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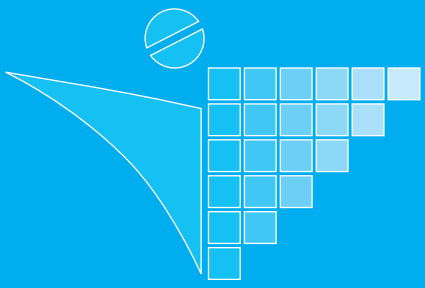


6th Adriatic Congress
of Pharmacoeconomics
and Outcomes Research

pharmaca

GLASILO HRVATSKOG DRUŠTVA ZA
KLINIČKU FARMAKOLOGIJU I TERAPIJU
I UDRUGE POSLODAVACA U ZDRAVSTVU

HRVATSKI ČASOPIS ZA FARMAKOTERAPIJU

PHARMACA Supplement 2016

Zagreb, 2016.

Final programme and abstracts from the

6th Adriatic Congress of Pharmacoeconomics and Outcomes Research

Bled, Slovenia, 21-24 April, 2016

Konačni program i sažetci

Šesti jadranski kongres farmakoekonomike i istraživanja ishoda liječenja

Bled, Slovenija, 21-24 April, 2016

Guest Editors / Gostujući urednici:
Dinko Vitezić, Rok Hren

PHARMACA Supplement 2016

CONTENT:
SADRŽAJ:

EDITORIAL

Once again Congress of Pharmacoeconomics and Outcome Research is before us. This year it will be organised in Slovenia, Bled, from April 21-24, 2016 and it is the 6th Adriatic Congress of Pharmacoeconomics and Outcomes Research. We should all be very proud of where are we today in the field of pharmacoeconomics and excited about where we are headed.

As organizers specified in their invitation this year Congress will be focusing on Health Technology Assesment which has become an active field internationally and has seen continued growth fostered by the need to support management, clinical, and policy decisions. Health policy decisions are becoming increasingly important as the opportunity costs from making wrong decisions continue to grow.

This year the Congress is organized by the ISPOR (International Society for Pharmacoeconomics and Outcomes Research) Slovenia Regional Chapter in partnership with the Section for Pharmacoeconomics and Outcomes Research of the Croatian Society for Clinical Pharmacology and Therapeutics, Croatian Medical Association, and under the auspices of EACPT, European Society of Clinical Pharmacology and Therapeutics.

As every year, a number of plenary sessions, round tables, issue panels, and research presentations will take place prior and during Congress and hopefuly there will be enough time for sharing thoughts, opinions and experience.

Health technology assessment as main topic of the Congress is for many reasons very important for Croatian clinical pharmacologists, all health care proffesionals and health policy as well.

On behalf of chief editor of the official journal of the Croatian Society for Clinical Pharmacology and Therapeutics I am very pleased to welcome all participants with the desire to spend a pleasant working and social moments

Ksenija Makar-Aušperger
Clinical pharmacologist, PhD, dr med
Editor-in chief Pharmaca

FOREWORD

Dear Colleague,

It is with great pleasure to extend our invitation to the 6th Adriatic Congress of Pharmacoeconomics and Outcomes Research, which will be held in Bled, Slovenia, from April 21-24, 2016. This year's Congress will be focusing on Health Technology Assessment, which has become widely accepted as a central tool in health system planning. However, as its implementation may vary among different European jurisdictions, we will discuss this pertinent topic particularly taking into account sustainability of the healthcare systems.

Our Congress is the forum (i) to share research and help advance the science of health economics within the Adriatic 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 five years our annual Congress has become a reference point in the field of pharmacoeconomics and outcomes research in our region since we are not shying away from explicitly discussing pressing challenges, such as conditions of severe economic constraints within our jurisdictions.

We encourage your participation by submitting research podium and poster abstracts. As every year, we will organize short course prior to the Congress and a number of plenary sessions, round tables, issue panels, and research presentations.

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

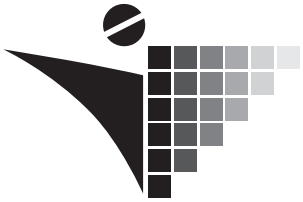
The Congress is organized by the ISPOR (International Society for Pharmacoeconomics and Outcomes Research) Slovenia Regional Chapter in partnership with the Section for Pharmacoeconomics and Outcomes Research of the Croatian Society for Clinical Pharmacology and Therapeutics, Croatian Medical Associa-

tion, and under the auspices of EACPT, European Society of Clinical Pharmacology and Therapeutics. The overall goal of our organizations is to advance public health care policies which maximize societal welfare and optimize diffusion of innovative health care technologies.

With best wishes,

Rok Hren, PhD, MSc IHP(HE)
Congress President
President, ISPOR Slovenia
Regional chapter

Prof. Dinko Vitezić, MD, PhD
Congress President
President, Section for Pharmacoeconomics and Outcomes Research and President, Croatian Society for Clinical Pharmacology and Therapeutics



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CONGRESS ORGANISED BY /
ORGANIZATOR KONGRESA:

Section for Pharmacoeconomics and Outcomes Research, Croatian Society for Clinical Pharmacology and Therapeutics, Croatian Medical Association and ISPOR Slovenia Regional Chapter /

Sekcija za farmakoekonomiku i istraživanje ishoda liječenja, Hrvatsko društvo za kliničku farmakologiju, Hrvatski liječnički zbor i podružnica ISPOR-a u Sloveniji

UNDER THE AUSPICES /
POD POKROVITELJSTVOM:

the Prime Minister of the Republic of Slovenia
Dr Miro Cerar

and

EACPT, European Association
of Clinical Pharmacology
and Therapeutics.

THURSDAY (21.4.2016)

Pre-Congress Training Course on Managed Entry Agreements (MEAs) in the Adriatic Region

9:15 From Assessment to Agreement: MEAs in the Adriatic region (Rok Hren, Slovenia)
9:45 Rationale and taxonomy of MEAs (Andras Inotai, Hungary)
10:15 MEAs: Case studies (Zoltan Kalo, Hungary)

10:45 ***Coffee break***

11:00 MEAs: Case studies (continued) (Zoltan Kalo, Hungary)
11:30 MEAs from the industry's perspective (Slobodanka Bolanča, Croatia)
12:00 Recommendations for implementation of MEAs (Zoltan Kalo, Hungary)
12:30 Final remarks, questions and course adjourn (Rok Hren, Slovenia)

13:00 ***Lunch break***

Opening ceremony

14:00 Welcome address by the Congress President, the President of CRO-CPT* and the EACPT** Executive Committee member - Six years history and vision of Adriatic Congresses (Dinko Vitezić)
14:15 Welcome address by the Executive committee chair of ISPOR*** Central & Eastern Europe network (Vlad Zah)
14:20 Statement by the Prime Minister of the Republic of Slovenia Dr. Miro Cerar
14:25 Welcome address by the Congress President and the President of ISPOR Slovenia Regional Chapter - Why HTA matters? (Rok Hren)

Keynote speeches: To 'HTA' or not to 'HTA': is that the question?

Chairmen: Rok Hren, Dinko Vitezić

14:40 An imperative of quality and safety within the health care (Dorjan Marušič, Slovenia)
15:05 Methodological and practical challenges of HTA for medicines (Mitja Kos, Slovenia)
15:30 ISPOR rare diseases special interest group report: challenges in assessing and apprasing rare disease diagnostics & treatment (Zoltan Kalo, Hungary)

15:55 ***Coffee break***

* CRO-CPT, Croatian Society for Clinical Pharmacology and Therapeutics
** EACPT, European Association for Clinical Pharmacology and Therapeutics
*** ISPOR, International Society For Pharmacoeconomics and Outcomes Researc

Keynote speeches: To 'HTA' or not to 'HTA': is that the question?

Chairmen: Rok Hren, Dinko Vitezić

16:15 Can we assure affordable and transparent patient access to innovative technologies without efficient HTA support? (Siniša Varga, Croatia)

16:40 Strenghts and weaknesses of HTA implementation in Hungary (Bertalan Nemeth, Hungary)

17:05 The future challenges in HTA (Valentina Rupel Prevolnik, Slovenia)

17:30 **Round table discussion:** Future of HTA and reimbursement challenges of innovative technologies in CEE countries

Moderator: Rok Hren (Slovenia)

Faculty: Dragana Atanasijević (Serbia), Livio Garattini (Italy), Zoltan Kalo (Hungary), Mitja Kos (Slovenia), Dorjan Marušič (Slovenia), Oana Mocanu (Romania), Siniša Varga (Croatia), Dinko Vitezić (Croatia)

18:30 ***Closure of Day 1***

18:45 ***Welcome reception***

FRIDAY (22.4.2016)

The Role of Generic Medicines and Biosimilars in Improving Health Care Policy and Practice

Chairmen: Igor Locatelli, Igor Francetić

9:00 Changing biological landscape (Davor Plavec, Croatia)

9:20 Significant cost savings potential of biosimilar drugs in the largest Croatian hospital (Viktorija Erdeljić Turk, Croatia)

9:40 Health technology assessment in CEE: the case of the second generation biologicals and the biosimilars (Laszlo Gulacsi, Hungary)

10:00 Review of studies addressing monoclonal antibodies switching: will we get an answer? (Tomislav Laptoš, Slovenia)

10:20 Criteria for the inclusion of biosimilars into hospital tenders - theory or practice? (Vesna Pavlica, Croatia)

10:40 ***Coffee break***

Patients' Perspectives in Health Technology Assessment

Chairmen: Valentina Rupel Prevolnik, Carmen Hadžić Kostrenčić

11:00 Whose quality of life measurements to use in health technology assessments: ones elicited from patients or from general population? (Marko Ogorevc, Slovenia)

11:20 Lessons to learn from the first fifteen years of EQ-5D in Central and Eastern Europe (Marta Pentek, Hungary)

11:40 Quality of life indicators in SHARE and their determinants (Andrej Srakar, Slovenia)

12:00 Impact of patient support program use on clinical outcomes among patients with rheumatoid arthritis (Andrew Ostor, UK)

12:20 Patient Reported Outcomes in (older) Diabetic Patients in Slovenia (Eva Turk, Norway)

12:40 Italian experience with registries as tools to assure access and sustainability of new innovative therapies/drugs. (Nello Martini, Italy)

13:30 ***Lunch break***

Contemporary Policy Practices and Challenges in Pricing and Reimbursement of New Technologies - Time for Cross Country Collaboration?

Chairmen: Boris Majcen, Siniša Varga

14:20 New regulatory developments from the Payer's perspective (Jurij Furst, Slovenia)

14:40 The evidence-informed policy network – its contributions to strengthening evidence-informed policy-making in Slovenia (Mario Ivanuša, Slovenia)

15:00 Pharmaceutical price schemes in Europe: time for a 'continental' one? (Livio Garattini, Italy)

15:20 Evolution of expenditures for prescription pharmaceuticals in Slovenia: separating the consumption, pure price and product mix effects (Petra Došenović Bonča, Slovenia)

15:40 The cost utility analysis of medical equipment in Croatian hospitals (Dragan Korolija Marinić, Croatia)

16:00 Patient access to medicines for rare diseases in Slovenia (Andreja Detiček, Slovenia)

16:20 ***Coffee break***

Methodological and Practical Aspects of HTA

Chairmen: Mitja Kos, Viktorija Erdeljić Turk

16:40 Management of anemia in patients with myocardial infarction: is there a more cost effective transfusion strategy? (Tabassome Simon, France)

17:00 Estimation of the value of evidence: a case of pharmacogenetic dosing of warfarin (Andrej Janžič, Slovenia)

17:20 Extrapolation of survival outcomes in cost-effectiveness modelling of cancer treatments (Igor Locatelli, Slovenia)

17:40 Challenges related to medicine price as the input parameter in cost-effectiveness analysis (Nika Marđetko, Slovenia)

18:00 Big problems of small countries: Impossibility of discrimination by direct segmentation (Davor Mance, Croatia)

18:20 ***Closure of Day 2***

20:00 ***Dinner***

SATURDAY (23.4.2016)

Selected Studies in Health Care Management of Oncology Patients

Chairmen: Maja Primic-Žakelj, Danko Vrdoljak

9:00 Reimbursement policies for oncological drugs: where to go? (Rok Hren, Slovenia)

9:20 Personalized medicine and economic evaluation in oncology: all theory and no practice? (Livio Garattini, Italy)

9:40 Expenditures for oncology drugs versus outcomes in South East Europe, is there a missing link? (Slobodanka Bolanča, Croatia)

