Croatian experience in Health Technology Assessment (HTA): National and international view

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- Population ~ 4.3 million
- GDP per capita ~14,000 US$ (10,245 €)

Croatian Health Care System

- Principles of social health insurance, financed from several sources
- The agreement and payment of the national mandatory health insurance is conducted through the Croatian Health Insurance Fund (HZZO)
- Total spending on healthcare (2000-12): ~ 6.8%-7.8% GDP
- Per capita spending on healthcare: ~ 800-1500 US$
Institutionalization of Agency for Quality and Accreditation in Health Care and Social Welfare

• Established under the Act on Quality of Health Care in 2007 as legal, public, independent, non-profit institution
• Three departments: 1) Department for Quality and Education, 2) Department for Accreditation in Health Care and 3) Department for Development, Research and HTA
• Formal activities in the field on HTA: October 2009
Plan for establishment of HTA process:

- **Croatian HTA Guideline**, [http://aaz.hr/hr/procjena-zdravstvenih-tehnologija](http://aaz.hr/hr/procjena-zdravstvenih-tehnologija)
- **International collaboration**, [http://aaz.hr/hr/projekti](http://aaz.hr/hr/projekti), [http://www.aaz.hr](http://www.aaz.hr)
- **National collaboration, education and HTA promotion** (congress, meetings, WSs, publications in Croatian language), [http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/edukativni-materijali](http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/edukativni-materijali)
- **Production of HTA Reports** (national, international), [http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/baza](http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/baza)
- **Scientific Publications**, [http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/publikacije](http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/publikacije)
- **Web page**, [http://www.aaz.hr/](http://www.aaz.hr/), [http://aaz.hr/hr/procjena-zdravstvenih-tehnologija](http://aaz.hr/hr/procjena-zdravstvenih-tehnologija); [http://aaz.hr/hr/projekti](http://aaz.hr/hr/projekti)
Challenges (limited legal framework, limited human resources, funding, appropriate stakeholders involvement in HTA process);

Factors facilitating HTA establishment in Croatia
### Annual HTA budget and permanent staff in Croatia

<table>
<thead>
<tr>
<th>Country</th>
<th>Since</th>
<th>Annual budget (US $ million)</th>
<th>Population served (million)</th>
<th>Permanent staff in HTA Department</th>
</tr>
</thead>
<tbody>
<tr>
<td>Croatia</td>
<td>2007</td>
<td>~0.4 (for whole Agency in 2009 and 2010)</td>
<td>4.3</td>
<td>4 (from December 2013; 1 - up to October 2013)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>~0.8 (for whole Agency in 2011 and 2012)</td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>~0.7 (for whole Agency in 2013)</td>
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Legal framework in Croatia

- **2006**, *Strategy of the development of the Croatian Health Care System 2006-2011*
- **September 2012**, *Croatian National Health Care Strategy 2012-2020* (Measures planned within the Priority 5: Fostering quality in health care - 5.9 Strengthening the health technology assessment),
  http://www.zdravlje.hr/programi_i_projekti/nacionalne_strategije/nacionalna_strategija_zdravstva

- **2007**, *Act on Quality of Health Care*
- **November 2011**, new *Act on Quality of Health Care and Social Welfare* (Ordinance on HTA process and reporting)
- **November 2012**, draft proposal *Ordinance on HTA process and reporting* to Croatian MoH (in process)
- **September 2015**, proposal of new *Act on Quality and Logistics in Health Care*

- **July 2013**, new *Ordinance regarding reimbursement on drugs, HTA not mandatory (if requested - 1 month timeframe)*
http://aaz.hr/hr/procjena-zdravstvenih-tehnologija

Contents

I Introduction and legal framework

II HTA process

1 Topics suggestion and selection process

2 Scope prepared

3 Assessment process

4 Advice (Appraisal) process

5 HTA Report

6 Guide for the Economic evaluation of health technologies: Croatia

Appendix I: Bibliography of recommended HTA Guidelines and methodology references

Appendix II: A Code of Practice for Declaring and Dealing with Conflicts of Interest in HTA process

Appendix III: Authorship

Appendix IV: Selected Data Sources on Croatian Population Health, Healthcare Resource Use and Costs
This 1st edition of The Croatian Guideline for Health Technology Assessment Process and Reporting is **based on, and accepted from**, HTA Guidelines from National Institute for Health and Clinical Excellence (NICE), The Canadian Agency for Drugs and Technologies in Health (CADTH), Belgian Health Care Knowledge Centre (KCE), Danish Centre for Health Technology Assessment, and EUnetHTA Core Models with adaptation to Croatian setting.

**Aim of Croatian HTA process and reporting** is to **produce credible and standardized information** that is **relevant and useful to decision makers** in Croatian publicly funded health care system, and to meet their needs for **reliable, consistent, timely and relevant HTA information**.

