong political commitment and central coordination. Capacity building, development of local HTA methodologies, instutionalisation of HTA and pilot HTA projects should be parallelly implemented.

HTAR: PREPARING FOR A EU HTA SYSTEM: HOW READY ARE WE AND WHAT DO MEMBER STATES NEED TO DO TO PREPARE?

Roisin Adams [1]

[1] National Centre for Pharmacoeconomics, Old Stone Building, Trinity Centre for Health Sciences, St. James's Hospital, Dublin, Ireland

The EU Regulation on Health Technology Assessment (EU) 2021/2282 entered into force in January 2022 and will be applied in January 2025. It sets up a legal framework for strengthened EU cooperation on health technology assessment (HTA). The aim is to improve access for EU patients to innovative technologies in the area of health such as medicines and medical devices. The HTA regulation also aims to reduce the duplication of efforts for national HTA authorities and industry and to increase business predictability and the long-term sustainability of EU HTA cooperation. The EU Member State HTA Coordination group (HTACG) will oversee the joint technical work carried out by its subgroups. The four subgroups: Joint Clinical Assessments, Joint Scientific Consultations, Methodology and Emerging Health Technologies are well established. The Stakeholder Network (SN) has also been convened and includes patient organisations, healthcare professional organisations, clinical and learned societies, as well as health technology developers and payers. The SN has met a number of times with the HTACG and Subgroup Chairs. The HTACG published the first of its scientific methodological guidelines in April 2024. The European Commission has published the first draft of one of six implementing acts. These implementing acts will provide procedural rules for joint clinical assessments and joint scientific consultations, as well as rules for the selection and consultation of experts and stakeholders, and rules on conflict of interest and confidentiality. This session will discuss how Member State HTA bodies

can take part in EU HTA under the regulation, what they can expect from a EU HTA system and how they might develop local infrastructure to most efficiently use the outputs of the HTA Regulation.

SHORT PODIUM PRESENTATIONS & NETWORKING - SELECTED HEALTH ECONOMIC AND POLICY TOPICS

VELMANASE ALFA VS. BONE MARROW TRANSPLANTATION IN PATIENTS WITH MILD TO MODERATE ALPHA-MANNOSIDOSIS: COMPARISON OF COST/UTILITY IN CROATIA, SERBIA AND MONTENEGRO

Slobodan M. Janković [1], Ana Antanasković [1], Ivana Stević [2], Dragana Lakić [2]

[1] University of Kragujevac, Faculty of Medical Sciences, Kragujevac, Serbia
[2] University of Belgrade, Faculty of Pharmacy, Belgrade, Serbia

In persons with deficit of alpha mannosidase oligosaccharides mount in lysosomes, which enlarge and compromise cell functioning, leading to premature apoptosis. Both neural and extraneural symptoms and signs appear, composing the clinical picture of alpha-mannosidosis. This complex disease could be treated by enzyme replacement therapy (ERT) with velmanase alfa or bone marrow transplantation (BMT). The aim of our study was to compare cost-utility of velmanase alfa vs. BMT treatment of mild to moderate alpha mannosidosis in three neighboring countries: Croatia, Serbia and Montenegro. Methods. For estimation of velmanase alfa vs. BMT cost/utility the Discrete-Event Simulation (DES) model was used. The lifetime horizon and the perspective of health insurance funds of the included countries were used. The model was simulated by cohort Monte Carlo simulation. Robustness of the results was tested by one-way and probabilistic sensitivity analyses. In all three investigated countries velmanase alfa was not cost/effective treatment option compared with the BMT. The velmanase alfa was less effective (ΔE = - 0.86, - 0.85 and – 0.87 quality adjusted life years in Croatia,

Montenegro and Serbia, respectively) and more costly than BMT (ΔT = 3,041,000 euro, 3,048,000 euro and 3,068,000 euro in Croatia, Montenegro and Serbia, respectively). Inferior effectiveness of velmanase alfa compared to the BMT could be explained by its weak penetration through bloodbrain barrier and progression of neurological deficit despite enzyme replacement therapy. On the other hand, the BMT is cost/effective compared to symptomatic therapy of alpha mannosidosis in all three countries investigated. Due to extremely high prices of enzyme replacement therapy, which many times surmount possible savings of healthcare services due to clinical improvement, the cost/effectiveness ratio of velmanase alfa vs. BMT is similar in Croatia, Montenegro and Serbia. In all three investigated countries the BMT is the most cost/effective treatment of mild to moderate alpha mannosidosis.

ORPHAN MEDICINES FOR THE MANAGEMENT OF SPINAL MUSCULAR ATROPHY: PHARMACOECONOMIC EVALUATIONS AND COMMENTS ON WILLINGNESS TO PAY THRESHOLDS

Andrej Belančić [1,2], Andrea Katrin Faour [3], Elvira Meni Maria Gkrinia [4], Dinko Vitezić [1,2]

[1] Department of Clinical Pharmacology, Clinical Hospital Centre Rijeka, Rijeka, Croatia
[2] Department of Basic and Clinical Pharmacology with Toxicology, University of Rijeka, Faculty of Medicine, Rijeka, Croatia
[3] Vancouver Coastal Health, Vancouver, Canada
[4] Independent Researcher, Athens, Greece

Gene deletions or mutations affecting the survival motor neuron (SMN1) gene cause spinal muscular atrophy (SMA), a rare, inherited autosomal recessive progressive disease of a varying phenotype. Currently, there are three orphan medicines (intrathecal antisense oligonucleotide – nusinersen, intravenous gene replacement therapy – onasemnogene abeparvovec-xioi, and peroral small-molecule splicing modifier – risdiplam) registered for the treatment of SMA. We have conducted a systematic literature review (as per PRISMA guidelines) on the pharmacoeconomic evaluations of all currently registered disease-modifying therapies to inform policy and highlight research gaps. Studies written in English, cost-effectiveness analyses (CEAs) and cost-utility analyses (CUAs) on orphan medicines registered for the treatment of SMA and comparisons of those regimens against each other, as well as best supportive care / standard of care, were considered for inclusion. The literature search yielded 1,364 records in total, of which, 900 were duplicates and excluded. Finally, 14 studies were included in this systematic review, with a total of eight CEAs and six CUAs. Besides providing incremental cost-effectiveness ratios (ICERs) for different SMA regimens and strategies, this study confirms

that pharmacoeconomic analyses should also be performed in cases when the cost of treatment is very high and the ICER values exceed the usual, acceptable values for standard therapy. Specific willingness to pay thresholds for orphan medicines are of the utmost importance, to allow patients with SMA to have access to safe and effective treatments. The present topic is important since with such economic evaluations, we get the possibility to compare the value of medications in the same indication; however, we should emphasise that in the interpretation of data and in making decisions about the use of medicines, the impact of new knowledge should be considered.

PGX TESTING ON DPYD VARIANTS C.496 AND *6 IN CROATIAN ONCOLOGIC PATIENTS – VALUE FOR MONEY OR NOT?

Sandra Knežević [1], Andrej Belančić [1,2], Tamara Janković [1], Jelena Rajič Bumber [1], Silvestar Mežnarić [1], Elitza Markova-Car [1], Jasenka Mršić-Pelčić [1], Dinko Vitezić [1,2]

[1] Department of Basic and Clinical Pharmacology and Toxicology, University of Rijeka, Faculty of Medicine, Rijeka, Croatia
[2] Department of Clinical Pharmacology, Clinical Hospital Centre Rijeka, Croatia.

Oncologic patients with dihydropyrimidine dehydrogenase (DPD) deficiency face an elevated risk of experiencing severe fluoropyrimidine (FP) related adverse events (AE). Approximately 4-7% of individuals exhibit pathogenic gene variations. Current guidelines recommend adjusting FP dosage based on genotype predicted DPD activity, considering four DPYD variants (DPYD*2A, c.2846A>T, DPYD*13 and c.1236G>A). We aimed to investigate if adding PGx testing for two additional variants - c.496A>G (rs2297595) and *6 c.2194G>A (rs1801160), could be useful in FP-related adverse events prediction/prevention, and finally is it value for money. We collected all pharmacogenetic testing (PGx) results performed at the Pharmacogenetic lab of the University of Rijeka, Faculty of Medicine, in the period from September 2023 till February 2024. The dose of FP was modified according to umbrella PGx recommendations, as per DPYD activity score, if DPYD*2A, c.2846A>T, DPYD*13 and c.1236G>A were identified. Patients in whom c.496A>G (rs2297595) and *6 c.2194G>A (rs1801160) were identified, were strictly prospectively followed in terms of effectiveness and safety outcomes, since those are still variants of “unknown clinical significance”. In the estimated period, a total of 116 patients (69% male) were tested for DPD deficiency in six gene variants. Overall, 30,2% (n=35) had one or more gene variations. The

prevalence of the variants of still “unknown clinical significance” were as follows: 19% for c.496A>G (4 homozygote – HoZ, and 18 heterozygotes – Hez), and 9.5% for *6 c.2194G>A (1 – HoZ, 10 – HeZ); which is 1,9 and 2,1 times higher than in general European population according to the current body of literature. Bearing in mind the gained clinical experience on effectiveness and safety outcomes in c.496A>G (rs2297595) and *6 c.2194G>A (rs1801160) carriers, a value for money will be thoroughly discussed. Further follow-up of c.496A>G (rs2297595) and *6 c.2194G>A (rs1801160) carriers is of high importance to assess the cost-effectiveness of PGx testing for these two additional variants. The obtained results may potentially improve the quality of life of oncologic patients receiving FP based protocols and lay the basis for the reassessment of PGx DPYD guidelines.