10:00 Melanoma screening – epidemiological impact and disease cost-savings (Goran Benčina, Croatia)

10:20 Counselling of Oncology Patients by the Oncology Pharmacists at the Clinic for Tumors, UHC Sisters of Mercy, Zagreb, Croatia (Vesna Pavlica, Croatia)

10:40 The role of clinical pharmacist as a member of the Multidisciplinary team involved in a treatment of oncology patients – case study (Marko Skelin, Croatia)

11:00 ***Coffee break***

Technology Assessment, Cost-Effectiveness Studies and Budget Impact Analysis of Selected Therapeutic Areas

Chairmen: Jurij Furst, Ljubica Suturkova

11:20 The implementation of HTA in decision making in Hungary (László Nagyjánosi)
11:40 Impact of ISPOR tools on national pharmacoeconomic practices: example Croatia (Josip Čulig, Croatia)
12:00 Methodological challenges and health policy development related to the implementation of MEAs in SEE (Slobodanka Bolanča, Croatia)
12:20 Methodology and the use of pooled analysis in the CEA for IDEGLIRA vs alternative intensification strategies in T2DM patients (Antonio Ramírez de Arellano, Spain)
12:40 Strengthening patient voice in HTA-EUPATI Serbia (Dragana Atanasijević, Serbia)

13:00 ***Lunch break***

Selected Studies in Health Care Management I

Chairmen: Andrej Srakar, Zoran Sterjev

14:00 Trends in utilization of statins in Republic of Macedonia 2013-2105 (Zorica Naumoska, Macedonia)
14:20 Changes in antihypertensive drugs usage in Croatia during 14-year period (Dinko Vitezić, Croatia)
14:40 Analysis of the consumption of drugs in the General hospital Zadar after a change in the model of hospitals financing (Aleksandar Knežević, Croatia)
15:00 Health and economic burden of acute otitis media infections in children (Goran Benčina, Croatia)
15:20 The cost-effectiveness of cythochrome P450 genotype screening for optimization of therapy with risperidone and clopidogrel treatment in R. Macedonia (Aleksandra Kapedanovska Nestorovska, Macedonia)
15:40 Pharmacoeconomic evaluation of opioid substitution treatment in Slovenia (Rok Hren, Slovenia)

16:00 ***Coffee break***

Selected Studies in Health Care Management II

Chairmen: Andrej Janžič, Aleksandar Knežević

16:00 HIV Antiretroviral Therapy (ART) – drug combinations and costs in Croatia (Goran Benčina, Croatia)

16:20 Prescription trends and expenditures of antimicrobial drugs during 5 years period in Croatia (Igor Francetić, Croatia)

16:40 Pharmacoeconomic aspects for analysis of treatment on infection from MRSA (Stevce Acevski, Macedonia)

17:00 Evaluation of the most commonly used antibiotics in pediatric population at Pulmonary Department of the Pediatric Clinic in Sarajevo, BIH (Svjetlana Loga Zec, Bosnia and Herzegovina)

17:20 Health care services utilization among elderly in Slovenia: critical assessment (Rok Hren, Valentina Rupel Prevolnik, Andrej Srakar, Slovenia)

17:40 Outpatient cost of BPH therapy 2011-2015 (Boris Benčina, Croatia)

18:00 ***Closure of the Congress***

SUNDAY (24.4.2016)

9:00 Joint Meeting of EACPT, ISPOR, CRO-CPT, UZEFI

10:30 ***Coffee break***

11:00 Joint Meeting of Scientific and Organizing Committees

12:15 ***Lunch and departures***

ABSTRACTS
SAŽETCI

Note: The organizers are not responsible for the contents of submitted abstracts.
Napomena: Organizatori ne preuzimaju odgovornost za sadržaj sažetaka.

AN IMPERATIVE OF QUALITY AND SAFETY WITHIN THE HEALTH CARE

Dorjan Marušič

Expert Panel at European Commission DG for Health and Consumers (DG Sanco), Slovenia

Improving quality and ensuring safety in health care represent a priority activity in all EU health systems. Consideration and introduction of internationally accepted principles of quality is the simplest way to provide quality health care: the best possible care with the best possible outcomes that people receive when it is needed. Such a level of service represents the optimal use of available resources and therefore should be the main objective of the operations of all parts, and thus the health care system from the steward via the payer to a single member. The Ministry of Health as a steward over strategic and legislative changes, the payer with a fair system of financing for the promotion of quality and secure methods of treatment as well as heath care providers - contractors with the optimal and rational use of all resources. Ensuring quality and safety in health care organization based on equal participation and interference of knowledge of all employees in the management processes for coordinated action by individual articles within the business. Thus, the results will be approaching the expectations of users – citizens in the healthcare system.

ISPOR RARE DISEASES SPECIAL INTEREST GROUP REPORT: CHALLENGES IN ASSESSING AND APPRASING RARE DISEASE DIAGNOSTICS & TREATMENTS

Zoltan Kalo

Syreon Research Institute, Hungary

Eotvos Lorand Tudomanyegyetem, Department of Health Policy and Health Economics, Hungary

An ISPOR Rare Diseases Special Interest Group (RD SIG) was initiated in June 2013. The first two objectives of RD SIG were to 1) review terminology and definitions of rare diseases and 2) to summarize challenges in assessment and appraisal of diagnostics and treatments in rare diseases. The presentation provides a summary of findings related to the second objective.

Attention to rare diseases has led to a substantial increase in the number of diagnostics and treatments. As the technologies have become available, a number of challenges become apparent in research, development and health technology appraisal (HTA) in rare diseases. These challenges confront multiple concerned stakeholders: regulatory bodies, HTA agencies, payers, industry, healthcare providers, academic, researchers and advocacy organizations, patients and their families.

Challenges were classified in two main categories: research-related and HTA-related. Among research-related challenges six major disease-related challenges and six major treatment-related challenges were identified. These obstacles, along with fundamental issues related to equity, lead to a great deal of uncertainty about safety and effectiveness, and consequent value assessment, which in turn have a negative impact on societal availability and patient access.

Not all the challenges will have a resolution that is entirely satisfactory to all relevant stakeholders. However, working together to fully identify and explore possible solutions will be an important next step in advancing the diagnosis and treatment in rare diseases.

CAN WE ASSURE AFFORDABLE AND TRANSPARENT PATIENT ACCESS TO INNOVATIVE TECHNOLOGIES WITHOUT EFFICIENT HTA SUPPORT?

Siniša Varga

Croatian Parliament

The Croatian Healthcare system has been ranked very high by the Euro Health Consumer Index in 2015 (4th place B4B, 16th place overall) with only 6,7% GDP per capita expenditure totaling just under 3 billion € for the population of 4,3 million with an average life expectancy at birth of 78.

Health technology assessment is becoming more important as rationale for setting standards for affordability and transparency of the healthcare system.

Demographic changes towards a predominantly elderly population demanding life extension is straining all healthcare financing systems globally.

Innovative technologies including personalized treatment regimens require a structured efficient HTA system in order to support the decision making process.

A major goal of the Croatian healthcare system is to increase life expectancy at birth from the current 78 to 80 years in the next 5 year period. Patient access to innovative technologies plays a major role in reaching this goal. HTA is the means by which government policies and payer decisions will be made in choosing which new drugs, technologies and procedures will be introduced (and which will be made obsolete) in order to maintain sustainability of the healthcare system without putting additional out-of-pocket financial burdens on patients.

STRENGTHS AND WEAKNESSES OF HTA IMPLEMENTATION IN HUNGARY

Bertalan Nemeth[1], Marcell Csanadi[1], Zoltan Kalo[1, 2]

[1] Syreon Research Institute, Hungary
[2] Eötvös Lóránd Tudományegyetem, Department of Health Policy and Health Economics, Hungary

OBJECTIVES: Our objectives were to assess the current implementation of health technology assessment (HTA) in Hungary, to identify country-specific patterns of challenges and potential improvements.

METHODS: We applied a structure that can be used to create HTA implementation roadmaps to evaluate various issues regarding HTA implementation. We gave a comprehensive description of the Hungarian HTA system according to relevant literature and the experiences of authors.

RESULTS: By investigating eight main components of HTA implementation we identified the most important strengths and weaknesses of the Hungarian system. More specifically we analyzed the emergence of HTA capacity, the establishment and current role of Department of HTA, the complex process of decision making, the quality elements developed in the near past and the activity of Hungarian experts at international collaborations.

CONCLUSIONS: We concluded that there is a sophisticated methodological and educational basis for HTA in Hungary. A permanent focus on capacity building and changes to the reimbursement procedure can further improve transparency and the scientific basis of decision making in the country.

THE FUTURE CHALLENGES IN HTA

Valentina Prevolnik Rupel

Institute for Economic Research, Ljubljana, Slovenia

Research activity in HTA varies considerably across Europe. An ageing population and diminishing workforce both require strong efforts to ensure effective and well-organized use of human resources and technologies in health care together with high need for innovative approaches toward health care delivery.

EU recognized the importance of HTA in article 15 Directive 2011/24, where it decided to support cooperation between national HTA Authorities, support member states in the provision of objective, reliable, timely, transparent , comparable and transferable information […] to enable effective exchange of information and avoid duplication of assessments.

While EunetHTA JA1 goal was mostly to develop tools for the HTA studies, JA2 tested the use of prepared tools and models on international level: as of March 2016, EUnetHTA has finalised 20 joint assessments: 2 joint assessments during EUnetHTA Project (2006-2008), 3 joint assessments during EUnetHTA JA1 (2010-2012) and 15 joint assessments during EUnetHTA JA2 (2012-2015). EUnetHTA JA3 goal is to translate pilots and projects into structured collaboration and coordination in HTA field among members states – the processes that lead to decision making in financing of health care technologies need to be improved to be able to successfully manage general challenges of the future.

CHANGING BIOLOGIC LANDSCAPE

Davor Plavec

Children's Hospital Srebrnjak, Zagreb, Croatia

Biologic drugs are almost on a daily basis changing the treatment of chronic inflammatory diseases. Originators are uniquely identified and differ in structure, have different mechanisms of action and undergo the same full clinical development pathways required for regulatory approval. Their switching typically only happens for medical reasons. During the last years biosimilar drugs developed by the process of reverse engineering or recreating the innovator's product, started entering the market. Biosimilar is not a generic equivalents of an original biologic drug because biologics are highly complex molecules produced in living cells and they significantly differ based on the manufacturing process. Different regulatory agencies approved biosimilar drugs for the market with different extrapolated indications based on the data from clinical trials of an original biologic drugs. Some of them even approved interchangeability. This regulatory situation is raising a lot of different efficacy and safety concerns. These concerns are based on the facts that immunogenicity of biologics is largely unpredictable and influenced by many factors that we still don't fully understand, that we are lacking a thorough risk–benefit analysis and robust post-marketing risk management programs for biosimilars. We are lacking the ability to trace all biologics/therapies as there is no clear consensus from regulatory authorities on nomenclature and no mandates for registries. Physicians and hospital pharmacists should remain alert to unexplained changes in drug efficacy or side effects.

SIGNIFICANT COST SAVINGS POTENTIAL OF BIOSIMILAR DRUGS IN THE LARGEST CROATIAN HOSPITAL

Viktorija Erdeljić Turk

University Hospital Zagreb, Zagreb, Croatia

OBJECTIVES: With the increased availability of biosimilars, the Hospital Drug Committee (HDC) in the largest Croatian hospital made recommendations to prescribers to start therapy with biosimilars in treatment-naive patient. However, the decision for treatment switching was left to the prescriber. The objective of this study was to evaluate the changes in utilization of original biologics and biosimilars between 2014 and 2015 in response to this recommendation, as well as to screen the attitudes and beliefs towards biosimilars among physicians and members of the HDC.

METHODS: Utilization of original biologics and biosimilars was compared between Jan2014-May2014 and Jan2015-May2015. The Laspeyeres, Paasche and Fischer index were calculated. Furthermore, an e-mail based survey was conducted among prescribers and members of the HDC on attitudes towards biosimilars utilization.