**If already published Core HTA and/or HTAs from other countries exist**, they will be critically appraised for quality by INAHTA checklist for the appraisal of HTA Reports and further **adapted to Croatian setting** according to EUnetHTA Adaptation Toolkit.
A Single Technology Assessment (STA) covers a single technology for a single indication. Whole process should be done in **time frame of 3 months**, specially if drugs and medical devices are assessed for reimbursement decisions and listing on Drug or Medical Devices Lists, when timelines from so called “Transparency Directive” should be respected (Council Directive 89/105/EEC of 21 December 1998 relating to the transparency of measures regulating the pricing of medicinal products for human use and their inclusion in the scope of national health insurance system).

A Multiple Technology Assessment (MTA) will normally cover more than one technology, or one technology for more than one indication. Timeline for full process and report should be in **time frame of 6 (maximum 9) months**. This timeline will be tested within the initial pilot HTAs, and the timing of each phase of HTA process and reporting will be mapped out in next version of the Guideline, for greater understanding and meeting public expectations. Agency recognizes **importance of timely production of information to fulfil decision-makers needs**.

Full HTA report should have the following **domains** (according to the EUnetHTA documents: HTA Core Model for Medical and Surgical Interventions, HTA Core Model for Diagnostic Technologies, HTA Core Model for Screening Technologies): 1 Current use of the technology (implementation level), 2 Description and technical characteristics of technology, 3 Safety, 4 Effectiveness (including Accuracy for diagnostic and screening techniques), 5 Costs, economic evaluation, 6 Ethical aspects, 7 Organizational aspects, 8 Social aspects and 9 Legal aspects.
HTA Report

Several types of the HTA report

• Full HTA report in English language and Summary for the larger international community

• Summary of full English report translated to Croatian language with short Advice to the Minister of Health or Croatian Institute for Health Insurance or Hospitals or health professionals in Croatian language

• Short Advice to patients, written in lay language

• Published on Agency’s website and subsequently in print

• Unique ID number, part of Agency Database on HTA
International collaboration, http://aaz.hr/hr/projekti, http://www.aaz.hr

“If you want to go fast, go alone. If you want to go far, go with other.”

- **EU Projects (EUnetHTA JAs, FP7, Horizon 2020)**

- **Memberships: HTAi, ISPOR, ISPOR HTA Roundtable Europe (from 2013: Germany and Croatia as Co-Chairs), ISPOR HTA Council (ISPOR HTA Training Programe, Pilot for CEE countries, Zagreb, Croatia, June 2015)**


- **WHO National Contact Point on HTA,** http://www.who.int/health-technology-assessment/en/
Important international documents on HTA


- 2011, Article 15 of Directive 2011/24/EU

- 2013, HTA Network, COMMISSION IMPLEMENTING DECISION of 26 June 2013 providing the rules for the establishment, management and transparent functioning of the Network of national authorities or bodies responsible for health technology assessment (2013/329/EU); 2014, Strategy paper for EU cooperation on HTA; 2015, Reflection paper on Reuse of Joint Work in national HTA activities

- 2014, 67th World Health Assembly Resolution: Health intervention and technology assessment in support of universal health coverage
International projects

- EUnetHTA Joint Action (2010-2012)
- EUnetHTA Joint Action 2 (2012-2015)
- FP7: European study on Quantifying Utility of Investment in Protection from Tobacco - EQUIPT (2013-2016)
European network for HTA Joint Actions (JA1, 2010-2012 and JA2, 2012–2015)
Possible JA3, 2016-2019
EUnetHTA Joint Action Project (2010-2012)

Croatian involvement

- WP8: Strategy and Business Model Development
- WP4, strand B: Development of two Core HTA
- WP7 New Technologies, strand B: Collaboration on (pre-coverage) assessments

EUnetHTA Joint Action 2 Project (2012-2015)

Croatian involvement

- WP2 (Education)
- WP4 (Full Core HTA)
- WP5 (Rapid Core HTA on pharmaceuticals and medical devices)
- Chair of EUnetHTA Plenary Assembly (2012-2014)
- Meetings in Zagreb, Croatia: EUnetHTA Plenary Assembly, March 2013; WP4 F-F meeting, October 2013
EUnetHTA JA 2010-2012

- Facilitation of national strategies for continuous development and sustainability of HTA
- HTA training and capacity building
- Anti-VEGF in diabetic macular oedema: A systematic review
- The pre-market clinical evaluation of innovative high-risk medical devices
- Prognostic tests for breast cancer recurrence
- Abdominal Aortic Aneurysm (AAA) screening

EUnetHTA JA2 2012-2015

- Fecal Immunochemical Test (FIT) versus guaiac-based fecal occult blood test (FOBT) for colorectal cancer screening
- Intravenous Immunoglobulins in MCI and Alzheimer disease
- Structured Telephone Support (STS) in adults with chronic heart failure
- Duodenal-jejunal bypass sleeve (EndoBarrier®) for the treatment of obesity with or without type 2 diabetes
- Transcatheter mitral valve repair in adults with chronic mitral valve regurgitation
- Canagliflozin for the treatment of Diabetes Mellitus Type 2
- Ramucirumab (Cyramza®) in combination with Paclitaxel as second-line treatment for adult patients with advanced gastric or gastro-oesophageal junction adenocarcinoma
- New pharmaceuticals in Chronic Hepatitis C
National adaptation - How?