CUTTING COSTS, NOT CARE: THE CASE FOR SUBCUTANEOUS HER2 THERAPY IN BREAST CANCER TREATMENT

Ivana Čegec [1], Viktorija Erdeljić Turk [1], Iveta Merćep [1,2]

[1] University Hospital Centre Zagreb, Department of Internal Medicine, Unit of Clinical Pharmacology, Zagreb, Croatia

In the treatment of early breast cancer, the combination of pertuzumab and trastuzumab with chemotherapy is recommended in two scenarios: as a neoadjuvant treatment for adult patients with HER2-positive, locally advanced, inflammatory, or early-stage breast cancer at a high risk of recurrence, and as adjuvant therapy for adults with HER2-positive early breast cancer, also at high risk of recurrence. Pertuzumab and trastuzumab, both recombinant humanized IgG1 monoclonal antibodies, specifically target the human epidermal growth factor receptor 2 (HER2). In the neoadjuvant setting, patients initially undergo six cycles of these monoclonal antibodies (beginning with a loading dose) in conjunction with chemotherapy, followed by surgery. If a complete pathological response is observed, an additional twelve cycles are administered. Traditionally, pertuzumab and trastuzumab have been administered through separate intravenous infusions during daily hospital visits, each lasting 30 minutes. However, since 2020, a combined subcutaneous administration of pertuzumab and trastuzumab has been approved, simplifying the treatment process. This subcutaneous formulation is also administered during regular hospital visits. Our aim was to compare the costs of the subcutaneous form of administration with the intravenous form of the drugs. We analyzed the costs of 18 cycles of intravenous administration of pertuzumab and trastuzumab against the subcutaneous injection of the same drug combination in neoadjuvant treatment, using drug prices from the Croatian Agency for Medicines and Medicinal Product's website, which regularly publishes lists of medicinal products with their maximum

allowed wholesale prices. A limitation of our study is that the prices may not reflect the actual prices negotiated between the manufacturer and the Croatian Health Insurance Fund. Considering that the price of one cycle of intravenous administration of pertuzumab plus trastuzumab is €3,808.20 (with a loading dose of €6,597.02), and the price of a cycle for subcutaneous administration is €3,682.78 (with a loading dose of €6,595.61), the total cost for 18 cycles amounts to €71,336.42 and €69,202.87, respectively. This represents a saving of €2,133.55 per patient. Based on data from the Croatian Institute for Public Health, in 2021, 2,928 women were diagnosed with breast cancer, and literature suggests that 20% of these cases are expected to be HER2-positive, equating to approximately 585 patients. Local experts estimate that almost all patients with early HER2-positive breast cancer undergo neoadjuvant therapy. Considering the price difference of €2,133.55 per patient, the total savings would amount to €1,249,406.88 for this clinical indication. In the treatment of early HER2-positive breast cancer, the combination of pertuzumab and trastuzumab for subcutaneous administration offers significant economic benefits, is easier to use, and saves more time for both patients and medical staff compared to the intravenous method. Our analysis focused solely on direct medical costs. If we had included the labor costs of medical staff, the projected savings could be even more substantial.

COST-EFFECTIVENESS OF PROSTATE CANCER (CAP) TREATMENT: CROATIAN AND CENTRAL AND EASTERN EUROPEAN COUNTRIES (CEE) PERSPECTIVE

Romano Oguić [1], Dag Zahirović [2], Dean Markić [1], Gordana Đorđevic [3], Josip Španjol [1], Antun Gršković [1]

[1] Department of Urology, Clinical Hospital Centre Rijeka, Croatia
[2] Cinical Institute of Oncology and Radiotherapy, Clinical Hospital Centre Rijeka, Croatia
[3] Department of Pathology and Radiotherapy, Clinical Hospital Centre Rijeka, Croatia

Standard procedure in treatment of metastatic hormone-sensitive prostate cancer (mHSPC) is androgen deprivation therapy (ADT) and abiraterone (ARATs), using apalutamide and enzalutamide, adding docetaxel chemotherapy + abiraterone (ARATs), including docetaxel + ADT (DAT), abiraterone acetate + prednisone + ADT (AAP), apalutamide + ADT (AAT), enzalutamide + ADT (ET), darolutamide + docetaxel + ADT (DAD), and AAP + ADT + docetaxel (AAD). Various treatments for metastatic castration-resistance prostate cancer (mCRPC) are including chemotherapy, endocrine therapy, immunotherapy and bone-targeting therapy. Survival benefits have been shown by adding docetaxel or recent androgen receptor axis-targeted therapies (ARATs) abiraterone, apalutamide, or enzalutamide to androgen deprivation therapy (ADT).. ADT+apalutamide and ADT+enzalutamide incurred higher costs and lower QALYs compared to ADT+abiraterone. Cost effectiveness among treatment options for HRPC using is a Markov model with three treatment: external-beam radiotherapy (EBRT)- 23 fractions by low-dose-rate (LDR), brachytherapy boost (ICER,19,47 €) and radical prostatectomy (RP) alone. In our Clinical Hospital Center, we treated 740 patients with high-

risk prostate cancer (HRPC) in the last 5 years (2019-2023), an average of 14-170 new cases per year, age 44-88 years. Radical prostatectomy (RP) was performed in 400 patients with prostate cancer (CaP), an average of 80 per year, radiotherapy EBRT 76Gy/38 fractions with the use of LHRH agonists in 100 patients per year, mostly non-operated, and approx. 40-45 "salvage" radiotherapy after radical prostatectomy. We use fractionated radiotherapy and we do not have available brachytherapy (cost 58,22 €.). The cost in our country is similar cost-effective strategy (ICER,19,47 € per QALY gained) to the available treatment strategies studied in the CEE. For (mHSPC) we also use the standard therapy of ADT+(ARATs), apalutamide and enzalutamide, chemotherapy with docetaxel and in combination with (ARATs), endocrine therapy. When mHSPC disease is of large volume (visceral and multiple bone grafts, a large number of lymph nodes) combinations of abiraterone acetate + prednisone + ADT (AAP), docetaxel and ADT (DAT), and darolutamide, docetaxel and ADT (DAD), are today the standard treatment considering all other clinical factors influencing the choice of therapy according to treatment guidelines. Many studies refer the financial burden and greater efficacy of using the combination of abiraterone+ prednisone+ ADT (AAP), versus docetaxel chemotherapy and this is standard practice today. Combination abiraterone acetate+prednisone+ androgen deprivation therapy (AAP) is a optimal first-line treatment for metastatic hormone-sensitive prostate cancer. Use of apalutamide and enzalutamide have a far better side effect profile than abiraterone and are equally or more effective than abiraterone acetate. Certainly, the combination of new drugs with ADT gives better efficiency than docetaxel, which is a form of cytotoxic chemotherapy, but the financial impact of new drugs (abiraterone, enzalutamide and apalutamide) is dramatically higher than docetaxel. In advanced mHSPC disease combinations of abirateron, docetaxel and ADT and darolutamide, docetaxel and ADT (DAT) is recommended according to treatment guidelines.

UPTAKE OF BIOSIMILARS IN ONCOLOGY IN CROATIA - NATIONAL AND HOSPITAL LEVEL

Suzana Mimica [1,2]

[1] University Hospital Centre Osijek, Croatia
[2] Faculty of Medicine University of Osijek, Croatia

Infliximab was the first approved biosimilar monoclonal antibody in the European Union (EU) in 2013 and the consequent uptake of infliximab and other anti-TNFα biosimilars has been heterogeneous throughout EU. As reassuring data on biosimilar efficacy and safety have emerged, the uptake of biosimilars in Oncology in the EU has been much faster. One year after its launch in July 2020, bevacizumab uptake rate in the EU reached approximately 70%. Biosimilars in Oncology now represent on average 75% of market share in the EU, in comparison to accessible and referenced market. The aim of this analysis was to evaluate the volume share of biosimilars of bevacizumab and trastuzumab in comparison to the referenced medicines in University Hospital Centre (UHC) Osijek and in Croatia, in the period from 1.1.2019. until 31.12.2023. Methods: For trastuzumab, the referenced market represents both intravenous and subcutaneous form of the referenced product. Data on volume of units and value were obtained from the hospital pharmacy at the UHC Osijek and IMS data for Croatia were used. Kadcyla (trastuzumab emtansine), Enhertu (trastuzumab deruxtecan), Perjeta (pertuzumab) and Phesgo (pertuzumab / trastuzumab) are considered a non-accessible market. The volume share of bevacizumab biosimilars in Croatia in comparison to the referenced biological was 0.85% in 2020, 27.35% in 2021, 69.98% in 2022 and 86.84% in 2023. The volume share of bevacizumab biosimilars at the same time in UHC Osijek was 0.1% in 2020, 13.8% in 2021, 67.6% in 2022 and 82.9% in 2023. The volume share of trastuzumab biosimilars in Croatia in comparison to the

referenced biological was 7.37% in 2019, 27.30% in 2020, 42.64% in 2021, 71.15% in 2022 and 74.37% in 2023. The volume share of trastuzumab biosimilars in UHC Osijek was 32,68% in 2019, 33,05% in 2020, 29,8% in 2021, 77,38 in 2022 and 93,1% in 2023. As compared to the prices per unit of the referenced bevacizumab in 2019, the current available price of cheapest biosimilar represents 32.4% of that price, while the current price of the referenced product is 46.2% of its previous price in 2019. The current price of subcutaneous trastuzumab represents 39.38% of the price in 2019, while the cheapest trastuzumab biosimilar and current price of the referenced IV product represent 35,95% and 37,7% of the initial price of the IV referenced product in 2019, respectively. For UHC Osijek only, estimated cost savings for bevacizumab from 2020. until end 2023 reached around 5 million euros and for Croatia around 40 million euros. Estimated cost savings for trastuzumab from 2019 until end 2023 in UHC Osijek are approximately 2 million euros. The uptake of trastuzumab and bevacizumab biosimilars in comparison to the referenced market is currently very high, both in UHC Osijek and in Croatia. The process of acceptance of those biosimilars was slower as compared to other European countries. Arrival of biosimilars enabled the price of the referenced products to drop by more than 50%, while the current price of biosimilars is approximately one third of the initial price of the referenced products. This enabled significant savings for the health system, both at the local and national level.