RESULTS: The expenditure on biologics with an available biosimilar alternative (epoetins, filgrastim, infliximab), increased by 12% (719,452.29 Croatian Kuna) in the evaluated period. The utilization of original biologics and biosimilars increased significantly, the index of utilization of original biologics and biosimilars in 2015 based on 2014 was 542. There was a marked increase in biosimilars utilisation (index range 115-3478) and a decrease in utilization of original biologics (index range 71-87). The prices of original biologics and biosimilars decreased in the range 8-20% and 4-18%, respectively. Overall, the Laspayeres, Paasche and Fischer indexes were 89.6; the lowest for original eritropoetins 79.9. The survey response rate was 34% (100/298) among hospital physicians and 74% (13/17) among HDC members. The average rating of attitudes toward generics and biosimilars was 3.9 and 3.7, respectively (1-5 scale). Most respondents showed positive attitudes toward using biosimilars for starting as well for switching treatment (72% and 59%, respectively). Most physicians believed that the best modality of biosimilars prescription is leaving the decision to the prescriber (53%). Fifty-two percent of respondents stated that the recommendations of the HDC are evidence-based. Members of HDC rated their attitudes toward generics and biosimilars higher as compared to other hospital physicians (4.2 and 4.5), stated better familiarity with biosimilars, and were more inclined to the use of biosimilars for starting as well as for switching treatment. Furthermore, 46% believed that all patients should receive biosimilars as soon as they become available.

CONCLUSION: HDC recommendations coupled with positive beliefs and attitudes of hospital physicians towards biosimilars resulted in a significant increase in biosimilars utilization on account of original biologics, with limited increase in expenditure.

HEALTH TECHNOLOGY ASSESSMENT IN CENTRAL AND EASTERN EUROPE: THE CASE OF THE SECOND GENERATION BIOLOGICALS AND THE BIOSIMILARS

László Gulácsi

Department of Health Economics,
Corvinus University of Budapest, Hungary

This presentation describes and discusses the development and use of health technology assessment (HTA) in the Central and Eastern European countries (CEE) with particular emphasis on transferability of the results of the cost-utility analysis of biologicals and biosimilars from other jurisdictions. In some extent financing thresholds issues also covered.

It offers an overview of similarities and differences between the individual CEE countries and discusses in detail the role of HTA by assessing its formalization and institutionalization, standardization of methodology, the use of HTA in practice and the degree of professionalization of HTA in the region. It finds that HTA has been to some extent implemented in all countries in CEE, with methodologies in accordance with international standards, but that challenges remain when it comes to the role of HTA in health care decision-making as well as to human resource capacities of the countries.

Suggestions are provided to strengthen HTA in CEE countries through cooperation, mutual learning, a common accreditation of HTA bodies and increased network building among CEE HTA experts.

REVIEW OF STUDIES ADDRESSING MONOCLONAL ANTIBODIES SWITCHING: WILL WE GET AN ANSWER?

Tomislav Laptoš

University Medical Centre Ljubljana, Ljubljana, Slovenia

OBJECTIVES: With infliximab as the first monoclonal antibody biosimilar being introduced in clinical practice in 2013 there are still questions raised regarding their use, especially interchangeability with their reference product. Without clear guidelines from EMA regarding the switching and different approaches from local medicine regulatory agencies the ongoing switching studies may provide some insight.

METHODS: On-going or planned studies including reference product infliximab and biosimilar infliximab were identified using EU or local clinical trial registries. Studies designs, inclusions and exclusion criteria and objectives were reviewed.

RESULTS: Three studies including patients with rheumatoid arthritis (RA), spondyloarthritis (SpA), psoriatic arthritis (PsA), Crohn's Disease (CD), Ulcerative Colitis (UC) and chronic plaque psoriasis were identified. Methotrexate (MTX) concomitant use when applicable as inclusion criterion was not conclusive across the studies.

The IFX4501 open-label, multicenter study will include up to 150 adult patients with CD, UC or RA in stable remission currently treated with reference infliximab. They will all be switched to biosimilar infliximab. The infliximab serum concentrations, antibody to infliximab (ATI) levels and disease activity scores will be compared to baseline.

Similarly, a parallel observational multicenter BIO—SWITCH study will include up to 200 adult participants with RA, SpA and PsA currently treated with innovator infliximab. They will be either switched to biosimilar infliximab or continue with the existing therapy. Primarily, disease activity scores will be compared at follow up to baseline for both arms as well as ATI levels and adverse and serious adverse events.

The NOR-SWITCH randomized double blind study with up to 500 included adult participants with RA, SpA, PsA, UC, CD and psoriasis is expected to give results in early 2017. Patients that have been on stable reference infliximab treatment are either switched to biosimilar infliximab or continue with reference product. Primary end points include occurrence of disease worsening based on appropriate disease activity scores during the 52-week study period. The study aims to evaluate safety and immunogenicity and cost-effectiveness of reference and biosimilar infliximab among other objectives.

CONCLUSION: The studies outcomes will shed light on the efficacy and safety of single switch from reference to biosimilar infliximab and most likely influence prescribing in Europe. However, as the study designs might not reflect real life situations of multiple switching, the practitioners may still be faced with current dilemmas.

WHOSE QUALITY OF LIFE MEASUREMENTS TO USE IN HEALTH TECHNOLOGY ASSESSMENTS: ONES ELICITED FROM PATIENTS OR FROM GENERAL POPULATION?

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Health technology assessment is the process in which we try to decide on the basis of thorough analysis whether it is worth financing a certain healthcare technology from public sources or not. In the process the technology is looked at from various angles, and one of the most important one is patients' perspective as they are the central reason of why we introduce the technology at all. There are different ways of including patients in the HTA process, however, there are claims from patients' side that »they are not being listened to as nothing changes«. The presentation will open the debate on the best way to include patients in the decision making processes by presenting the results of the empirical analysis of differences in preferences towards health states between patients and general population. The arguments for using one or the other will be explored and it will be shown that patients are more experienced in valuing health states and using general population values for priority setting hence does not prove to be valid.

LESSONS TO LEARN FROM THE FIRST FIFTEEN YEARS OF EQ-5D IN CENTRAL AND EASTERN EUROPE

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The presentation provides a systematic review and analysis of the use of the EQ-5D questionnaire eight Central and Eastern European (CEE) countries (Austria, Bulgaria, Czech Republic, Hungary, Poland, Romania, Slovakia, Slovenia. Altogether 143 studies (152 country-specific results) were retrieved involving 81,619 respondents. Cardiovascular, neurologic and musculoskeletal diseases were the most frequently studied clinical areas. Hungary and Poland emerge from the other countries of the region, especially with regard to the number of publications, sample sizes, covered clinical areas and methodological expertise. Overall an increasing use of EQ-5D is observed throughout CEE. However, population norms and national value sets are available only in three and two countries, respectively. Improvement in methodological quality of reporting and collaboration between CEE countries should be strengthened.

QUALITY OF LIFE INDICATORS IN SHARE AND THEIR DETERMINANTS

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Quality of life is a multidimensional concept, that can be defined in many ways, making its measurement and incorporation into scientific studies difficult (see e.g. Theofilou, 2013). These evaluations include one's emotional reactions to life occurrences, disposition, sense of life fulfilment and satisfaction, and satisfaction with work and personal relationships (Diener, Suh, Lucas & Smith, 1999). In our study we use CASP-12 (CASP stands for‚control',‚autonomy',‚pleasure' and‚self-realization') index which is a broadly accepted composite measure of quality of life and use data from Wave 5 of SHARE (Survey of Health, Ageing and Retirement in Europe) to study determinants of this index. We assume socioeconomic indicators will not be sufficient to explain the variation in the level of this index, but also institutional, health, leisure and other indicators will have a significant influence. We furthermore explore the correlation of CASP-12 (which is an individual-based measure) to happiness indicators using Veenhoven's database on happiness which is a country-based dataset (the data are on country level and don't vary by individuals). In this manner we are able to determine the distinction between quality of life on individual as well as country specific level. In conclusion we provide discussion and policy relevance of the study.

IMPACT OF PATIENT SUPPORT PROGRAM USE ON CLINICAL OUTCOMES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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OBJECTIVES: To assess the impact of a patient support program (PSP) on adalimumab (ADA) effectiveness for RA treatment in routine practice.

METHODS: PASSION (NCT01383421) is a post-marketing observational study to explore and describe the effectiveness of ADA on the course of RA treatment and patient satisfaction over time in the context of utilization of the PSP. The study enrolled patients (pts) with active RA with an insufficient response to standard treatment and initiated ADA therapy. ADA was prescribed according to the local product label and participants had an option to utilize the PSP. The PSP comprised "Core elements" (starter pack, call center/hotline, nursing services, educational material, and injection guide) and "Other elements" (eg, refill reminders, email, newsletters). The primary endpoint is the % of pts achieving the minimal clinically important difference (MCID; improvement of ≥0.22) in the Health Assessment Questionnaire Disability Index (HAQ-DI) at week (wk) 78 vs baseline (BL). Secondary clinical parameters include % of pts achieving MCID in HAQ-DI at other timepoints vs BL and changes in the 28-joint Disease Activity Score (DAS28), Simplified Disease Activity Index (SDAI), and Clinical Disease Activity Index (CDAI).

RESULTS: 852 pts completed 52 wks of treatment. Mean BL disease scores were 1.5 for HAQ-DI, 5.3 for DAS28 based on C-reactive protein (CRP), 35.8 for SDAI, and 33.4 for CDAI. Overall, 49.9% of enrolled pts utilized the PSP. Improvement in physical functioning was greater at all study time points in pts utilizing the PSP vs those who were non-PSP users, as reflected by mean decreases of 0.61 and 0.46, respectively, in HAQ-DI from BL to wk 52 (P=0.07). More pts using the PSP achieved an MCID in the HAQ-DI vs non-PSP users (73.8% vs 67.2%) at wk 52 (P=0.18). Significant changes (P≤0.005) from BL to wk 52 were observed for pts using the PSP vs non-PSP users in DAS28(CRP), SDAI, and CDAI scores. Study discontinuation rates were significantly (P=0.003) lower among PSP users vs non-PSP users.

CONCLUSIONS: In pts with active RA who initiated ADA, better improvement in functional and clinical outcomes was achieved in the PSP users vs the non-PSP us-

ers. Improvements were maintained at all time points throughout the study, most likely due to better adherence rates among PSP users. The findings have health economic implications as poor disease control equates with higher healthcare costs. PSP should be therefore be integral to RA management.

PATIENT REPORTED OUTCOMES IN (OLDER) DIABETIC PATIENTS IN SLOVENIA

Eva Turk

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The aim of the study was to measure patient reported outcomes, such as health related quality of life (HRQoL) of older diabetic patients in Slovenia. We conducted a cross-sectional study of diabetes mellitus patients. The Audit on diabetes-dependent quality of life (ADDQoL) and EQ-5D surveys were the applied questionnaires. A total of 563 patients participated in the study, of which 482 (85.6%) were diabetes mellitus type 2 patients, ranging from 22-93 years (average 61.9 +/-12.8). Twenty four (4.3%) patients reported no impact of diabetes on their HRQoL at all, while in the remaining respondents, particular reference was put to the effects on freedom to eat, dependency on others and family life.

The findings of the present study highlight the impact of diabetes mellitus on HRQoL. Diabetes Mellitus imposes a personal burden on individuals. Information on the quality of life of diabetes patients is important to Slovenian policy makers and family physicians in order to identify and implement appropriate interventions for achieving better management of diabetes and ultimately improving the HRQoL of diabetes patients.

NEW REGULATORY DEVELOPMENTS FROM THE PAYER'S PERSPECTIVE

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Current EMA projects on establishing adaptive pathways to marketing authorisation have been observed by the payers and nongovernmental organizations with concerns. They will result in lowering the standards for regular marketing authorisation and providing less data on drugs. There are already concerns with the established modified - conditional approvals. In the recent article problems with drugs approved conditionally by EMA were presented (1). There were delays or discrepancies in the fulfilment of EMA's obligations in more than one third of the authorisation procedures. Speeding up access to new medicines via adaptive pathways is to be achieved by using data based on phase II clinical data. It was shown that the combined success rate at Phase III and submission has fallen to around 50%. Two thirds of are terminated due to lack of efficiency, more than 20% due to safety issues (2). This clearly proves that preliminary data from earlier phases of development overestimate the potential benefit of a treatment and do not allow a robust assessment of risks and benefits. Studies with smaller populations will lead to fragmentation of populations and extrapolation of results. Finally, adaptive licencing will result in shift of costs on public payers. Managed Entry Agreements and new financing schemes are supposed to support reimbursement but they bear high transaction and administrative costs and are not easily implemented.