FINANCIAL IMPACT OF GENERIC THERAPEUTIC INTERCHANGE OF ABIRATERONE

Hana Kalinić Grgorinić [1]

[1] Pula General Hospital, Pula, Croatia

Therapeutic interchange to lower- cost generic product offers significant cost savings to payers and patients while maintaining equivalent drug effectiveness. In January 2023 was introduced The list of interchangable drugs by Agency for Medicinal Products and Medical Devices of Croatia. In September 2023 the List was updated and abirateron was included. Our institution recognized the significance of the matter and used the opportunity to reduce the cost. Thus, since October 2023 we started to use generic abirateron for all patients, instead of expensive original drug. Our data were collected by retrospective analysis using the hospital database for patients treated with abirateron from September 2023 till February 2024. There were 11 patients. Before the intervention, in September 2023, the number of patients treated with generic abirateron was 2, and the number of patients treated with original drug was 9. One month therapy cost for one patient with generic abirateron was 171,47 EUR, and with original drug 1.904,49 EUR. In October 2023 we switched all 11 patients on generic variant of abirateron. Thus, our monthly cost for all those patients was 1.886,17 EUR. The difference in the actual cost vs estimated cost led to a savings of 15.597,18 EUR for a month, and 77.985,9 EUR for 5 months (October 2023- February 2024). Therapeutic interchange of original abirateron with generic abirateron generated significant savings. Continued extension of the List of interchangable drugs created by Agency for Medicinal Products and Medical Devices of Croatia could generate significant cost savings, with maintaining equivalent drug effectivness.

PATIENT EXPERIENCES RELATED TO REPORTING SUSPECTED VACCINE SIDE EFFECTS

Sara Karmel[1], Željko Jovanović [2]

[1] Community Health Centre of the Primorje-Gorski Kotar County, Croatia
[2] Faculty of Health Studies, University of Rijeka, Croatia

Reporting suspected adverse reactions allows monitoring of vaccine safety and identification of new, rare or serious adverse reactions that may not have been observed during clinical trials. When an adverse reaction is suspected, health professionals have a legal obligation and patients have the opportunity to report it to the relevant bodies such as the Croatian Agency for Medicinal Products and Medical Devices in order to contribute to a broader understanding of the potential risks and benefits of vaccines. Our goals were to analyze whether healthcare workers report suspected vaccine side effects to the Croatian Agency for Medicines and Medical Products, to analyze whether patients report suspected vaccine side effects to the Croatian Agency for Medicines and Medical Products and, if not, for what reasons, and to analyze the share of reported and unreported suspicions of a side effect of the vaccine. Data were collected via an online anonymous questionnaire on the Facebook social network in the period from 01.02.2023. until 15.04.2023. years. A study was conducted on 275 adults of both sexes who were vaccinated and/or had vaccinated their child/children. 90.76% of the respondents stated that the healthcare worker did not report the suspected side effect of the vaccine to the competent institutions. 88.21% of respondents did not report suspected vaccine side effects to the Croatian Agency for Medicines and Medical Products, and the most common reasons for not reporting by respondents were: "I didn't know I could do it myself" in 39.18% of cases and "a healthcare worker told me that it is an expected side effect that should not be reported" in 19.30%

of cases. Of the total number of suspected vaccine side effects, 11.79% were reported to the Croatian Agency for Medicines and Medical Products, while 88.21% of suspected vaccine side effects remained unreported. Improving patient education, communication, trust and empowerment may be key to encouraging adverse event reporting and thus improving vaccine safety and consequently greater acceptance of vaccination.

THE USE OF LARGE LANGUAGE MODELS IN PHARMACOECONOMICS

Igor Rubinić [1,2], Dinko Vitezić [1,2]

[1] Department of Clinical Pharmacology, Clinical Hospital Centre Rijeka, Rijeka, Croatia
[2] Department of Basic and Clinical Pharmacology with Toxicology, Faculty of Medicine, University of Rijeka, Rijeka, Croatia

Large language models (LLMs), a subset of artificial intelligence (AI), have emerged as powerful tools utilized in various fields. LLMs enable individuals without programming knowledge to engage with artificial intelligence tools through natural conversation, making advanced technologies more accessible to a wider audience. The aim of this study is to explore the application of LLMs in pharmacoeconomics research. The objectives include understanding LLMs' capabilities, identifying challenges, and exploring new opportunities for their use in pharmacoeconomics. A literature review was conducted, targeting studies that specifically employed LLMs in pharmacoeconomic analyses. By utilizing specific keywords, relevant research articles from academic databases were identified. Extracted findings focused on cost-effectiveness modelling, systematic reviews, and health technology assessments were synthesized. Additionally, LLM limitations and associated risks were assessed. LLMs have been employed in various pharmacoeconomic contexts. They can be used in cost-effectiveness modelling, systematic reviews, and health technology assessments. By analysing extensive datasets, LLMs facilitate evidence synthesis and inform policy decisions. However, their efficacy hinges on the quality of training data, ensuring unbiased, representative data is paramount. Furthermore, comprehending LLM decision-making remains challenging, exacerbating existing ethical and jurisdictional

complexities. Privacy concerns, patient consent, and legal implications demand meticulous consideration. The integration of LLMs in pharmacoeconomics holds promise. Collaborative efforts among researchers, policymakers, and industry stakeholders are essential. LLMs can revolutionize evidence-based decision-making, leading to more efficient and equitable healthcare systems.

ASSESSING THE CURRENT LANDSCAPE OF HEALTH TECHNOLOGY ASSESSMENT KNOWLEDGE AND SKILLS AMONG CLINICIANS IN CROATIA

Miro Vuković [1], Mirjana Huić [2], Željko Krznarić [3], Ljubo Znaor [4], Ana Marušić [1]

[1] University of Split, School of Medicine, Croatia
[2] EBM Center, Zagreb, Croatia
[3] Croatian Medical Association, Zagreb, Croatia
[4] University Hospital Center Split, Croatia

This study investigated the levels of knowledge and skills required for HTA among clinicians at university hospitals in Croatia, in light of the upcoming EU regulation. The questionnaire that was distributed to medical and dental medical doctors who work in the three largest university hospitals in Croatia (UHC Zagreb, UHC Sestre Milosrdnice, and UHC Split) included questions about basic demographic data, previous scientific and regulatory experience, and HTA-related experience. The main part of the survey focused on questions for selfassessment of the following skills: clinical effectiveness and safety, searching for the studies, critical appraisal skills, summarizing study characteristics and preparing for synthesis, qualitative evidence synthesis, grading the certainty of the evidence, understanding key concepts in data synthesis and analysis, ethics, health economics, and public and patient involvement. The final part of the survey focused on the subjective needs of each respondent toward future education in this field.

So far, the survey was completed by 363 clinicians working at university hospitals in Split and Zagreb. The majority of the respondents were female (63.24%) aged 31-40 years (33.85%). 87.27% of respondents reported that they were never involved in an HTA process, while 77% of them never used the results of an HTA report. When analyzing the skills

related to the HTA process, all categories had median scores of either 2 or 3 out of a maximum 5. Updated results will be available upon finalizing the sample size and completion of the final analysis. The level of HTA knowledge and skills among Croatian clinicians is currently inadequate to meet upcoming EU regulatory standards. Significant investments into HTA infrastructure, education, and practical training are therefore urgently needed. However, using targeted education based on the results of this study could aid in maintaining the target goals laid out in the EU regulation regarding the HTA.

COST-EFFECTIVENESS OF USING PROBIOTICS TO ENHANCE CHECKPOINT INHIBITOR THERAPY RESPONSE

Marija Kurtov [1], Robert Likić [2,3]

[1] Clinical Hospital Sveti Duh, Department of Internal Medicine, Unit of Clinical Pharmacology and toxicology, Zagreb, Croatia
[2] University of Zagreb, School of Medicine, Zagreb, Croatia
[3] University Hospital Centre Zagreb, Department of Internal Medicine, Unit of Clinical Pharmacology, Zagreb, Croatia

Checkpoint inhibitors (CIs) are monoclonal antibodies used in treating malignant diseases by targeting immune checkpoints, enhancing the ability of the immune system to recognize and attack cancer cells. The most commonly used CIs are ipilimumab, nivolumab, and pembrolizumab. Despite their efficacy, individual responses to CI therapy vary, posing a challenge in cancer treatment. Recent studies suggest a link between gut microbiome composition and CI therapy response, potentially offering new avenues for improving treatment outcomes. These findings have paved the way for manipulating the gut microbiome through the subsequent administration of probiotics to enhance CI therapy response, providing a promising adjunct therapy. Discussion Probiotics are living microorganisms similar to the beneficial bacteria naturally found in the human gut. They are often taken as dietary supplements to help maintain a healthy balance of gut microorganisms, which is crucial for digestive and overall health. As mentioned earlier, using probiotics alongside CI therapy has been linked to improved overall survival and progression-free survival in NSCLC patients compared to CI therapy alone. The exact mechanism behind this effect remains unclear. Furthermore, recent research published in Cell suggests that orally consumed Lactobacillus reuteri can enhance CI therapy response by releasing indole-3-aldehyde, a compound derived from tryptophan metabolism that stimulates anti-

tumor IFNγ+CD8+ T cells. This reinforces the idea that dietary supplementation with probiotics may be a beneficial adjunct therapy for patients undergoing CI treatment. According to the Croatian Institute of Public Health, there were 932 newly diagnosed cases of melanoma in 2021. With the rising incidence of melanoma and the substantial financial burden it imposes on healthcare systems, optimizing treatment strategies is imperative. Immunotherapy with CIs has become a cornerstone in the treatment of metastatic melanoma. However, due to significant individual variability in treatment response, it has been reported that only 22% of melanoma patients treated with ipilimumab experience prolonged survival. Moreover, ipilimumab can induce autoimmune adverse effects in up to 60% of patients. As per national guidelines, ipilimumab and nivolumab combination therapy for a duration of one year can cost approximately €121,000, while a monthly probiotic supplementation may range from €10 to €50. Although promising, the incorporation of probiotics into clinical guidelines requires further validation through larger randomized clinical trials. If validated, a modest investment in a monthly probiotic supplement could potentially reduce the need for multiple treatment cycles or lower the dosage of CIs, thereby diminishing the risk of adverse effects and alleviating the burden of their hospital management. Checkpoint inhibitors have transformed cancer treatment, yet variability in patient response remains a challenge. Emerging research suggests probiotics could enhance CI therapy, potentially improving survival rates and reducing adverse effects. Further clinical trials are needed to validate this approach before its widespread implementation in clinical guidelines

IMATINIB AND THE TREATMENT OF CML

Andro Koren [1], Robert Likić [1,2]

[1] University of Zagreb, School of Medicine, Zagreb, Croatia
[2] University Hospital Centre Zagreb, Department of Internal Medicine, Unit of Clinical Pharmacology, Zagreb, Croatia

Imatinib and the treatment of CML Why would chemotherapy be something avoidable for a patient with chronic myeloid leukaemia? After all, it is quite efficient. However, it isn`t very specific in it`s damage to tissues. Classic Chemotherapy kills all cells of high MI, including mucosal cells, skin, blood cells, hair... Moreover, several specific complications include idiopathic lung fibrosis, dilated cardiomyopathy and cardiotoxicity and nephrotoxicity with various others. Therefore, the finding of bcr-abl translocation in CML patients and targeted treatment with imantinib made a real revolution in oncology patients. One simple pill for treating a tumour patient in comparison to aggressive hospital treatment. This has opened the door for specialized, personalised treatment of many other tumours, especially of haematological decent such as MPN, MDS, AML. In addition to pathology, all recently diagnosed leukemia patients get a name and surname of their disease with rigorous cytogenetic and immunopathological findings that pave the way to the possibility of localised treatment of a tumour. Targeting a tumour tyrosine kinase makes it virtually impossible of displaying a negative effect in a tissue without this abnormality. CML accords for 15% of newly diagnosed cases of leukaemia in adults and it is often an accidental finding in a person`s lab work. Therefore, it is mostly diagnosed in the latent phase, before Richter transformation into AML or ALL and beneficial of TKI treatment. With the finding of imatinib, it is possible to sustain a greater major molecular response and prolong life expectancy. It has been shown more efficient than classical chemotherapy, interferon therapy and radiotherapy with less complications for the patient. Perfect, isn`t it? Five-year survival rates of

CML patients in 1993 (without TKI treatment) vs. 2023 (with TKI treatment) – 31% vs. 90%. There is only one question to be posed here? Is it sustainable and affordable? Of the 12 drugs approved by the FDA - 11 were priced above $100 000 per year. It would be beneficial to try and open them to smaller markets due to numerous patients. However, the numbers speak for themselves: with the initial price of imatinib of 30 000 dollars and 30 000 patients in 2013 the generated revenue from hospital bills was 900 million dollars. The treatment of CML with imatinib has shown that rigorous tumour treatment can be exchanged for only one pill: a TKI with favourable adverse drug profile and greater efficacy than traditional chemotherapy.

THE COST-EFFECTIVENESS OF VITAMIN D SUPPLEMENTATION IN VITAMIN D DEFICIENT POPULATION IN ORDER TO PREVENT ACUTE RESPIRATORY INFECTIONS

Karolina Majstorović Barać [1], Robert Likić [2,3]

[1] Clinical Hospital Sveti Duh, Department of Internal Medicine, Unit of Clinical Pharmacology and toxicology, Zagreb, Croatia
[2] University of Zagreb, School of Medicine, Zagreb, Croatia
[3] University Hospital Centre Zagreb, Department of Internal Medicine, Unit of Clinical Pharmacology, Zagreb, Croatia

Acute respiratory infections (ARI) account for two-thirds of all infections in the population and approximately 30% of total morbidity. ARIs are the primary reasons for visits to primary care, as well as absences from work and school. Adults typically experience three to five episodes annually, while children may suffer up to ten times. There are over 500 different microorganisms that cause ARIs, with viruses constituting the majority (85%). ARIs are the most common justification for prescribing antibiotics, representing about 70% of all prescribed oral antibiotics. The greatest misuse of antibiotics occurs when viral infections are treated unnecessarily, ineffectively, and harmfully. Annually, nearly 2.5 million Croatians suffer from ARIs (1). Approximately 18,000 Croatians are on sick leave due to ARIs every day (2, 3), leading to significant financial burdens from absence costs, diagnostic and treatment expenses, whether outpatient or hospital-based. The opportunities to prevent ARIs remain limited. Observational studies have consistently shown independent associations between low serum concentrations of 25- hydroxyvitamin D (the major vitamin D metabolite) and increased susceptibility to ARIs (4, 5). Vitamin D metabolites aid in the induction of antimicrobial peptides in response to viral and bacterial stimuli (6-8), among other effector mechanisms, such as autophagy induction and the synthesis of reactive nitrogen and oxygen intermediates (8). Vitamin D deficiency is prevalent worldwide, with high rates of deficiency

observed in American (25%), Canadian (36%), European (40%), and South Asian populations (61%), across various age groups (10-13). A meta-analysis of individual participant data (IPD) from 25 randomized controlled trials in the UK, involving 10,933 participants, demonstrated a protective effect of vitamin D supplementation against acute respiratory tract infections (number needed to treat [NNT] = 33). The benefits were greater in those receiving daily or weekly vitamin D without additional bolus doses (NNT = 20), especially in those with profound vitamin D deficiency (levels < 25 nmol/L) at baseline (NNT = 4) (14). These findings underscore the necessity for health sectors to effectively screen and educate high-risk populations, and intervene with vitamin D supplements when necessary, to establish preventive and therapeutic measures.

COMPARATIVE PHARMACOECONOMIC ANALYSIS OF ERAVACYCLINE AND COLISTIN IN MULTI-DRUG RESISANT INFECTIONS

Lovro Pendić [1], Fran Posavec [1], Robert Likić [1,2]

[1] University of Zagreb, School of Medicine, Zagreb, Croatia
[2] University Hospital Centre Zagreb, Department of Internal Medicine, Unit of Clinical Pharmacology, Zagreb, Croatia

The emergence of multi-drug resistant (MDR) bacterial infections underscores the pressing need for new antibiotics. Traditional antimicrobials like colistin, while potent, are fraught with significant side effects including nephrotoxicity and neurotoxicity. Conversely, eravacycline, a member of the tetracycline class, has been approved for managing complicated intraabdominal infections (c-IAI) in adults, showing efficacy against MDR Gram-positive and Gram-negative bacteria without impairing kidney function. This presentation will explore a pharmacoeconomic comparison between eravacycline and colistin, focusing on cost-effectiveness ratios (CER) and incremental cost-effectiveness ratios (ICER) based on Defined Daily Dose (DDD) costs, cure rates, treatment duration, and the incidence of acute kidney injury (AKI). Data for the analysis are drawn from distributor-provided DDD costs for Xerava in Croatia and cure rates, among other parameters, as documented by Alexander et al., 2024. Findings indicate that eravacycline, despite a higher direct cost per DDD, offers a more favorable cost per percentage point of cure rate than colistin. However, the substantial additional cost for each additional percentage point of cure when transitioning from colistin to eravacycline invites a nuanced discussion on the overall cost-effectiveness, particularly when factoring in the costs associated with diagnosing and managing drug-induced side effects. This analysis not only highlights the economic considerations in antibiotic choice but also emphasizes the importance

of evaluating the broader implications of side effects in treatment decisions.

AI-ENHANCED DETECTION OF ADVERSE DRUG REACTIONS IN MULTIMORBID PATIENTS: HYPERSENSITIVITY PNEUMONITIS CASE STUDY

Fran Posavec [1], Lovro Pendić [1], Robert Likić [1,2]

[1] University of Zagreb, School of Medicine, Zagreb, Croatia
[2] University Hospital Centre Zagreb, Department of Internal Medicine, Unit of Clinical Pharmacology, Zagreb, Croatia

This presentation will delve into the utilization of Artificial Intelligence (AI) to identify adverse drug reactions (ADRs), focusing on a challenging case of hypersensitivity pneumonitis (HP) in a patient with a complex medication regimen. Amidst the challenges faced by patients with multimorbidity and the associated polypharmacy, the risk of ADRs, such as HP, significantly escalates. The innovative application of AI techniques, including machine learning, natural language processing (NLP), and deep learning, offers a nuanced approach to dissecting intricate patient data and drug interactions. This case report illuminates the AI-driven process that underscored the critical medication suspects contributing to HP, thus enhancing healthcare professionals' ability to refine treatment plans and bolster patient care. By illustrating the integration of AI in detecting ADRs, the presentation underscores the complementary role of AI in augmenting clinical insights, while also pondering the technological limitations and the envisioned trajectory of AI in tailoring patient-specific healthcare solutions. This discussion promises to offer profound insights into the future of AI in personalizing medicine and its pivotal role in advancing healthcare outcomes.