1. Banzi R, et al. Approvals of drugs with uncertain benefit–risk profiles in Europe, Eur J Intern Med 2015; http://dx.doi.org/10.1016/j.ejim.2015.08.008

2. Arrowsmith J. Trial watch: Phase II failures: 2008–2010. Nature Reviews Drug Discovery 2011; 10, 328-329; http://dx.doi:10.1038/nrd3439

THE EVIDENCE-INFORMED POLICY NETWORK – ITS CONTRIBUTIONS TO STRENGTHENING EVIDENCE-INFORMED POLICY-MAKING IN SLOVENIA

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Policies influenced by sound scientific evidence and best practices significantly improve the achievement of positive public health outcomes. Research, however, does not automatically feed into policy and practice, e.g. 30-40% percent of patients in Europe fail to receive cost-effective interventions justified by the best-available scientific evidence.

In order to promote the systematic and transparent use of research evidence in policy and practice, the World Health Organization (WHO) Regional Office for Europe launched in 2012 the Evidence-informed Policy Network. EVIPNet Europe is a regional network that aims to increase the capacity of its member countries to develop health policies based on the best available evidence. Country-specific activities commenced in Slovenia, one of the network's focus countries, in 2013. A situation analysis on evidence-informed policy-making (EIP) was conducted, based on which an initial proposal to institutionalize EIP through the establishment of an EIP advisory body – so-called Knowledge Translation Platform – was presented. In parallel, a first evidence brief for policy on primary health care was performed, feeding into the health system reform process.

The evidence briefs for policy summarize the best available global and local evidence on a high priority issue in a systematic and transparent manner and present the evidence in a user friendly way to catalyze research uptake. In contrast to Health Technology Assessment (HTA), which have been successful in informing clinical policy-making, guidelines development and reimbursement decisions in many countries in relation to drugs, vaccines, devices, clinical interventions and some public health programs like screening and vaccination, EVIPNet evidence briefs for policies support decision-making related to the "higher level" health management and health system interventions. In both cases, it is important to consider that evidence is but one factor influencing the policies. A wide variety of factors on the individual, organizational as well as system level come into play such as values, beliefs and resources, which impact how and to what extent research is being used.

PHARMACEUTICAL PRICE SCHEMES IN EUROPE: TIME FOR A 'CONTINENTAL' ONE?

Livio Garattini

Mario Negri – Institute for Pharmacological Research, Italy

Regulation schemes for drug prices have been an unavoidable policy response to control public health expenditure. Here we discuss the current EU price schemes starting from three main conceptual approaches to price a good.

The cost-based pricing approach implies that the price of a product reflects the sum of its main cost items. A reference-based pricing (RbP) approach can be applied to clusters of products competing with each other in the same 'market arena'. The value-based pricing (VbP) approach aims at setting a price mainly on the perceived value of the product to the customer.

Negotiation has now become a major common feature in most EU countries for price setting. The lack of transparency caused by national negotiations has hidden the true prices of many new drugs and jeopardized all traditional price schemes. Here we put forward a very general proposal for a European price scheme for new drugs. A first reasonable step could be to classify new drugs approved at European level according to their potential innovation: i) drugs offering more limited therapeutic gains; ii) innovative drugs addressing important 'unmet needs'. The first group of drugs could be subject to RbP based on the actual prices in domestic markets, the second to VbP by estimating a 'cost per QALY' from the third payer's perspective on the basis of economic data sourced from a basket of countries.

EVOLUTION OF EXPENDITURES FOR PRESCRIPTION PHARMACEUTICALS IN SLOVENIA: SEPARATING THE CONSUMPTION, PURE PRICE AND PRODUCT MIX EFFECTS

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OBJECTIVES: The key objective is to investigate pharmaceutical expenditure in Slovenia in the 2001-2015 period and selected sub-periods. The analysis focuses on the dynamics and breakdown of expenditures on prescription pharmaceuticals but is coupled also with the examination of expenditures for OTC medicines and medicines consumed in the hospital setting.

METHODS: Expenditure growth for prescription pharmaceuticals is decomposed into three components including quantity growth where consumption of pharmaceuticals is measured in the number of defined daily doses (DDDs), price changes calculated by the Laspeyres price index and changes in the mix of pharmaceuticals.

RESULTS: Following the 2008 economic crisis, health spending has slowed notably across Europe after years of continuous growth. This slowdown affected all health spending categories but to varying degrees also in Slovenia. According to data of the Health Insurance Institute of Slovenia, consumption of prescription pharmaceuticals has been on the rise both before and after crisis. Expenditures, however, started to decline after crisis. In the 2009 2015 period, total expenditures for prescription pharmaceuticals decreased by 4%, which is about -1% annually on average. The decomposition of this decline shows that a 13% increase in the quantity of consumed medicines was accompanied by a 34% decline of their prices and a mix effect that pushed the expenditures upwards for 28%. The mix effect reflects changes in the structure of consumed medicines due to regulation and also entry and exit of pharmaceuticals. The mix component has offset a substantial part of the decline in prices of prescription pharmaceuticals.

The decrease of expenditures for prescription pharmaceuticals was coupled with a notable rise of expenditures for OTC medicines, i.e. 12 percent annually on average in real terms in the 2008-2013 period. Data on pharmaceutical expenditure from the National Health Accounts does not include the costs of medicines used in hospitals that are part of inpatient spending. On average, these expenditures raise the

pharmaceutical bill by around 20% in OECD countries. Data for Slovenia indicate that costs for pharmaceuticals in hospitals are about one third of the value of all prescription pharmaceuticals currently included in the National Health Accounts.

CONCLUSION: Annual price changes and the altered structure of consumption explain why Slovenia was able to maintain a positive trend of consumption of prescription pharmaceuticals, while cutting total expenditures for prescription pharmaceuticals since 2010.

THE COST-UTILITY ANALYSIS OF MEDICAL EQUIPMENT IN CROATIAN HOSPITALS (AUG 2014 – JULY 2015)

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Medical equipment usage and status together with doctors' performance and efficiency have not been analysed since recently. The new team in the Cabinet of Minister of health decided to make such an analysis to enable decision-making processes. The decisions regarding equipment purhcasing and human resources planning were on top of our priorities inside the hospital sector. Long wait-list in elective care could not be adressed without these data, also.

The Ministry of health organised and coordinated these activites for various types of exuipment and medical activities. Most of the analyses were done in field of radiology, cardiology, gastroenterology, neurology and ophtalmology. The reason for that is a continous and high demand from patients on mentioned areas of hospital services.

Results were collected, analysed and presented to all the hospital directors first, and in public medica later on. This data served us and the hospital directors in better planning of providing public health-care services, equipment tendering and human resources planning. The data have shown a great variability in performance between hospitals. Secondly, results have shown a significant room for improvement of doctors' efficiency and performance. Alltogether, with other set of activities in the Cabinet, we have provided one million of hospita services more in 2015 compared with 2014, what presents an increase of 11 %.

PATIENT ACCESS TO MEDICINES FOR RARE DISEASES IN SLOVENIA

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Medicines for rare diseases (RD) usually represent the only treatment possible for a certain RD. The incentives in development of medicines for RD are increasing and today these medicines represent around 20% of all innovative medicines. Therefore, countries are facing challenges in providing patient access to these technologies. While different countries have different health technology assessment processes and decision-making policies, the purpose of the study was to assess the patient access to medicines for RD in Slovenia and compare their market introduction with selected European countries in the last decade.

The medicines for rare diseases that obtained marketing approval between 2005 and 2014 via centralised procedure at EMA were included in the study. Further, the IMS Health database was used for first launch and sales data in Slovenia and the selected European countries that represent important European pharmaceutical markets (France, Germany, Netherlands, Norway, Sweden and United Kingdom) and the neighbouring countries. The number of medicines present in each country and time to first launch were compared between the countries.

In total, 125 medicines for RD were approved between 2005 and 2014. Among them, 71 have orphan designation and 54 are non-orphan medicines. Due to lack of sales data in all the countries five products were excluded from the comparison between the countries. Of the remaining 120 products, Germany and the United Kingdom have introduced around 70 %. In Slovenia, 66 (55%) of all the medicines for RD were launched – 40 orphan and 26 non-orphan. Among medicines available, 50 medicines (76%) were placed on one of the reimbursement lists. The analysis of times to launch between the countries revealed that the two leading countries in the number of accessible medicines (Germany and the United Kingdom) were also one of the the fastest in introducing them to the market. Slovenia offers a comparable number of medicines for RD to Sweden, France and Italy and made available more medicines than the other neighbouring countries. The total pharmaceutical expenditure for these medicines in 2015 in Slovenia amounted to around 44 million euros.

In Slovenian healthcare system patient accessibility to medicines for RD is good – more than a half of the medicines approved in Europe are accessible to the patients which ranks Slovenia in the middle. However, it takes longer to introduce these medicines to the market than in the other important European pharmaceutical markets.

ESTIMATING THE VALUE OF EVIDENCE: A CASE OF PHARMACOGENETIC DOSING OF WARFARIN

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When a new health technology seeks reimbursement, it often goes through extensive evaluation such as health technology assessment. The most valuable seems to be the estimation of benefits and financial costs, often combined in a cost-effectiveness analysis. An important part is also the assessment of surrounding uncertainty which emerges from the parameter variability. With measuring expected cost of uncertainty, interpreted as expected value of perfect information (EVPI), we can determine the financial consequences of taking the decision. We estimated the EVPI about clinical benefits of pharmacogenetic (PG) dosing of warfarin. The estimation was made twice, first after early clinical trials and second after relatively big randomized clinical trials had been published. First assessment included evidence available up to 2007 and revealed that EVPI for clinical benefit of PG dosing would be around 80 EUR. That is also the amount that a decision-maker would be willing to pay for additional research which should completely resolve the uncertainty about clinical benefit of PG dosing. However, if the costs of the research exceed EVPI, it would be rational to make a decision, take over the possible opportunity costs of the decision made and not investing into additional clinical trials. Nevertheless, after 2007 several clinical trials have been conducted. Each trial contributed to the more precise estimation of clinical benefits, but overall it had minor effect on EVPI. This means that these trials do not represent a significant value for the potential founders of this novelty. However, several other parameters and their variability might also be important for reimbursement decision makers as they directly impact the result of a cost-effectiveness analysis. One of such is the price of PG testing which reduced significantly in the recent years and can therefore affect the reimbursement decision.

EXTRAPOLATION OF SURVIVAL OUTCOMES IN COST-EFFECTIVENESS MODELLING OF CANCER TREATMENTS

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Pharmacoeconomic modelling of cancer treatments is often based on survival analysis of clinical outcome data; namely, overall survival, progression free survival or time to subsequent cancer therapy analysis. A parametric survival function such as Weibull, Generalized Gamma, Lognormal, Log logistic, Gompertz or Exponential function, are commonly assumed and tested for goodness of fit for the baseline treatment in clinical practice. In order to evaluate new treatment a hazard ratio is estimated from clinical trials or meta-analysis and applied to the to the survival function of baseline treatment on the basis of proportional hazard assumption. This assumption can be validated for the time period of the data from clinical trials. However, as a time horizon in cost effectiveness study is normally set to lifetime, an extrapolation of the survival curves is needed. Violations of the constant hazard ratio can lead to biased estimates of cost-effectiveness results. The strengths and weaknesses of survival data extrapolations were shown on a case clinical data of new cancer treatment; olaparib (PARP inhibitor). Patients' survival time was estimated using four state Markov model; maintenance therapy, first subsequent chemotherapy, second subsequent chemotherapy and death. Significant differences in mean but not median survival times were observed using various survival functions and survival modelling approaches.

CHALLENGES RELATED TO MEDICINE PRICE AS THE INPUT PARAMETER IN COST-EFFECTIVENESS ANALYSIS

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Medicine cost could be a key factor affecting Incremental Cost-effectiveness Ratio (ICER); therefore it should reflect the actual medicine price whenever possible. The price included in the analysis depends on transparency of actual medicine prices in a selected country. In addition, discounting as a parameter related to medicine cost affects the result of cost-effectiveness analysis (CEA). The purpose of the presentation is to present the effect of medicine cost input parameters on the results of CEA. The effect of following medicine cost parameters were evaluated in the CEA: use of different medicine price types, inclusion (exclusion) of value added tax, and application of different discount rates. Models from the literature or our own were used in order to simulate the results. Examples of CEA including strategies which differ in proportion of medicine cost in relation to all costs and CEA differing in time of health gains of the new medicine were selected for this purpose. Inconsistency in the application of the same price level affects ICER the most when medicine cost presents the majority of the total costs. This is more likely to be the characteristics of new and innovative medicines. The use of different price level, for example including (excluding) value added tax is recognized as a change of the ICER for the same proportion irrespective of whether the cost increment is high or low. However, the absolute value of ICER depends on the amount of cost increment, as higher cost increment means higher ICER. Including value added tax could therefore result in that the suggested cost-effectiveness threshold is exceeded. In the case of Slovenia, value added tax could affects result even for the high priced hospital medicines, as it is reimbursed by the Health insurance institute. Furthermore, the difference in discounting affects the results of CEA analyses regardless of the time when the health gains of the new medicine occur, however the more distant are health gains the greater is the impact. Therefore, the greatest impact appears in the case of prevention or screening programmes, such as infant vaccination programmes or cancer screening. The guidelines on the uniform application of the CEA analysis should be established in order to obtain comparable and transparent results.