STANDARD HEALTHCARE VERSUS CLINICAL TRIAL CARE - OVERVIEW OF BENEFITS THROUGH NATIONAL FUND AND PATIENTS PERSPECTIVE USING A MODEL OF DYSLIPIDEMIA

Nataša Skočibušić [1,2,3], Andrej Belančić [1,4], Marin Gobac [5], Dinko Vitezić [1,4]

[1] Department of Clinical Pharmacology, Clinical Hospital Centre Rijeka, Croatia
[2] Clinical research unit, Specialty hospital Medico, Rijeka, Croatia
[3] University of Rijeka; Faculty of Health Studies, Rijeka, Croatia
[4] Department of Basic and Clinical Pharmacology with Toxicology, University of Rijeka, Faculty of Medicine, Rijeka, Croatia

Participation in clinical trials entails taking part in the discovery of effects of health care interventions. At the same time, clinical trial care is associated with various clinical and economic benefits compared to standard healthcare in a similar setting. Aim: To provide an overview of benefits through national fund and patients' perspective using a model of a patient with dyslipidemia under a (primary) lipid-lowering management through standard healthcare versus clinical trial care. The model of standard healthcare was projected based on clinical experience, interviews with Croatian general practitioners alongside analysis of medical records. The model of clinical care was projected as per protocol of a 5-year long clinical trial using drug X, due to statin intolerance, for the treatment (primary prevention) of dyslipidemia. To assess patients' perspective benefits, differences in the number of medical procedures, consultations, and other healthcare therapeutic and diagnostic regimens utilized over a 5-year period were evaluated. The prices used in the economic calculations were derived from the Croatian Health Insurance Fund tariff schedule, ensuring consistency and accuracy in cost estimation across both models of care. Results: Alongside notable direct and indirect healthcare system / national fund

benefits, it is important to highlight that a patient under clinical care received 10 specialist/consultant outpatient visits, 8 electrocardiograms, 1 echocardiography, and 8 laboratory panels more, when compared to a patient under standard healthcare. From the single patient's economical perspective, the latter difference in number of medical procedures is approximately equal to benefit of €1108,63. Although we here presented benefits in the dyslipidemia setting, they can easily be extrapolated to other indications and subpopulations. To deduce, our findings highlight that clinical trials offer multifaceted benefits both to patients and healthcare system / national fund at large.

A LITERATURE REVIEW OF ECONOMIC EVALUATIONS OF RIVAROXABAN WITH OR WITHOUT ASPIRIN IN STABLE CARDIOVASCULAR DISEASE

Melissa Seven[1], Andrea Faour [2], Sandra Knežević[3], Andrej Belančić [3,4], Dinko Vitezić [3,4]

[1] University of Rijeka, Faculty of Medicine, Rijeka, Croatia
[2] Vancouver Coastal Health, Vancouver, Canada
[3] Department of Basic and Clinical Pharmacology with Toxicology, University of Rijeka, Faculty of Medicine, Rijeka, Croatia
[4] Department of Clinical Pharmacology, Clinical Hospital Centre Rijeka, Rijeka, Croatia

Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS) trial demonstrated that the risk of major adverse cardiovascular events is significantly lower with the combination of rivaroxaban (2.5 mg twice daily) plus aspirin than with aspirin alone (100 mg once daily), when used in the management of stable cardiovascular disease. Keeping in mind the findings of COMPASS trial as well as the notable healthcare burden of cardiovascular disease, we aimed towards overviewing the published evidence on the cost-effectiveness of rivaroxaban (2.5 mg twice daily) plus aspirin versus aspirin alone (100 mg once daily), in stable cardiovascular disease setting, on a global scale. On 9th February 2024, we searched PubMed using the following search strategy: rivaroxaban AND aspirin AND cost-effectiveness. By the latter search we identified 39 manuscripts. After applying the prespecified inclusion criteria, which were based on COMPASS population, intervention and comparator characteristics, we included nine manuscripts in our review. Data extraction was conducted manually. Results: All of the included cost-effectiveness analyses (CEAs) encompass perspectives from national healthcare payers; Italy, the Netherlands, France, Germany, the United Kingdom, Australia, the USA, Canada, China, and Taiwan. Overall, the aforementioned CEAs

indicate that the combined regimen (low-dose rivaroxaban + aspirin) is cost-effective when compared to aspirin alone, in the prevention of recurrent cardiovascular events, both in patients with coronary artery disease and peripheral artery disease. Interestingly, only CEA from Taiwan diverged in its conclusion, suggesting that combined regimen might not be as cost-effective in preventing recurrent cardiovascular events. Prescribing low-dose rivaroxaban on top of aspirin to patients with stable cardiovascular disease is cost-effective. The presented pharmacoeconomic findings offer valuable insights for the management of patients with stable cardiovascular disease, thus, directly impacting policy, and laying the basis and directions for clinical strategies/ guidelines.

EFFICACY OF SENOLYTIC RESEARCH IN COST CONTROL OF CHRONIC AGE-RELATED DISEASES

Luciana Koren [1], Robert Likić [1,2]

[1] University of Zagreb, School of Medicine, Zagreb, Croatia
[2] University Hospital Centre Zagreb, Department of Internal Medicine, Unit of Clinical Pharmacology, Zagreb, Croatia

The emergence of multi-drug resistant (MDR) bacterial infections underscores the pressing need for new antibiotics. Traditional antimicrobials like colistin, while potent, are fraught with significant side effects including nephrotoxicity and neurotoxicity. Conversely, eravacycline, a member of the tetracycline class, has been approved for managing complicated intraabdominal infections (c-IAI) in adults, showing efficacy against MDR Gram-positive and Gram-negative bacteria without impairing kidney function. This presentation will explore a pharmacoeconomic comparison between eravacycline and colistin, focusing on cost-effectiveness ratios (CER) and incremental cost-effectiveness ratios (ICER) based on Defined Daily Dose (DDD) costs, cure rates, treatment duration, and the incidence of acute kidney injury (AKI). Data for the analysis are drawn from distributor-provided DDD costs for Xerava in Croatia and cure rates, among other parameters, as documented by Alexander et al., 2024. Findings indicate that eravacycline, despite a higher direct cost per DDD, offers a more favorable cost per percentage point of cure rate than colistin. However, the substantial additional cost for each additional percentage point of cure when transitioning from colistin to eravacycline invites a nuanced discussion on the overall cost-effectiveness, particularly when factoring in the costs associated with diagnosing and managing drug-induced side effects. This analysis not only highlights the economic considerations in antibiotic choice but also emphasizes the importance of evaluating the broader implications of side effects in treatment decisions.

THE PHARMACOECONOMIC IMPACT OF FOLATE (B9) IN ENHANCING ANTIDEPRESSIVE ACTIVITY

Karlo Petković [1], Zdeslav Strika [1], Robert Likić [1,2]

[1] University of Zagreb, School of Medicine, Zagreb, Croatia
[2] University Hospital Centre Zagreb, Department of Internal Medicine, Unit of Clinical Pharmacology, Zagreb, Croatia

The pharmacoeconomic impact of folate (B9) in enhancing antidepressive activity Objectives: explore potential savings by integrating folate supplementation into Croatian psychiatric disease treatment guidelines Abstract: This article explores the multifaceted benefits of folate (B9) supplementation in augmenting antidepressive activity, leading to reduced pain, decreased dependency on costly antidepressants, fewer paid leaves, and prolonged remission. The potential savings and societal advantages of integrating folate supplementation into Croatian psychiatric disease treatment guidelines are discussed through a pharmacoeconomic lens.

COST EFFECTIVENSS AND ROLE OF AI AS A MEDICAL ASSISTANT

Zdeslav Strika [1], Robert Likić [1,2]

[1] University of Zagreb, School of Medicine, Zagreb, Croatia
[2] University Hospital Centre Zagreb, Department of Internal Medicine, Unit of Clinical Pharmacology, Zagreb, Croatia

Cost effectiveness and role of AI as a medical assistant Medical triage is a process of determining the priority of patients' treatments based on the severity of their condition. Traditionally, this is the responsibility of general practitioners (GP) who must assess each patient's illness and provide care accordingly. However, with the advancements in artificial intelligence (AI), there is growing potential to revolutionize the triage process. By automating this initial assessment, AI can significantly reduce the time required for each patient encounter, allowing GPs to focus their attention on those in need of urgent care. Moreover, AI-driven triage systems could also have significant economic benefits. We analysed all patients presenting to the emergency room (ER) with cough as their primary symptom over a period of 2 months. Our study compared the costs of traditional medical ER assessment with potential savings accrued through the utilization of an AI-powered chatbot (CodyMD) for medical triage. This comparative study aimed to evaluate the economic impact and diagnostic efficacy of integrating AI technology in the triage process for cough-related ER visits. In the past 2 months, 270 patients presented to the ER of Clinical Hospital Centre Zagreb with cough as their chief symptom. For the purpose of this analysis, we assumed that all patients had acute respiratory infection (ARI). Most patients presenting with cough are not acutely endangered and represent a significant burden on healthcare expenditure if evaluated in an ER of a university hospital where such an assessment per patient has a projected cost of €150 (€40 for a specialist examination, €50 for chest X-ray, and the remainder for ECG and

laboratory analysis). The projected costs of ER assessment for ARI for all 270 patients would be €40,500. However, if CodyMD was used to evaluate all 270 patients at home, and reliably diagnosed 50% of them with acute, viral respiratory disease, thereby allowing 135 (50%) patients to forego visiting the ER, the savings accrued over 2 months would amount to €20,250 and €121,500 and €607,500 over 1 and 5 years respectively. By utilizing CodyMD AI powered chatbot, the patients can achieve a correct diagnosis being made with a precision of 65-70%. Traditional triage in medicine relies on GPs to allocate care based on symptom severity, but AI could soon change this paradigm. By automating initial assessments, AI streamlines patient encounters, allowing GPs to focus on urgent cases. Additionally, our analysis demonstrates significant potential cost savings arising from integration of AI-powered triage systems, highlighting the economic benefits of adopting such technology in healthcare settings.

SEMAGLUTIDE VERSUS TIRZEPATIDE IN THE TREATMENT OF OBESITY: A SYSTEMATIC REVIEW OF ECONOMIC EVALUATIONS

Art Sefedini [1], Ana Sekulić [1], Sandra Knežević [2], Carla Sans Pola [3], Andrea Faour [4], Andrej Belančić [2,5], Dinko Vitezić [2,5]

[1] University of Rijeka, Faculty of Medicine, Rijeka, Croatia
[2] Department of Basic and Clinical Pharmacology with Toxicology, Faculty of Medicine, Rijeka, Croatia
[3] Department of Clinical Pharmacology, Vall d'Hebron Hospital Universitari, Barcelona, Spain
[4] Vancouver Coastal Health, Vancouver, Canada
[5] Department of Clinical Pharmacology, Clinical Hospital Centre Rijeka, Croatia

This systematic review aimed to overview the body of evidence on cost-effectiveness of semaglutide and tirzepatide for managing obesity in adults, in order to obtain both direct and indirect pharmacoeconomic comparisons between the latter agents. We have conducted a systematic literature review (as per PRISMA guidelines). Studies written in English, cost-effectiveness analyses (CEAs) and cost-utility analyses (CUAs) on semaglutide (2.4 mg once weekly) and/or tirzepatide for the treatment of obesity and comparisons of those regimens against each other, as well as with no treatment/diet and exercise alone, were considered for inclusion. A comprehensive search [(obesity) AND (semaglutide) AND (econom* OR economic evaluation); (obesity) AND (tirzepatide) AND (econom* OR economic evaluation)] was conducted across PubMed/Medline, Global Health, Embase, and Health Management Consortium databases on 7th February 2024. Data was manually extracted. The literature search yielded 103 records in total, of which, 48 were duplicates and excluded. Following screening in Covidence, 8 CEAs were included for further analysis. Markov model was identified as the predominant modelling approach, whilst

healthcare sector was the most commonly applied perspective. Economic outcomes of the included studies varied widely. All studies compared semaglutide with diet and exercise/lifestyle modification but one, which provided an indirect comparison between semaglutide and tirzepatide. Gómez Lumbreras et al. provided an indirect comparison (with phentermine plus topiramate-PpT as a comparator) from the US payer's perspective; the ICERs for semaglutide versus PpT and tirzepatide versus PpT were $24,274,467/QALY and $355,616/QALY, respectively. In the absence of both direct and indirect pharmacoeconomic evaluations comparing semaglutide and tirzepatide, no firm conclusion on their comparative cost-effectiveness can be made yet. Future research should focus on resolving uncertainties in economic evaluations and broaden the scope to include MACE benefits, renal benefits, and prevention/management of obesity related complications into calculations when yielding ICERs.

SELECTED HEALTH ECONOMIC AND POLICY TOPICS

UNLOCKING THE COST OF MENTAL HEALTH: NAVIGATING THE PHARMACOECONOMICS OF PSYCHIATRIC DRUGS IN EUROPE

Iveta Merćep [1,2], Dominik Strikić [1]

[1] University Hospital Centre Zagreb, Zagreb, Croatia
[2] University of Zagreb, School of Medicine, Zagreb, Croatia

The pharmacoeconomics of psychiatric drugs is a critical area of study given the substantial burden of mental health disorders in Europe. In 2017, approximately 123 million individuals across Europe were affected by mental health disorders, with depression being the most prevalent. Alarmingly, those grappling with mental health issues exhibit higher mortality rates compared to their counterparts, engage in riskier health behaviors such as smoking and alcohol consumption, and experience diminished overall life quality. Notably, suicide poses a mortality risk equivalent to gastric or pancreatic cancer in Croatia, underscoring the severity of the issue. Economically, mental health disorders impose a significant financial strain, with approximately 4.1% of the European GDP allocated towards their treatment, including healthcare expenditures and productivity losses. Projections indicate a staggering increase in expenditure, with estimates reaching 14.5 trillion euros by 2030, making mental health disorders the largest expense in healthcare. Furthermore, these disorders rank third in Disability Adjusted Life Years (DALYs), with predictions placing them at the forefront within the next five years. The economic impact extends to the workforce, as mental health disorders account for roughly 50% of all sick leaves in Europe, with durations twice as long as those for other diseases. Despite these figures, allocation towards mental health from healthcare funds falls short of the World Health Organization's

recommended 10%, with Croatia spending only around 4%. Clinical trials for psychiatric drugs, particularly antidepressants, are prolonged compared to other medications. However, the market sees limited innovation, with only seven new antidepressants introduced in the last two decades, despite a 22% increase in usage in Croatia alone. Understanding the pharmacoeconomic landscape of psychiatric drugs is vital for policymakers, healthcare providers, and pharmaceutical companies to address the escalating burden of mental health disorders effectively. Balancing cost considerations with the need for innovation and access to treatment is paramount to improve outcomes and alleviate the societal and economic impacts of these disorders.

PREDICTING THE RISK OF HIGH HEALTHCARE COSTS FOR PATIENTS WITH ALZHEIMER'S DISEASE

Jelena Sušac [1], Siniša Debogović [2], Jakša Vukojević [1], Dinko Vitezić [3,4], Ninoslav Mimica [1,5]

[1] University Psychiatric Hospital Vrapče, Zagreb, Croatia
[2] General Hospital Brežice, Brežice, Slovenia
[3] School of Medicine, University of Rijeka, Rijeka, Croatia
[4] University Hospital Centre Rijeka, Rijeka, Croatia
[5] School of Medicine, University of Zagreb, Zagreb, Croatia

The study aimed to create a statistical, multivariable, predictive model of the highest costs of formal care, treatment, and informal care for patients diagnosed with dementia. We conducted a prospective cohort study at the Health Center “Zagreb-Zapad”. The targeted population included patients aged 60–80 years, diagnosed with dementia, residing in private households, and their informal caregivers. The outcome was the share of costs of informal care (IC) in the total costs of care estimated using the Resource Utilization in Dementia questionnaire. We used profile analysis of six principal components of the Alzheimer’s Disease Cooperative Study ADLs inventory, Neuropsychiatric Inventory and Mini-Mental State Examination, and conducted statistical analysis. We enrolled 240 patients with a median age of 74, and 186 (78%) were women. The total annual costs at the population level were estimated at 594 million EUR, with around 70% attributed to informal care costs. The final predictive model included eight variables: age, age at the time of the first episode of dementia, the number of comorbid chronic physical conditions, diabetes, and four factors related to activities of daily living. The overall accuracy in predicting the upper quartile of total healthcare costs was 90%. The model underwent internal validation after six months, and its accuracy in the validation measurement was 83%. We

concluded that the population of people with dementia is heterogeneous, and there are relatively large differences in the costs attributed to them. This perspective provides new insights into adequately planning therapeutic goals and expectations.

ANXIOLYTICS PRESCRIBING IN CROATIA: HOW TO MAKE PRESCRIBING PATTERNS MORE RATIONAL

Marta Kučan Štiglić [1], Tea Strbad [2], Andrej Belančić [3,4], Dinko Vitezić [3,4]

[1] Medicalia d.o.o, Rijeka, Croatia
[2] Croatian Health Insurance Fund, Zagreb, Croatia
[3] Department of Clinical Pharmacology, Clinical Hospital Centre Rijeka, Rijeka, Croatia
[4] Department of Basic and Clinical Pharmacology with Toxicology, Faculty of Medicine, Rijeka, Croatia

The most frequent anxiety disorder in primary care is generalized anxiety disorder which is associated with a high economic burden (decreased work productivity and increased use of health care services, particularly primary health care). Benzodiazepines are the most frequently prescribed anxiolytics that have been widely used due to their wide therapeutic application. A problem that is directly related to their uncontrolled and irrational use relates to prescribing on private prescription. This refers to a situation where a healthcare professional prescribes medicines to a patient outside of the publicly funded healthcare system. All available anxiolytics are fully or partially reimbursed by Croatian Health Insurance Fund (CHIF), but physicians could prescribe through private prescriptions for CHIF insured persons. In this case a full price of the medicine is paid by a patient. Since private prescriptions are not documented in CHIFs database there is a possibility for private prescriptions abuse. The aim of the study is to determine and analyse changes in the prescribing trends and patterns of anxiolytics in Croatia within the past 15 years, using the International Medical Statistics (IMS) database and CHIF's database. The total usage of anxiolytic drugs increased from 61.13 DDD/1000 in 2006 to 84.24 DDD/1000 in 2021 (maximal consumption) and then decreased to 82.78 DDD/1000 in 2022. During 17-year period, consumption in DDD/1000 increased 35.42%, while the financial expenditure in the

same period decreased 15.57% (from 14.4 million EUR in 2006 to 12.17 million EUR in 2022. The mean price per DDD of all anxiolytic drugs remained stable or decreased during the investigated period, except for bromazepam (it raised from 0.26 EUR in 2006 to 0.33EUR in 2015, and then started decreasing to 0.32 EUR in 2022). The price per DDD of two most prescribed anxiolytics (diazepam and alprazolam) remained stable and lowest among all anxiolytics available in Croatia (0.09 EUR per DDD). Despite being either not recommended by clinical guidelines or of doubtful efficacy in many cases, prescribing of anxiolytics is common. According to the results of our investigation there is a need for enhanced national regulatory framework for anxiolytics prescribing in Croatia for the benefit for the patients.