BIG PROBLEMS OF SMALL COUNTRIES: IMPOSSIBILITY OF DISCRIMINATION BY DIRECT SEGMENTATION

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OBJECTIVES: To show how the legal and institutional system of the European Union prohibiting price discrimination of third degree, i.e. direct segmentation according to country of origin, has a negative impact on smaller markets, and to find alternative marketing, bundling, distribution, pricing, and reimbursement policies acceptable for both producers and national health providers.

METHODS: A theoretical approach is supported by a practical example. A game theoretical approach is used to find optimal producer and national health provider policies and game equilibria.

RESULTS: High wage, high income countries have higher health opportunity costs, higher willingness to pay and higher capabilities to pay, i.e. their demand curves are above the curves of lower income countries and have lower elasticities. Without discrimination and resale, low income countries as price-takers, face higher prices of pharmaceuticals than they alternatively would have. Common market nationals cannot be charged higher prices because of their nationality or country of residence, but discrimination according to some other criteria is permitted! Such direct segmentation price discrimination would enable low income countries to pay lower prices. Alternative bundling and marketing methods for pharmaceuticals may bring benefits for both consumers and producers. To circumvent the non-discrimination clause, instead of direct pricing, the industry needs to bundle the pharmaceuticals horizontally and vertically with other services to the point where no direct product costing may be established. The pay per cure reimbursement method guarantees efficient results, and new efficient therapies enable such policies. Differences in wages due to Balassa-Samuelson and Baumol-Bowen effects may mask the underlying direct segmentation discrimination. A cooperative approach of several smaller countries vs. the pharma industry and their common negotiation of prices may additionally provide for even lower costs.

CONCLUSION: Third degree price discrimination requires the supplier to have enough market power to be able to set different prices to different groups of consumers as well as the ability to prevent resale. These practices are on the common

market clearly prohibited. In the particular case of pharmaceuticals, a price discrimination of third degree is of interest to both pharmaceutical companies and national health providers. Competition and new pay-per-cure reimbursement methods reduce not only prices, but also its variance, reducing thereby the overall risk for the national health providers.

REIMBURSEMENT POLICIES FOR ONCOLOGICAL DRUGS: WHERE TO GO?

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Oncological drugs have had a tremendous impact on the advancement of the global health care within the last decade. It is thus a prerogative that the new oncological drugs are made continuously accessible to the patients, while also taking into account the sustainability of the reimbursement systems.

In this presentation, various policies which are currently used by the authorities to reimburse innovative oncological drugs will be critically assessed. Special care will be given to understanding the value-based pricing (VBP) as one of the central tools, which have been widely applied in assessing the innovativeness of new technologies. Several challenges that VBP poses on novel cancer treatments along with potential solutions will be discussed. Among others, we will argue that when estimating economic value of innovative cancer care, its impact should be broadened by considering both benefits and costs beyond the healthcare system.

PERSONALIZED MEDICINE AND ECONOMIC EVALUATION IN ONCOLOGY: ALL THEORY AND NO PRACTICE?

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The clinical definition of personalized medicine (PM) is closely related to that of pharmacogenomics. Ideally, PM could lead the pharmaceutical industry to differentiate products by subgroup of patients with the same pathology and find new gene targets for drug discovery.

Here we focus on the potential impact of PM on the design of clinical trials and economic evaluations limited to oncology (its first and main field of application). Then we assess the European economic evaluations focused on trastuzumab (TR) and cetuximab (CX), the two drugs usually mentioned as emblematic examples of targeted therapies. Clinical results of PM in oncology have not been as encouraging as hoped so far. Of course, economic evaluations on targeted therapies cannot help overcome the lack of clinical evidence for most of them. The two paradigmatic examples of CX and TR indicate that the methodological implications on economic evaluations debated in the literature are more theoretical than practical.

EXPENDITURES FOR ONCOLOGY DRUGS VERSUS OUTCOMES IN SOUTH EAST EUROPE, IS THERE A MISSING LINK?

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INTRODUCTION: Public health expenditures for treating oncology patients is already significant and with rising trend. The overall risk of dying from the malignant disease is decreasing in Europe, due to improvements in screening, diagnosis and treatment, however important variations between countries still remain despite the increased level of investments. There are number of publications demonstrating regional and national differences in cancer survival rates in Europe, stimulating public debates and political actions towards designing new policies to reduce regional and international variances in health outcomes.

OBJECTIVES: The objective of this study was to analyze the utilization of oncology drugs during the five years period in selected South East Europe countries (Croatia, Romania, Serbia and Slovenia) in correlation with observed outcomes in order to assess country specific effectiveness of healthcare interventions in oncology.

METHODS: Drug utilization data at the molecule (INN) level used in this study are derived from the IMS database and are presented in volume, as days of treatment (DOTs) and in value, as consumption in Euros (€).While more comprehensive study is still being conducted, the pilot analysis presented here included only L02 group (endocrine treatment), being of appropriate size and with a good mix of innovative and generic drugs. From the outcome perspective the following diseases, mostly connected to the utilization of L02 drugs, have been analyzed: breast, prostate and endometrial cancers.

RESULTS: There are significant differences and trends observed over the five years period in the parameters analyzed in this pilot study:

	Life expectancy (years)	Incidence* (per 100.000)	Mortality* (per 100.000)	Positive outcome'** (per 100.000)	Positive outcome'** (as % of incidence)	Volume investment - DOT per capita change (5y period)	Value investment - Price per DOT change (5y period)	Cost of 'positive outcome' (€)	Difference to Slovenian investm. per 'positive outcome' (€)	Positive outcome gain'** (per 100.000) with Slovenian investm.	Positive outcome gain'** (in abs.terms) with Slovenian investm.
Croatia	78	173,5	55,0	118,5	68%	13%	-46%	1.912	815	10,7	453
Romania	74	115,7	40,3	75,4	65%	24%	-35%	1.611	1.115	10,7	2.139
Serbia	75	172,5	58,5	114,0	66%	29%	-27%	559	2.168	14,4	1.029
Slovenia	80	234,1	59,8	174,3	74%	2%	12%	2.727	n.a.	n.a.	n.a.

CONCLUSION: Among the analyzed countries, Slovenia appears to be the most effective in terms of ensuring the biggest positive outcome for their patients (difference between incidence and mortality). Although additional parameters have to be included in the analysis, from this pilot study it seems that Health authorities in

Slovenia have achieved the observed positive results by investing in L02 treatments in terms of value, introducing new, more costly but more effective technologies, while maintaining reasonable cost per positive outcome and ensuring positive contribution from the L02 group to overall life expectancy which is respectfully the highest in the SEE region. Ensuring appropriate investment in L02 group could, in absolute terms, prevent death from breast, prostate or endometrial cancer in 452 patients in Croatia, 1.029 in Serbia and 2.139 in Romania. This conclusion could be methodologically challenged for good reasons, but the aim of it is to increase debate and further analysis derived from drug utilization data. Missing links between investment in health and outcomes have to be identified for each country, and are probably related to inefficiencies of (1) national cost effectiveness analysis and lack of threshold indicators, (2) HTA process as a transparent platform for reimbursement decision, (3) stakeholder education, (4) clinical guidelines availability and consistency in implementation, (5) long-term healthcare strategy with key health outcome indicators.

MELANOMA SCREENING – EPIDEMIOLOGICAL IMPACT AND DISEASE COST-SAVINGS

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OBJECTIVES: Melanoma is a malignant skin tumor and it counts for less than 5% of all skin cancers. The incidence of melanoma is growing all over the world, also in Croatia. Due to the increase in the incidence of melanoma it is important to assess the economic impact and the cost of diagnosis and treatment of melanoma. The diagnosis of cutaneous melanoma at an early stage can save lives, reduce treatment costs and generate substantial savings. From 2008 Croatia is part of project „Euromelanoma" for early detection of skin cancers.

METHODS: Melanoma (C43) incidence and mortality data for period 2003-2007 and 2008-2012 were collected. Comparison of incidence and incidence by stages (local disease, regional disease - melanoma with lymph node involvement, distant disease - metastatic melanoma and unknown stage) were made. The source of data is Croatian Cancer data registry which provides national data on melanoma incidence and mortality. Secondary goal was to estimate the costs through types of care and types of costs.

RESULTS: The incidence of melanoma between 2003 and 2007 is 2 420 while in the period 2008-2012 during „Euromelanoma" program is 2 808. In the period between 2003 and 2007 there was 756 local, 377 regional and 234 metastatic melanoma. During „Euromelanoma" program there was 990 local, 499 regional and 213 metastatic melanoma. Total cost of melanoma in the period 2003-2007 was 5 352 243 EUR and 4 983 208 for period 2008-2012.

CONCLUSION: The results show that there is a significant difference in the incidence of melanoma by stages and costs in period without screening period and in the period during the program „Euromelanoma". In Croatia melanoma is still diagnosed in late stages and with poor survival rates. Despite many public health campaigns and education melanoma health burden is still increasing and close monitoring will be needed. The screening of melanoma can save lives, reduce treatment costs and generates significant savings directly and indirectly.

DISCLOSURE STATEMENTS: Goran Benčina is employee of the GlaxoSmithKline group of companies. GlaxoSmithKline was not involved in any stages of study conduct, including analysis of the data.

COUNSELLING OF ONCOLOGY PATIENTS BY THE ONCOLOGY PHARMACISTS AT THE CLINIC FOR TUMORS, UNIVERSITY HOSPITAL CENTRE SISTERS OF MERCY, ZAGREB, CROATIA

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INTRODUCTION: In the past ten years the oncology pharmacy in Croatia has been developing rapidly and intensely. It has been recognized by physicians, medical oncologists, nurses and health care administration, as well as by the Faculty of Pharmacy and Biochemistry of the University of Zagreb in Croatia. In order to develop this specific segment of pharmacy, we drafted a development plan which encompasses: the central preparation of antineoplastic drugs within hospital pharmacies, the legal regulations related to central preparation, the acceptance and development of multidisciplinary approach in the treatment of oncology patients, optimization of pharmacotherapy, prevention of medication errors, practice at wards which dealt with all the above, and finally, direct interaction and work with the oncology patient and their family together with healthcare personnel involved in treatment of the oncology patient.Patient counselling is intended for all oncology patients and their family members who want to get educated related to over-the-counter drugs and food supplements, whether they were treated in our Clinic or in any other health care institution in the Republic of Croatia.

The title of our project is: Pharmaceutical counselling of oncology patients related to the application and harmonization of drugs and food supplements.

PURPOSE OF THE PROJECT: It is conducted with the purpose of preventing medication errors, drug interaction and coordination of therapy, as well as for the counseling of the patient on how to apply therapy (increase adherence) and education on the need of strict control of herbal drugs and food supplements. Also patients are advised on mitigation of side effects of their officially prescribed pharmacotherapy, which is a very common problem in oncology setting due to low safety profile of antineoplastic drugs. Concomitant use of complementary alternative medicine , often unaware by prescribers, can lead to undesired side-effects, which could then postpone the official therapy. Consequently it can put at stake the outcome and

success of treatment and damage the quality of life of the patient. Money spent in that way is considerable for both the society and for the individual.In case of the analysis of the pharmacotherapy of hospitalized patients, the medical oncologists or any other specialist will send an internal referral slip stating: opinion of the oncology pharmacist requested. Likewise, we shall be on call for the outside patients in the outpatients clinic in the course of the day. Every opinion written by oncology pharmacist has a seal of oncology pharmacy specialist and makes a part of medical documentation of patient.

METHOD: All the official medical documentation is analysed and through the interview with the patient we get insight into all drugs, herbal drugs and food supplements that they take.

RESULTS: Based on the acquired data, we conduct the analysis of pharmacotherapy, herbal drugs and food supplements and we counsel oncology patients and members of their family. Also, we educate patients on proper intake of their therapy.

CONCLUSION: By educating and counselling oncology patients, oncology pharmacists can contribute to positive outcomes of pharmacotherapy. By doing so, they can motivate patients to follow their pharmacotherapeutic plan, provide patients' safety and considerable reduction of overall expenses.These are the main reasons why oncology pharmacists must be part of the multidisciplinary team.

THE ROLE OF CLINICAL PHARMACIST AS A MEMBER OF THE MULTIDISCIPLINARY TEAM INVOLVED IN A TREATMENT OF ONCOLOGY PATIENTS – CASE STUDY

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INTRODUCTION: In this presentation we are going to present two cases form our daily practice regarding counseling of oncology patient at the Clinic for Tumors in Zagreb. Also we are going to show you a role of Clinical pharmacist as a part of multidisciplinary team involved in a treatment of oncology patient.

METHODS: Clinical pharmacist involved in a treatment of oncology patient as a part of multidisciplinary team is going to present two cases of its practice and results of its interventions through two case reports.

RESULTS: In a two presented case participants will have insight on results of work of clinical pharmacist on an oncology ward setting. Results will demonstrate its clear benefit regarding improvement in a treatment efficiency and safety. Consequently, we can expect to have a reduction of treatment expenses.

CONCLUSION: Clinical pharmacist involved in a treatment of oncology patient as a part of multidisciplinary team can improve treatment quality and reduce its costs.

THE IMPLEMENTATION OF HTA IN DECISION MAKING IN HUNGARY

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The Hungarian HTA office evaluates medicines and medical devices for decision makers (Ministry of Human Capacities, Ministry of National Economy, National Health Insurrance Fund) since 01/05/2004, based on the in the year 2002 developed Hungarian Guideline for Health Technology Assessment and internal rules, codes of procedures. Since 2002 approx 1500 medicines and 900 medical devices were evaluated. The acceptance of evaluations of the HTA office is two-sided; both the willingness of decision makers to take output of evaluations into account and the adequate information of HTA to make decision are important and needed.

The presentation is going to introduce the implementation of medical, cost-effectiveness and budget impact evaluations in Hungary, based on our experiences and the main differences between the output of Hungarian HTA, the needs of decision maker and the opportunities are going to presented as well.

IMPACT OF ISPOR TOOLS ON NATIONAL PHARMACOECONOMIC PRACTICES:EXAMPLE CROATIA

Josip Čulig

ISPOR Chapter Croatia

ISPOR is the leading global professional society in pharmacoeconomics and outcome research. Founded in 1995 of multidisciplinary membership, ISPOR advances the policy, science and practice in pharmacoeconomics. The ISPOR Task Forces are helping to drive a discussion for creating incentives in health care systems to achieve better outcomes and creating the tools and systems to measure performance. They develop consensus guideline reports on good practice standards for outcome research and their use in health care decision making processes. Currently, the ten Task Forces are working on new guideline tools and 47 Good Practices on various matters are already available on the ISPOR webpage.

Drug policy in Croatia is regulated by various directives. The important sub-law that regulates drug reimbursement is the Ordinance of the Ministry of Health which establishes the criteria for the inclusion of medicinal products in the Basic and the Supplementary List of the Croatian Institute for Health Insurance (2009, revision 2013). Among those criteria for inclusion is the budget impact analysis (BIA). The two ISPOR Good Practices are directly mentioned as obligatory tools for BIA execution: Principles of Good Practice for BIA (Report of ISPOR Task Force 2007) and the Principle of Good Practice for decision analytic modelling in health-care evaluation (report of ISPOR Task Force 2003). The Principle of Good Practices for BIA II was announced in 2014. Furthermore, some new useful tools were developed, as, for example, the Clinical Assessment in Rare Diseases Clinical Trials, presented at the 18th Annual Congress held in Milan in 2015. Rare Diseases therapies are very expensive and specific, so proper evaluation is needed to preserve the equal position of those drugs on the reimbursement lists of health providers.

This is especially the case for countries with a fragile economy and low GDP per capita. The analytical models are based on the evidenced data from the randomized clinical trials. This is not always identical to real world data. Different ISPOR Task Forces have developed relevant tools to help researches and decision makers providing drug policy according to available databases: for example, Observational Study Database Methods for Use of Real World Data (2007), Design and

Analysis of Non-Randomized Studies of Treatment Effects Using SecondaryDatabases (2009), Multiple Criteria Decision Analysis for Health Care Decisions(2016). The ISPOR Good Practices are useful tools for researchers and decision makers for establishing scientifically founded criteria in creating national drug policies.

METHODOLOGICAL CHALLENGES AND HEALTH POLICY DEVELOPMENT RELATED TO THE IMPLEMENTATION OF MEAS IN SOUTH EAST EUROPE

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INTRODUCTION: Due to recession and cost containment measures in public healthcare funding over the last decade, pharmaceutical expenditure has been in focus of the most European markets despite comprising only the minor part of total public healthcare budget. Alternative funding arrangements were thus needed, in order to minimize the budget uncertainties for the public payers as a prerequisite for the reimbursed access to patients. The variety of different financial models and arrangements are today called Managed Entry Agreements (MEAs). The most commonly used definition of MEA is published by Klemp et al in 2011: *'An arrangement between a manufacturer and payer/provider that enables access to (coverage/reimbursement of) a health technology subject to specified conditions. These arrangements can use a variety of mechanisms to address uncertainty about the performance of technologies or to manage the adoption of technologies in order to maximize their effective use, or limit their budget impact.'*

OBJECTIVES: To assess current methodological challenges and health policy development related to the implementation of MEAs in South East Europe (SEE).

RESULTS AND DISCUSSION: Among several policy challenges identified in the areas of the implementation and monitoring of MEAs, the legal issues emerge as the most important: (1) National legal frameworks related to MEAs in SEE are very limited or not existing, thus if not appropriately regulated and managed at the national level, they may raise concerns from the perspectives of the Transparency Directive and the Competition law. Additional methodology and policy related concerns have been identified: (2) Limited or nonexistent cross country collaboration in SEE, which is the reason for observed repetitive implementation hurdles; (3) Data verification through patient registries or similar databases is usually not possible, limiting the opportunities for performance based agreements in SEE; (4) Confidentiality of MEAs potentially jeopardized in some countries due to the implementation of agreed financial conditions through distribution chain, which is directly and artificially supporting parallel trade beyond regular commercial circumstances; (5) Risk of unequal treatment of different pharmaceuticals through different conditions imposed by MEAs in countries without formal thresholds and HTA; (6) It is

observed that in the first years of the MEA implementation, National Health Administration commonly exercise the position of power, and is being closed for the scientific dialogue and professional argumentation.

CONCLUSION: More detailed introduction of MEAs into national legislation in SEE countries could increase the trust of all stakeholders, expedite and improve the access of innovative technologies to patients in needs, and limit the areas of uncertainties and concerns for both the payers and the pharmaceutical industry.

METHODOLOGY AND THE USE OF POOLED ANALYSIS IN THE CEA FOR IDegLira VS ALTERNATIVE INTENSIFICATION STRATEGIES IN T2DM PATIENTS

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OBJECTIVES: IDegLira is a once-daily combination of insulin degludec (IDeg) and liraglutide. Trials directly comparing IDegLira with alternative strategies for intensifying basal insulin are ongoing. While awaiting results, this analysis was performed to indirectly compare different strategies. METHODS: A pooled analysis of all available completed Novo Nordisk randomized clinical trials conducted in patients inadequately controlled on basal insulin (five trials) was used to compare indirectly (1) IDegLira (N=199) with (2) addition of liraglutide to basal insulin (N=225); (3) basal/bolus (BB) insulin (insulin glargine [IGlar] + insulin aspart) (N=56); or (4) up-titration of IGlar (N=329). All trials had comparable inclusion/exclusion criteria, baseline characteristics and titration targets (in strategy 2 the basal insulin could not be up-titrated beyond baseline dose). Patient-level data were analyzed using multivariable statistical models with baseline heterogeneity accounted for using explanatory variables. RESULTS: For strategies 1–4, at end-of-study (26 or 52 weeks) change in A1C (%) was –1.7, –1.3*, –1.4* and –1.0* respectively; change in body weight (kg) was –2.9, –3.5, +4.0* and +1.2*; mean daily basal insulin dose (U) was 37.8, 36.6, 62.4* and 60.7*; confirmed hypoglycemia rate (events/100 patient-years) was 122.8, 124.4, 1060.8* and 286.1* (*p

STRENGTHENING PATIENT VOICE IN HTA-EUPATI SERBIA

Dragana Atanasijević

ISPOR Chapter Serbia

In last 15 years Serbia has passed through a period of considerable political and economic changes. The same time, Serbia is classified by the World Bank as an upper middle-income economy. Notable achievements in poverty reduction in 2000s were almost canceled by the global economic crisis (2008) and moreover Serbia nowadays continues to face major economic challenges. Poverty that was decreased almost double from 2002 to 2008 jumped back in 2010, with about 230,000 people below the poverty line. The unemployment rate rose from already high base up to 20 % in 2012 and Serbia is facing significant demographic transition.Population of Serbia is decreasing in the last twenty years (for about half million), which coincides with a period of instabilities in the country. The population has been brought to the brink of demographic ageing due to decreasing of birth rate and increasing of economic migration. Growing share of population above 65 years together with growing unemployment rate challenges the sustainability of the system, especially because of escalated demand for health and social care and reduced productivity.

To address growing burden of non-communicable diseases within a constrained fiscal space, Serbia has already started interventions to improve health financing system, in order to find way how to prize quality and efficiency at both primary care and hospital levels.

Following EU orientation of the Serbian Government and the Ministry of Health who recognize explicit and transparent way of developing solutions for improving health care quality and patient safety, ISPOR Chapter Serbia expresses its own desire to contribute the process of creating conditions that will maximize realization of a modern and sustainable, patient centered health care system. In that manner ISPOR Chapter Serbia has supported the establishment and development of national platform EUPATI in Serbia as part of a wider European initiative which is the model of cooperation between patient organizations, regulatory bodies, scientific and academic community and pharmaceutical companies.

TRENDS IN UTILIZATION OF STAINS IN REPUBLIC OF MACEDONIA 2013-2105

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INTRODUCTION: Statins are indicated for patients on risk or with diagnosed cardiovascular diseases and Type 2 diabetes, as well as patients with high LDL cholesterol level. Rational use of statins has a major and increasing importance for public health and allocation of financial resources by Health Insurance Funds (HIF). The total expenders for lipid lowering drugs have progressively increased worldwide in the past two decades. In R.Macedonia 22 different brands of statins (atorvastatin(8), rosuvastatine(7), simvastatine(5) fluvastatine(1) and lovastatine(1)) are marketed.

OBJECTIVES: The aim of the study was to evaluatethe market share and utilization trends of statins in R. Macedonia from 2013 to 2015.

MATERIALS AND METHODS: Retrospective analysis and data comparison the utilization of HMG-CoA inhibitors (C10AA) in R. Macedonia. The data were obtained from HIF, IMS Health Macedonia, Pharmaceutical Industry and Marketing Authorisation Holders.

RESULTS AND DISCUSSION: According to the official data about prescriptions and expenditures of medicines in R.Macedonia, cardiovascular drugs are most commonly prescribed and used drugs.The average HIF cost for this group of drugs was 110778658.00EUR in period 2013-2015, with increasing trend of approximately 6.5-7.1% each year. Regarding to the official data from HIF atrovastatine is constantly on the list of ten most commonly utilized drugs in R. Macedonia since 2012, and it accounts the highest expenses from the reimbursement (1612603.00euros in 2013, 1845528.00 euros in 2014 and 3452432.00 in 2015. Rosuvastatineis also one of ten drugs that account the highest costs from the HIF (1271544.00euros in 2014). In line with the trend of increasing spending on statins are the records obtained from IMS Health data basis for the period from 2013 to 2015. In comparison with official HIF data the noticeable differencesare confirmed for the dispensed generic drugs and variations in their average costs of 3409350.00eur in 2013, 2119062.00eur in 2014 and 1184725.00eur in 2015, fact that indicates on out of pocket expenditure and possible irrational use of this drugs.

CONCLUSION: Rapid increase in statin use worldwide and in R.Macedonia can mostly be attributed to an increase in consumption volume. In order to evaluate

drug expenditure effectively when chronic diseases remain on the rise globally, it's inevitable to widen the price reduction concept with initiatives that may control statine consumption amounts, such as educational programs for rational drug utilization and targeting eligible population.