PHARMACOECONOMIC ASPECTS OF TREATING IBD

Željko Čabrijan [1,2,3]

[1] Division of Gastroenterology, Hepatology and Clinical Nutrition, University Hospital Dubrava, Zagreb, Croatia
[2] University of Applied Health Sciences Zagreb, Croatia
[3] School of Medicine, Osijek, Croatia

IBD presents a complex landscape for pharmacoeconomic evaluation because it significantly impacts patients' lives and healthcare systems. Pharmacoeconomic evaluation becomes crucial for understanding the economic implications of various treatment strategies. Several studies underline the rising prevalence of IBD globally, emphasizing the need for effective and economically sustainable treatments. Patients have a wide range of responses to various treatments. What works for one might not have the same impact on another. Genetic variations, disease severity, and individual immune responses contribute to this variability. Challenge is determining the most cost-effective treatment strategies, a treatment that proves highly effective for some patients may not be as beneficial for others. Pharmacoeconomic assessments need to consider the heterogeneous nature of patient responses to ensure that the economic evaluation is reflective of real-world scenarios. Incorporating this variability into pharmacoeconomic models can improve the accuracy of pharmacoeconomic analysis and support development of personalized medicine approaches.

IMPACT OF BIOSIMILAR APPROVAL ON FINANCIAL CONSUMPTION: A SIMPLE MODELLING STUDY ESTIMATING COST SAVINGS FOLLOWING INFLIXIMAB BIOSIMILAR APPROVAL

Robert Marčec [1]

[1] Clinical Hospital Center Zagreb, Zagreb, Croatia

The increase in utilisation of monoclonal antibodies is associated with substantial financial strain for healthcare systems. Biosimilars have the potential for cost-saving, however the cost-savings depend on their actual utilisation. We aimed to investigate if the approval of infliximab biosimilars had an impact on the drug's financial consumption and estimate the potential cost-savings accrued in Croatia. A simple economic model was constructed to estimate the savings made after the approval of the first infliximab biosimilar in 2013. Data regarding annual drug utilisation and total annual cost was retrieved from annual drug utilisation reports published by HALMED. The model is based on a comparative simulated scenario in which no biosimilar was approved and the price of 1 defined daily dose (DDD) of infliximab was fixed at 20.72358€ (mean cost of 1DDD 2009- 2014) in the simulated years 2014–2022 with the presumption that drug utilization remained the same. Following the approval of the first infliximab biosimilars in 2013, the cost of 1 DDD of infliximab decreased on average 6% per year. The average yearly cost-savings amounted to 2 852 911€, with the highest savings accrued in 2022 being equal to 6 864 125€. The total savings estimated by our model are significant and amounted to 25 676 202€ in a 9-year period (2014–2022). Following the approval of the first infliximab biosimilar in 2013, the financial consumption of 1 DDD of infliximab started decreasing and according to our model resulted in significant cost savings.

THE COST OF DIALYSIS IN CROATIA: A COMPREHENSIVE ASSESSMENT OF HEMODIALYSIS AND PERIOTONEAL DIALYSIS COSTS BEYOND THE PAYER'S PERSPECTIVE

Viktorija Erdeljić Turk [1]

[1] Division of Clinical Pharmacology, Department of Medicine, University Hospital Zagreb, Zagreb, Croatia

This study aims to provide a comprehensive analysis of the costs associated with hemodialysis (HD) and peritoneal dialysis (PD) in Croatia, offering a detailed comparison from both healthcare payers' and societal perspectives. It seeks to assess the financial implications of these dialysis therapies, emphasizing the broader economic impacts on the healthcare system and society. A multifaceted approach was employed to evaluate the direct and indirect costs of HD and PD. The direct medical costs considered include the expenses related to dialysis procedures, medical supplies, medications, hospitalizations, personnel, and the overheads of running a dialysis center. Indirect costs encompass lost productivity, transportation, and caregiver expenses. The study compares these costs within the context of Croatia's healthcare infrastructure and reimbursement policies, providing a holistic view of the economic burden posed by different dialysis modalities. The analysis reveals significant differences in resource utilization and economic outcomes between in-center HD and PD. Direct medical costs dominate the overall costs for both dialysis modalities, with variations largely influenced by the choice of dialysis modality and the associated healthcare delivery methods. Difficulties in accurately quantifying indirect costs, such as travel to the dialysis center and loss of productivity, were encountered due to limited local input data. However, indirect costs also have a considerable impact, reflecting broader economic implications on patients' quality of life and societal productivity. The study uncovers the challenges in quantifying

the comprehensive economic impact, highlighting the variability in cost effectiveness across different patient populations and the difficulties in assessing intangible costs like psychological well-being. This comprehensive cost analysis underscores the necessity of a nuanced evaluation of dialysis modalities in Croatia, considering both economic and health outcomes. The findings advocate for informed healthcare decision-making, incorporating a balanced view of financial sustainability and patient-centered care. The study calls for a broader consideration of dialysis costs, urging stakeholders to account for the full spectrum of economic consequences when making decisions about dialysis treatment modalities. It is essential to recognize that the cost-effectiveness of each dialysis modality directly depends on its suitability for the individual patient, with modalities being unique and often complementary, necessitating a tailored approach to optimize patient outcomes and healthcare costs.

THE PHARMACIST'S PRESCRIPTION: A POTENTIAL CURE FOR CROATIA'S HEALTHCARE OVERLOAD

Dominik Strikić [1], Ivan Gornik [1], Iveta Merćep [1,2], Robert Likić [1,2]

[1] Clinical Hospital Centre Zagreb, Zagreb, Croatia
[2] University of Zagreb Medical School, Zagreb, Croatia

The Croatian healthcare system is under a noticeable strain, which is particularly evident in the burden on emergency departments. The ER strain is exacerbated by a remarkable influx of unnecessary visits, that are often seen as the easiest entry point into the healthcare system. As medical professionals struggle to cope with the overwhelming number of patients, the search for alternative strategies is inevitable. Working closely with other healthcare professionals, particularly pharmacists, appears as a promising option. Pharmacists have the expertise to support primary care teams in treating patients with common problems such as seasonal viral infections, who typically present with symptoms such as cough or fever, by providing symptomatic treatment. To better understand the issue of unnecessary visits, we conducted a retrospective cohort study in the Department of Emergency Medicine at the University Hospital Zagreb from 1 January to 15 March 2024. We identified patients who presented to the emergency department without a referral from the primary care physician and who had a cough as their primary symptom without the presence of other symptoms. We excluded individuals under 18 years of age. During the study period, we assessed 25,709 patients in the emergency department, with 232 patients (0,9%) meeting our inclusion criteria. Of these patients, none had visited repeatedly, six required hospitalisation for a variety of conditions, particularly pneumonia, and five were referred for further urgent outpatient diagnostic procedures. Furthermore, 221 patients (approximately 95%) were discharged with treatment recommendations (54 with antibiotic prescriptions), mostly involving symptomatic therapies. Laboratory tests, including CBC and biochemistry, were

performed on 228 patients (99%), and chest x-rays were performed on 219 patients (94%). Based on the Croatian Medical Chamber's price tariff, the average price for screening examinations is €40, chest X-ray is €35, and laboratory testing is €20. According to our observational study, more than 95% of patients could have potentially been treated by pharmacists, resulting in reduced healthcare expenditures and an overall reduction in healthcare costs by more than €21,000 during the study's period. The use of pharmacists and pharmacies for a range of procedures, including simple consultations and vaccinations, is commonplace in developed countries. Indeed, modern medicine thrives on the collaboration of different experts, and utilising the knowledge of pharmacists could facilitate easier access to the healthcare system and ultimately reduce the cost burden.

MEDICAL DESERTS: A GROWING GLOBAL CONCERN

Robert Likić [1,2]

[1] Clinical Hospital Centre Zagreb, Zagreb, Croatia
[2] University of Zagreb Medical School, Zagreb, Croatia

Medical deserts" refer to regions with severely limited access to healthcare, characterized by a scarcity of healthcare professionals and facilities, which results in poor health outcomes and pronounced health inequalities. This issue has historically plagued remote and rural areas but has intensified with 20th and 21st-century urbanization, leading to a stark urban-rural healthcare divide. Predominantly, these areas suffer due to low population density, making it economically unviable to sustain healthcare services, and disparities in regional resources, infrastructure, and professional distribution. In Europe, including countries like Croatia, these disparities manifest through differences in age demographics, economic conditions, and travel distances to healthcare facilities. Socioeconomic and demographic factors also shape medical students' willingness to work in these underserved areas. Personal backgrounds, aspirations for urban amenities, and perceived professional opportunities deter many from rural postings. Addressing these challenges requires comprehensive strategies. Research from the Zagreb Medical School highlights that while some medical students are open to working temporarily in medical deserts, a significant number are reluctant. This points to the necessity for targeted policy interventions that offer incentives such as student loan forgiveness, housing allowances, and tax benefits to attract and retain healthcare workers in these regions. Moreover, collaboration among governments, academic institutions, and healthcare organizations is vital. Enhancing medical education to include rural health exposure and mandating rural postings as part of the curriculum can prepare future healthcare professionals for the realities of working in underserved

areas. Combating the plight of medical deserts demands a multifaceted approach that not only improves immediate access to healthcare but also addresses the broader socio-economic barriers contributing to this global concern. Ensuring equitable healthcare access for all, regardless of location or background, is crucial for global health equity.