CHANGES IN ANTIHYPERTENSIVE DRUGS USAGE IN CROATIA DURING THE FOURTEEN-YEAR PERIOD

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OBJECTIVES: Cardiovascular diseases (CVD) represents a huge burden to society in terms of morbidity, mortality and economic losses. Therapy of CVDs has a huge impact to the financial expenses of healthcare systems. Monitoring of national trends in hypertension treatment can provide important insight into the effectiveness of efforts for reducing cardiovascular diseases. The choice of pharmacological treatment for people with hypertension has important both therapeutic and financial implications. The aim of our study was to identify and analyze changes in the usage of common used groups of antihypertensive drugs (AH) in Croatia from 2000-2013 and to identify the changes in prescription patterns as well as the average price for 1 DDD.

METHODS: Data on the consumption have been obtained from the database IMS (International Medical Statistics) for Croatia. According to the World Health Organization Collaborating Centre for Drugs Statistics Methodology annual volumes of drugs are presented in defined daily doses/1000 inhabitants/day (DDD/1000), while financial expenditure data are presented in Euros (€).

RESULTS: Consumption of CV drugs in Croatia during period from 2000-2013 increased 146.97% (from 190.186 DDD/1000 in 2000. to 469.67 DDD/1000 in 2013), while the financial expenditure in the same period increased 85.81% (from 70.6 mil € in 2000 to 131.2 mil € in 2013), but achieved its maximum in 2006 (149.1 mil €). Prescription patterns in the same period changed, and the most frequently prescribed subgroup were Agents acting on RAS. Their share among antihypertensive drugs increased from 39.13% (2000) to 52.67% (2013). On the opposite, the share of prescribed Diuretics in the same period decreased from 20.16% in 2000 to 12.25% in 2013.

CONCLUSION: Prescription of CV drugs in Croatia during 2000-2013 continuously increased. Prescription patterns among antihypertensive drugs changed and the average cost per DDD gradually decreased. Changes in prescription patterns could be possible result of legal changes introduced by Croatian National Insurance Company and pharmaceutical promotion of new AH drugs (particularly advertising). Changes in price of 1 DDD could be mainly result of the introduction of generics and the implementation of restrictive measures on prices on the both original and generic drugs on Croatian drug market.

ANALYSIS OF THE CONSUMPTION OF DRUGS IN THE GENERAL HOSPITAL ZADAR AFTER A CHANGE IN THE MODEL OF HOSPITALS FINANCING

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Up to 1.01. 2015 hospitals in Croatia are from CIHI (Croatian Institute for Health Insurance) paid to the so-called. limits (flat) which are required to justify the performed services, although it was for most hospitals difficult. Hospitals which have done more service than was provided to the allocated funds are not received new funding for the excess services. One of these hospitals is OB Zadar. From 01.01.2015. hospitals have received funding under the performed services. The aim is to analyze the development costs for drugs in these two different modes of financing. In 2014 total revenue OB Zadar was 257 894 699 kuna, as 2015 was 308 918 975 Kn an increase of 19.8%. At the same time the cost of the medication was 2014 45 069 096 Kn, and a year later 52 702 851 Kn an increase of 16.9%. At the same time for especially expensive drugs (which are particularly hospital refunded) spent 2014 22 518 096 Kn and 2015 30 187 616 Kn an increase of 34.0%. In doing so, the 2014 especially expensive drugs accounted for 49.9% of total consumption of drugs, and 2015 57.3% of the total consumption of drugs. Based on these data, it is evident that the method of financing the hospital according to the performed services lead to better therapy and lower interest costs for drugs in the total revenues of the hospital and at the same time a larger share of modern medicines in total consumption. The only question is how this model is sustainable in the long run we will see when this year CIHI will close new contracts on the financing of hospitals.

HEALTH AND ECONOMIC BURDEN OF ACUTE OTITIS MEDIA INFECTIONS IN CHILDREN

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BACKGROUND: Acute otitis media (AOM) is one of the most common infections for which antibacterial agents are prescribed for children. By three years of age, at least one episode of AOM occurs in more than 80% of all children. Diagnosis and management of AOM has significant impact on the health of children, antibiotics usage and healthcare costs. Also there is significant social burden due to absenteeism.

METHODS: Publicly available data were collected on the incidence and costs of treatment of AOM. As sources of data Croatian Health Service Yearbook for 2014, list of codes diagnostic-therapeutic groups and drugs lists of the Croatian Institute for Health Insurance were used. These data were collected for the age group 0-6 years. Using the collected data direct medical costs of treatment were calculated.

RESULTS: In 2014, in Croatia, there were total 179 375 cases of AOM in all age groups. In age group 0-6 years incidence was the highest (34,74 %) with 62 316 cases of AOM. Total cost of AOM in age group 0-6 years was 2.582.417 €. Largest share in the total costs of treatment refers to the cost of treating AOM in outpatient setting (2.203.494 €). The share of drug costs in the cost of treating AOM was 33,76%.

CONCLUSION: AOM is an important public health problem and one of the most common reasons for prescribing antibiotics in primary care. The costs of primary health care are up to 85,33% of all costs in the treatment of AOM. Further prevention strategies are needed due to the antibiotics resistance and their consumption, and share in the costs for the health system.

THE COST-EFFECTIVENES OF CYTOCHROME P450 (CYP2D6 AND CYP2C19) GENOTYPE SCREENING FOR OPTIMIZATION OF THERAPY WITH RISPERIDONE AND CLOPIDOGREL TREATMENT IN R. MACEDONIA

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INTRODUCTION: The high degree of individual variability in drug response combined with attendant long term care and numerous comorbidities impose substantial economic burden and have important implications for both, patients and health care systems. The clinical integration of pharmacogenetics (PGx), as a contemporary approach for personalization of pharmacotherapy and improved disease managment, requires an evidence of clinical utility. Appraising the drug related function of CYP450 genetic variants is the core for efficient modeling of population specific cost-effective PGx platform for individualization of drug therapy.

OBJECTIVE: To assess cost-effectivenes of CYP2D6 and CYP2C19 PGx platform for individualized treatment with Rispiridone and Clopidrogrel in R.Macedonia.

METHODS: Decision tree model, incorporating state transition probabilities form CATIE (Clinical Antipsychotic Trials of Intervention Effectiveness) and TRITON-TIMI 38 (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel–Thrombolysis in Myocardial Infarction) study, was developed to evaluate the economic viability of the PGx application in individualization of Rispiridone and Clopidrogel therapy. The base case scenario included national frequencies of CYP450 genetic variants, direct costs related to drug treatment, PGx test, treatment of major adverse events and hospitalization, obtained utilizing official, publicly available data. The quality-adjusted life years (QALY), defining the health benefit for the two treatment strategies (PGx guided and traditional), were extracted from the published data.

RESULTS: The PGx defined Risperidone dose strategy (assuming 99% test accuracy) was associated with €7.6 /month/patient increase in total treatment cost and health gain of 0,11 QALY, yielding an ICER of €69.32/ QALY, compared to the traditional approach. Reduced PGx test accuracy (95% and 50%) augmented the ICER (€610.73/QALY and €2300.22/QALY, respectively), due to the €30.53/ month increase in the treatment for each incorrect genotyped patient. Total accumulated cost of Clopidrogel per patient for the PGx guided therapy was

€ 99.049 versus € 107.62 for the traditional treatment strategy while the mean drug-associated cost was e € 21.09 and € 9.68, respectively. The cost associated with and due to side events hospitalization was 1,5-fold less in PGx compared to the traditional treatment.

CONCLUSION: Economic assessment of genetic screening testing for mutations that affect the level of expression and functional activity of CYP2D6 and CYP2C19 genes justifies the application of PGx individualized treatment with Risperidone and Clopidogrel in R. Macedonia.

PHARMACOECONOMIC EVALUATION OF OPIOID SUBSTITUTION TREATMENT IN SLOVENIA

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OBJECTIVES: We analyzed cost effectiveness of buprenorphine/naloxone combination and sustained realease (SR) morphine when compared to methadone in patients treated for opioid dependence in Slovenia. To compare the expected costs of treatment with buprenorphine/naloxone combination and SR morphine, cost-minimization analysis was performed.

METHODS: We adapted a micro-simulation decision model to the real-life conditions in Slovenia by using locally-specific data for maintenance treatment costs of buprenorphine/naloxone, SR morphine, and methadone with the average dose of treatment set at 10.68 mg/day for buprenorphine/naloxone, 592 mg/day for SR morphine, and 82 mg/day for methadone. Additional costs of in-pharmacy methadone preparation were not considered. All other direct costs were based on COBRA (Cost-Benefit and Risk Appraisal of Substitution Treatment in Routine) study and adjusted to conditions of the local jurisdiction. In the base case, hospital/clinic visits, office visits, outpatient treatment, treatment of infections, and other medication costs were considered. In sensitivity analysis, special care was taken not to overestimate the difference in costs for patients treated with buprenorphine/naloxone combination, SR morphine, and methadone; accordingly, 50% lower direct costs (other than drug costs) were also included. Indirect costs were not included in the study. Main outcome measures were costs, gains in quality adjusted life years (QALYs), and incremental cost-effectiveness ratios (ICERs).

RESULTS: Our model has shown that under base case scenario buprenorphine/naloxone dominated methadone (by saving €60 and gaining 0.153 QALY per patient over one year); when comparing SR morphine and methadone, the resulting ICER was €5,434 per QALY. Cost-minimization analysis revealed lower treatment costs with buprenorphine/naloxone combination than those with SR morphine by 45% (€894 per year per patient), with treatment costs of buprenorphine/naloxone and SR morphine accounting for 28% and 41% of total direct costs, respectively. The sensitivity analysis showed robustness of our findings.

CONCLUSION: Results of our study suggest that treating patients with buprenorphine/naloxone combination instead of methadone or SR morphine appears to be cost-saving in Slovenia. This result is particularly relevant for implementation of treatment guidelines and for those patients who can receive as an intervention of choice either buprenorphine/naloxone combination, SR morphine or methadone.

HIV ANTIRETROVIRAL THERAPY (ART) – DRUG COMBINATIONS AND COSTS IN CROATIA

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OBJECTIVES: Antiretroviral therapy (ART) consists of the combination of antiretroviral drugs to maximally suppress HIV virus, stop the progression of HIV disease and prevent onward transmission of HIV. ART for HIV infection has resulted in outstanding decreases in HIV- related morbidity and mortality. According to WHO recommendation ART should be initiated for all people with HIV as soon as possible after diagnosis without any restrictions of CD4 counts. This study evaluated drug therapy received by adult HIV patients in Croatia in order to compare prescribed drug therapy to established guidelines (DHHS, BHIV, EACS) and costs.

METHODS: In this study we have determined ART drugs used between 2013 and 2015 in Croatia and combinations by categories: 1) nucleoside reverse transcriptase inhibitors (NRTIs), 2) 3rd drug regimens and 3) single pill regimens (SPR). In 3rd drug regimens there were 3 categories: 1) non-nucleoside reverse transcriptase inhibitors (NNRTIs) based regimens, 2) protease inhibitors (PIs) based regimens and 3) integrase inhibitors (INIs) based regimens.

RESULTS: Most prescribed NRTIs were abacavir/lamivudine and tenofovir/emtricitabine (66,5% and 33,5% patients). In 3rd drug category NNRTIs were prescribed in 58,8% (efavirenz), PIs (darunavir and lopinavir) in 29,8% and INIs (raltegravir and dolutegravir) in 11,4% patients. From 2015 only 2 single pill regimens were available (abacavir/dolutegravir/lamivudine and tenofovir/emtricitabine/elvitegravir/cobicistat) and prescribed for total 33 patients in 2015. Highest share in costs has backbone therapy abacavir/lamivudine - 1.631.337 EUR in average 2013-2015.

CONCLUSIONS: The prescribing quality of ART for HIV in Croatia is very good and in line with the guidelines. Although from 2015 efavirenz is not anymore first line in guidelines, it's still the most prescribed NNRTI. It is expected that this change in guidelines will have more impact on prescribing in the near future.

DISCLOSURE STATEMENTS: Goran Benčina is employee of the GlaxoSmithKline group of companies.

PRESCRIPTION TRENDS AND EXPENDITURES OF ANTIMICROBIAL DRUGS DURING FIVE YEARS PERIOD IN CROATIA

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OBJECTIVES: The objective of this study is to analyze the utilization of antimicrobial agents in Croatia over the period of 5 years, in order to identify changes in the prescription practices which could potentially lead to inadequate antimicrobial treatment. There is increasing presence of infections caused by antibiotic-resistant bacteria which is likely related to numerous factors such as: frequent use of broad-spectrum antibiotics in both out- and in-patient settings; prolonged hospitalization of patients with high risk of person to person transmission of antibiotic-resistant infections and the reduction in nursing staff due to economic reasons. Inadequate antimicrobial treatment is closely associated with the antibiotic resistance of clinically most important pathogens.

METHODS: Drug utilization data used in this study are based on the WHO ATC and DDD classification system which are the gold standard for international drug utilization research. Source of data is the IMS database which collects sell out information from wholesalers, and are thus highly reliable, especially on the INN level. IMS data are presented as volume consumption, in days of treatment (DOTs which equals DDDs) and as value consumption, in Euros (€).

RESULTS: The most prescribed ATC class of antimicrobial agents in the period of 2011-15 in Croatia, in volume, is J01C group with more than 20 million DOTs consumed per year, meaning that every Croatian citizen consumed between 4,85 DOTs of J01C antibiotic in 2011 and 4,92 DOTs in 2015. Fixed combination of amoxicillin and clavulanic acid comprised over 65% of utilized J01C antibiotics which is a clear sign of inadequate antibacterial treatment. In value terms , 64% of total expenditures for antibiotics in 2011 and 70% in 2015 were spent for two ATC classes, J01C and J01D. The ATC class with the biggest increase in expenditure was J01X, among which linezolid and colestin increased the most, which could indicate a rise of resistant Acinetobacter infections. The five most utilized antibiotics in DOTs, in the period of 2011-15, are: amoxicillin with clavulanic acid, amoxicillin, cefuroxime, azithromycine and doxycycline and in terms of expenditure: amoxicillin with clavulanic acid, azithromycine, cefuroxime, ciprofloxacin and meropenem.

CONCLUSION: Drug utilization research of antimicrobial agents should be performed continuously at national and regional levels, available data should be analyzed by the professional community and published for future reference. This is needed in order to identify early alerts of inadequate antimicrobial treatment which could lead to increased resistance and unjustifiable expenditures. Revision of national and regional antimicrobial clinical guidelines should be done based on the drug utilization research. Implementation of clinical guidelines should be closely monitored by relevant professionals and compared with changes in antibiotic resistance data.

EVALUATION THE MOST COMMONLY USED ANTIBIOTICS IN PEDIATRIC POPULATION AT THE PULMONARY DEPARTMENT OF THE PEDIATRIC CLINIC IN SARAJEVO

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OBJECTIVE: Etiological causative agents of bronchopneumonia are bacteria, viruses, parasites and fungi. Since pediatric population is vulnerable and specific, clinical features are often non-specific and conditioned by numerous factors. These factors include certain age group, presence of comorbidity, exposure to risk factors, carried out immunization etc. , frequent use of antibiotics leads to a rise in bacterial resistance. Bacterial resistance, along with limitations in establishment of timely diagnosis and difficult ethiological classification, often leads to severe clinical features and inadequate response to therapy, which results in increased number of treatment days, as well as increased consumption of antimicrobials.

METHODS: The study included patients under 18 with diagnosis of bronchopneumonia, patients with detailed history of the disease and detailed information on diagnostics and treatment carried out at the Pediatric Clinic, and patients who were hospitalized in the pulmonary department in the period from 1st July to 31st December 2014.

RESULTS: We present the results of 104 patients who were hospitalized at pulmology department of the Pediatric Clinic with diagnosis of bronchopneumonia. First and third generation cephalosporins (cephazolin and ceftriaxone, respectively) and penicillin antibiotics (ampicillin) were most commonly used antimicrobial agents with the average duration of antibiotic therapy of 4.3 days, all of which is consistent with the guidelines.

CONCLUSION: The Pediatric Clinic of the University Clinical Center of Sarajevo has also based its principles of treating bronchopneumonia on observing guidelines

and protocols, as well as principles of good clinical practice. For the purpose of preventing bronchopneumonia in pediatric population, specific epidemiological measures ought to be taken, and they should involve all levels of health care.

HEALTH CARE SERVICES UTILIZATION AMONG ELDERLY IN SLOVENIA: CRITICAL ASSESSMENT

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OBJECTIVES: To analyze health care service utilization among elderly in Slovenia.

METHODS: Health care service utilization among elderly depends on many factors. However, it is important to realize that older people in their consumption of health care services are not a homogeneous group as they may be particularly exposed to personal income and social inequalities. To better understand the factors that influence the use of health care resources among the elderly in Slovenia, we used a panel database of Wave 4 of the Survey of Health, Ageing and Retirement in Europe (SHARE). The SHARE data were self-reported and included indicators of health care services utilization, such as the number of contacts with general practitioners and specialists, hospital admissions within the last 12 months, and number of medications taken at least once a week. The results were presented according to age (in 5-year intervals), gender, education and subjective perception of income. Analyses of bivariate relationship dependency were performed by Pearson's chi-square test and Cramer's contingency coefficient.

RESULTS: We presented results separately for ambulatory medical care, medication and hospital admissions. For utilization of ambulatory medical care, the following results were obtained: (i) the number of contacts with physicians (either general practicioners or specialists) in the past twelve months significantly ($p < 0.0001$) depended on age; (ii) as expected, the proportion of individuals who did not consult a physician in the last twelve months was the largest (around 20 per cent) in the 50-59 age group and decreased to cca 11.5 per cent in the age groups from 65 to 79 years, but then - interestingly - started increasing at the age 80 and above; (iii) similar trend was observed when considering seven or more consultations, with the lowest proportion of individuals in the age group 50-59 and 85+; (iv) the number of contacts solely with general practitioners in the past twelve months was also strongly dependent on age ($p < 0.0001$); (v) gender was not significantly related to the number of contacts with general practitioners or specialists or solely with general practitioners; (vi) education and subjective perception of income were inversely associated with the distribution of the number of contacts with general practitioners or specialists ($p < 0.012$ for education and $p < 0.0001$ for income) or

solely with general practitioners ($p < 0.0001$ for both education and income). When considering medication use, we observed that the number of medications taken at least once weekly significantly ($p < 0.0001$) depended on age, but as in ambulatory medical care, larger proportion of individuals in the age group 85+ than in the age group 70-84 were taking no medications, while smaller proportion were taking four or more drugs. Proportion of individuals who were hospitalized over the past 12 months siginificantly depended on age ($p < 0.005$) and subjective perception of income ($p < 0.028$), but not on educaton or gender.

CONCLUSIONS: Our findings confirmed that high health care services utilization among elderly is dependent upon various factors. Results are important as the basis for the planning and implementation of health care policies in Slovenia, particularly in the current conditions of changing demographic structure and rapid technological progress of medicine.

OUTPATIENT COST OF BPH THERAPY 2011-2015

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OBJECTIVES: Benign prostatic hyperplasia (BPH) is an enlarged prostate gland. The prostate gland surrounds the urethra, the tube that carries urine from the bladder out of the body. As the prostate gets bigger, it may squeeze or partly block the urethra. This often causes problems with urinating. BPH is a very common condition. The histological prevalence in the general male population is estimated to be over 50% of men aged 51-60 years, and increases to 90% in those aged 81-90. The prevalence in Europe of moderate-to-severe symptoms of BPH in men ranges from 14% to 30%.

METHODS: Cost (in EUR) and volumes data for BPH market in Croatia were collected for time period of 2011-2015. Alpha-1–receptor blockers (tamsulosin and silodosin), alpha-adrenergic receptor blockers (finasteride and dutsteride) and combinations (tamsulosin and dutasteride) were taken into account. Using the collected data outpatient cost of BPH treatment was calculated.

RESULTS: In the period of 2011-2015, there were in average 877 618 units prescribed (743 067 – 970 098). Average total market value was 6 789 496 EUR, with lowest value in 2015 – 6 474 911 EUR. Total cost for BPH therapy in period 2011-2015 was 33 947 481 EUR. Most prescribed therapy was tamsulosin 2 906 220 units and cost of 20 121 679 EUR for the period 2011-2015. Finasteride was most prescribed alpha-adrenergic receptor blocker with 1 065 643 units and cost of 6 862 704 EUR.

CONCLUSIONS: BPH is a progressive disease and can lead to serious complications like BPH related surgery. BPH has a significant social and economic burden. Total cost for outpatient BPH therapy in period 2011-2015 was 33 947 481 EUR. Alpha-1–receptor blockers accounts for 59,8%, alpha-adrenergic receptor blockers 35,2% and combinations for 5% of total costs.

DISCLOSURE STATEMENTS: Goran Benčina is an employee of the GlaxoSmithKline group of companies.

PHARMACOECONOMIC ASPECTS FOR ANALYSIS OF TREATMENT ON INFECTION FROM METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS (MRSA)

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Pharmacoeconomic researches are identifying, measuring and comparing costs and outcomes from therapy in healthcare systems, which are common criteria`s for making decision in health policies. Bacterial infections from Methicillin resistant Staphylococcus aureus (MRSA) are serious epidemiological problem. Pharmacoeconomic evaluation on therapy for MRSA is hard, but of excellence meaning. Antibiotic resistance is growing; multi resistant species are identified every day. If we want to make analysis of the key factors in process for dealing with MRSA, then we should examine more perspectives, but precise clinical outcome of every individual should be made. Antibiotics choice is one way how to reduce cost for the treatment. When evaluating antibiotic choice, there are some factors that should be taken in consideration:

1. Basic infection
2. Efficacy of the drug
3. Adverse reactions
4. Compliance
5. Availability of health resources
6. Health insurance
7. Possibility of self-care
8. Costs for intravenous administration
9. Availability of PO therapy
10. Cost of therapeutic failure

Studies show that "switch" therapy, from intravenous to per oral, cuts the costs of therapy without influence on efficacy, short course of intravenous treatment followed with per oral administration for the rest of the treatment has multiple advantages. Switch therapy is commonly used practice in the developed countries. Development of resistance to antimicrobials is natural phenomenon, increased use of antimicrobials leads to increased resistance, but reduction of use does not reduce resistance. When deciding which antibiotic treatment should be used for treating

MRSA infection, antimicrobial resistance should be one of the factors in deciding. Knowledge of antimicrobial resistance can help make proper antibiotic choice and lower risk of failure and antibiotic misuse. Cost efficacy of the antimicrobial treatment starts with the initial therapy, after clinical evaluation of the patient and start of antibiotic treatment. Clinical evaluation, results from microbiological testing, can lead to additional treatment, change of antibiotic or switch to per os. Everyday evaluation, adverse effects and comorbidities have influence in better cost efficacy ratio. Main factor in evaluation of antimicrobial agents used in treatment of MRSA infection is patient. Factors that are evaluated are multiple, complex, interconnected and changeable in time. Best perspective for is: evaluation of patient with possible infection, if possible start aggressive treatment, in time adjust it as you get clinical and laboratory data. Observe data for antimicrobial resistance, so you could make proper antibiotic choice. Make continuously cost effectiveness evaluations so you could follow costs.

HEALTH AND ECONOMIC BURDEN OF ACUTE OTITIS MEDIA INFECTIONS IN CHILDREN

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OBJECTIVES: Acute otitis media (AOM) is one of the most common infections for which antibacterial agents are prescribed for children. By the age of three, at least one episode of AOM occurs in more than 80% of all children. Diagnosis and management of AOM has significant impact on the health of children, antibiotics usage and healthcare costs. Also there is significant social burden due to absenteeism.

METHODS: Publicly available data were collected on the incidence and costs of treatment of AOM. As sources of data Croatian Health Service Yearbook for 2014, list of codes diagnostic-therapeutic groups and drugs lists of the Croatian Institute for Health Insurance were used. These data were collected for the age group 0-6 years. Using collected data, direct medical costs of treatment were calculated.

RESULTS: In 2014, in Croatia, there were total 179 375 cases of AOM in all age groups. In age group 0-6 years incidence was the highest (34.74 %) with 62 316 cases of AOM. Total cost of AOM in age group 0-6 years was 2.582.417 €. Largest share in the total costs of treatment refers to the cost of treating AOM in outpatient setting (2.203.494 €). The share of drug costs in the cost of treating AOM was 33,76%.

CONCLUSIONS: AOM is an important public health problem and one of the most common reasons for prescribing antibiotics in primary care. The costs of primary health care are up to 85,33% of all costs in the treatment of AOM. Further prevention strategies are needed due to antibiotics resistance and their consumption, and share in the costs for the health system.

DISCLOSURE STATEMENTS: Goran Benčina is employee of the GlaxoSmithKline group of companies.

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