PRICE AND POTENTIAL SAVINGS IN SECOND-LINE TREATMENT OF PATIENTS WITH ACTIVE CROHN'S DISEASE AND ULCERATIVE COLITIS IN CROATIA

Iva Mikulić [1], Robert Likić [1,2], Iveta Merćep [1,2]

[1] Clinical Hospital Centre Zagreb, Zagreb, Croatia
[2] University of Zagreb Medical School, Zagreb, Croatia

Treatment options for adult patients with moderately to severely active Crohn's disease (CD) and ulcerative colitis (UC) who respond inadequately or not at all to conventional therapy or a tumor necrosis factor-alpha antagonist (infliximab, adalimumab) or in whom there are medical contraindications for such therapies, include the anti-integrin agent vedolizumab and the anti-interleukin (IL)12/23 agent ustekinumab. Both second-line therapies are priced significantly higher than first-line therapy in Croatia. Ustekinumab was first marketed in the European Union (EU) in 2009 by Janssen-Cilag International under the brand name Stelara. In January 2024, the European Commission approved a biosimilar called Uzpruvo®. In addition, the Committee for Medicinal Products for Human Use recommended the approval of Pyzchiva®, another biosimilar, in February 2024. This decision facilitated market entry of biosimilars following the expiry of the European Supplementary Protection Certificate for Stelara in July 2024. We calculated the annual cost of one year of treatment with biologics for the treatment of CD and UC in Croatia. We also calculated the potential savings that could be achieved if ustekinumab biosimilars entered the market. In 2023, the one-year treatment cost for a patient in Croatia amounted to € 2,669 for infliximab alone, € 9,795 for adalimumab, € 15,176 for vedolizumab and € 22,518 for ustekinumab. Based on the market entry model for adalimumab biosimilars in 2019, we have calculated the potential savings from ustekinumab biosimilars. The first adalimumab biosimilar was priced 11% below the originator product Humira® in the first year. In the following year, the original

product was 20 % cheaper and all biosimilars were 3 % cheaper. In the second year, the price of the originator product was 23% below its original price and the biosimilars were 9% cheaper. In the third year, there was a further price reduction of 11%, with all adalimumabs having the same price. A price reduction of 30 % is to be expected for ustekinumab over the next three years after biosimilars' market entry. With one intravenous and six subcutaneous administrations, ustekinumab offers lower medical costs compared to eight intravenous administrations of vedolizumab, and with the 30% lower price for a year's treatment (around €15,763), the cost of treatment with ustekinumab would be lower than the cost of vedolizumab. Competition from biosimilars following the expiry of EU exclusivity rights for Stelara offers a significant opportunity to improve patient access at the same or even lower cost to European healthcare systems.

EDUCATIONAL WORKSHOP:

Principles of transforming the pharmaceutical pricing and reimbursement systems in lower income European countries

Zoltán Kaló [1,2]

[1] Center for Health Technology Assessment, Semmelweis University, Budapest, Hungary
[2] Syreon Research Institute, Budapest, Hungary

Patient access to new pharmaceuticals is more limited in lower income European countries than in higher income countries. As pharmaceutical R&D increasingly focusing on high-cost medications for narrow patient populations, inequity in patient access to medical innovation will be even more important in the near future. As a consequence, transformation of the pharmaceutical pricing and reimbursement to increase the system preparedness in countries with limited resources is inevitable. Objectives and directions of potential changes may not be the same for different stakeholder groups. Therefore, transformation of pharmaceutical pricing and reimbursement systems should be guided and balanced by key principles to ensure that improvement in one objective does not compromise other objectives. The educational workshop will shed light on these principles and will highlight specific policy tools for public policy-makers, industry representatives and academic researchers especially from lower income European countries.

abbvie

Inovativna znanost. Potpuna predanost.

Najteže zdravstvene izazove savladavamo pomoću inovativne znanosti.

Potpuno smo predani pomoći onima kojima je to najpotrebnije.

HR-ABBV-180006, rujan 2023.

AstraZeneca

We are leading a revolution in oncology to redefine cancer care

CALQUENCE® (akalabrutinib)

IMJUDO™ tremelimumab

Lynparza® olaparib

IMFINZI™ durvalumab

ENHERTU® trastuzumab derukstekan

TAGRISSO® osimertinib

Sastavni dio ovog materijala su Sažetci opisa svojstava lijekova Imjudo, Calquence, Lynparza, Imfinzi, Enhertu i Tagrisso sukladno članku 14. i članku 15. Pravilnika o načinu oglašavanja o lijekovima ("Narodne novine" broj 43/15). Prije propisivanja lijeka, molimo pročitajte zadnji odobreni Sažetak opisa svojstava lijeka i Uputu o lijeku.
SAMO ZA ZDRAVSTVENE RADNIKE.

Enhertu (trastuzumab derukstekan) ▼Ovaj je lijek pod dodatnim praćenjem. Time se omogućuje brzo otkrivanje novih sigurnosnih informacija. Od zdravstvenih radnika se traži da prijave svaku sumnju na nuspojavu za ovaj lijek. Upute za prijavljivanje dostupne su na www.halmed.hr.

AstraZeneca d.o.o., Ulica Vjekoslava Heinzela 70, 10000 Zagreb,
Tel: +385 1 4628 000, www.astrazeneca.com
Veeva ID: HR-HR-5295. Pripremljeno ožujak 2024., vrijedi do ožujak 2026.

Daiichi-Sankyo | AstraZeneca

Lp(a) – stara ploča, nova muzika

Gotovo 60 godina nakon što ga je prvi put opisao Norvežanin, liječnik i genetičar, Kare Berg, lipoprotein (a) je postao prihvaćen kao nasljedni, uzročni čimbenik rizika za kardiovaskularnu bolest i kalcificiranu stenozu aortnog zaliska.[1]

Što je lipoprotein (a)?

- **Molekula slična LDL-čestici koja uključuje dvije proteinske komponente; apolipoprotein (a) i apoB100.[1-3]**
- **Glavni je prijenosnik oksidiranih fosfolipida (OxPL) u plazmi što je čini izuzetno aterogenom.[2]**
- **Brojne studije pokazale su povezanost između povećanog Lp(a) i aterosklerotske kardiovaskularne bolesti (ASKVB), kalcificirane bolesti aortalnog zalistka/ aortalne stenoze (CAVD/AS), moždanog udara, zatajenja srca ili periferne arterijske bolesti (PAD).[1,2]**

Europske smjernice o liječenju dislipidemija iz 2019. sugeriraju mjerenje Lp(a) barem jednom u životu svake odrasle osobe.[3-5]

Literatura: 1. Dermot R, Neely G. Br J Cardiol 2022;29(suppl 1):S3–S6. **2.** Pasławska A, Tomasik PJ. Cells. 2023 Oct 17;12(20):2472. **3.** Cegla J, et al. Atherosclerosis 2019;291:62-70. **4.** Mach F, et al. Eur Heart J. 2020 Jan 1;41(1):111-188. **5.** Kronenberg F, et al. Eur Heart Journal 2022;42(39):3925-3946.

NOVARTIS | Reimagining Medicine

Novartis Hrvatska d.o.o., Radnička cesta 37b, 10 000 Zagreb, tel. 01 6274 220, novartis.hrvatska@novartis.com / Broj odobrenja: HR2403228960 / Datum odobrenja: 23.03.2024.

Debljina

nije problem
pojedinca već

odgovornost zajednice!

Pokrećemo promjene u debljini

Novo Nordisk Hrvatska d.o.o.
Ulica D. T. Gavrana17 - 10020 Zagreb HR24CO00008
Datum sastavljanja: 03/2024

novo nordisk®

BIOMARIN®

BOLESNICI SU U SREDIŠTU SVIH NAŠIH NASTOJANJA

"Znamo da za BioMarin rade ljudi koji nam žele živote učiniti boljima"

majka djeteta kojem je dijagnosticirana genetska bolest

FORUM OF INTERNATIONAL RESEARCH & DEVELOPMENT PHARMACEUTICAL COMPANIES, EIG

Eli Lilly (Suisse) S.A. Predstavništvo u RH, Ulica grada Vukovara 269 G, 10 000 Zagreb
Tel: +385 1 2350 999, Fax: +385 1 2305 870
SAMO ZA ZDRAVSTVENE RADNIKE,
PP-MG-HR-0008, 19.3.2024.

MSD
INVENTING FOR LIFE

Istražujemo za život.

Koristimo znanost za intenzivna istraživanja u potrazi za medicinskim otkrićima koja će koristiti bolesnicima i društvu danas, sutra i generacijama koje dolaze.

Jamieson MC
PRIRODNI IZVORI
Od 1922.

SALUS
Zagreb

MERCK

CONTRIBUTORS

ewo pharma since 1959

EXCEED ORPHAN

MEDIS Therapeutics

MEDIA SPONSOR

PHARMABIZ

UNDER THE AUSPICES OF

Ministry of Health of the Republic of Croatia

MEDRI

Faculty of Medicine of the University of Rijeka

pharmacoeconomics-congress.eu