- Translation of Summary of relative effectiveness to Croatian language
- Recommendations for national decision makers – Croatian language
- Whole Rapid REA document as Appendix
**Barriers**

- **Topic relevance** (not always in line with national requests on HTA-medical devices; positive example of canagliflozin and ramucirumab-joint assessment finished before Manufacturers national application for reimbursement; HepC drugs assessment-in line with national request)
- **Human resources**
- **Time**
- **Legal framework limited**
- **Language**
EUnetHTA documents and tools

Methodological Guidelines

Endpoints used for REA of pharmaceuticals

1. Clinical endpoints
2. Composite endpoints
3. Surrogate endpoints
4. Safety
5. Health-related quality of life

Comparators and comparisons

6. Criteria for the choice of the most appropriate comparator(s)
7. Direct and indirect comparison

Levels of evidence

8. Internal validity
9. Applicability of evidence in the context of a relative effectiveness assessment

Tools

- Core Model (as flexible format and content)
- Planned and Ongoing Projects Database (POP)
- Submission template for pharmaceuticals and medical devices
**Added value**

- Learning by doing; possibility to recognize barriers and facilitating factors; to make further changes and improvement on European and national level

- Less time for the production of national HTA reports (the **number and quality of national reports** will be **increased**)

- National awareness and political recognition of concrete benefits of HTA

- Effective communication and cooperation with relevant policy-and decision-makers

- Improved local competence and capacity in HTA

- Increased international visibility of the participating organizations (scientific visibility through scientific papers)

- Core HTA information based on good practice in HTA methods and processes: **objective, reliable, transparent, transferable, timely, fit for purpose**
National collaboration, education and HTA promotion, http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/edukativni-materijali

Congresses, meetings, WSs, publications in Croatian language, educational documents on web page
• Meeting with international experts for main HTA users (January 2010)

• HTA symposiums during the Croatian congresses on pharmacoconomics and outcome research with international participation (2010-2013)

• 1st National Conference, 2013 (Health Care Quality, Accreditation and HTA)

• TAIEX Project, http://ec.europa.eu/enlargement/taiex/dyn/taiex-events/detail_en.jsp?EventID=43260, December 2010, organized by the Technical Assistance Information Exchange Instrument of the European Commission (TAIEX) in co-operation with our HTA Department: 2 days Workshop - “Health Technology Assessment; main principles, HTA process and report” (110 participants from different stakeholders+8 EU experts), Commission funding 100%

• Procjena zdravstvenih tehnologija u Hrvatskoj: uloga Agencije za kvalitetu i akreditaciju u zdravstvu. HČIJZ. 2011;7:e.


• Ekonsmske analize kao dio procesa procjene zdravstvenih tehnologija. Liječničke novine, 2010.
“MoH Projects incubator”

Project proposal „Development of Health Technology Assessment“, January 2013 (to Croatian MoH for possible application on EU Funds)
• **Production of HTA Reports** (national, international), [http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/baza](http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/baza)

• **Web page**, [http://www.aaz.hr/](http://www.aaz.hr/), [http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/](http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/); [http://aaz.hr/hr/projekti](http://aaz.hr/hr/projekti)
Agency HTA Database, [http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/baza](http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/baza)

HTA reports (27 finished), 2011- July 2015

<table>
<thead>
<tr>
<th>Rapid HTA at national level</th>
<th>HTA at national level</th>
<th>HTA at international level</th>
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<tr>
<td>4</td>
<td>15</td>
<td>8</td>
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</table>
VASCULAR-ENDOTHELIAL-GROWTH-FACTOR-INHIBITORS (ANTI-VEGF) IN DIABETIC MACULAR OEDEMA

SYSTEMATIC REVIEW

VIENNA AND ZAGREB, MARCH 2011
The whole range of health technologies in national HTA Reports (examples)

- Transcatheter Aortic Valve Implantation-TAVI
- Insulin glargine and insulin detemir in combination with oral antidiabetic therapy in patient with type 2 diabetes mellitus
- Sitagliptin and sitagliptin with metformin therapy in patients with type 2 diabetes mellitus
- Tandem mass spectrometry in expanded newborn screening for inherited metabolic disorders
- Particle Beam Radiation Therapies for Cancer
- Intensity-Modulated Radiation Therapy, IMRT
- Endovascular abdominal aortic aneurysm (AAA) repair
- Biofeedback and Neurofeedback treatments for psychiatric disorders
- Impact of triclosan-coated sutures on surgical site infection
- Nucleic acid testing for screening blood donations on HBV, HCV and HIV
- Blood glucose meters for self-monitoring of blood glucose
- Drugs in the treatment of lung cancer (afatinib, erlotinib, gefitinib, crizotinib, pemetrexed)
- Sofosbuvir in Chronic Hepatitis C
- Drugs in the treatment of prostate cancer (cabazitaxel, enzalutamide, abiraterone)
Scientific publications, http://aaz.hr/hr/procjena-zdravstvenih-technologija/publikacije

- European collaboration on relative effectiveness assessments: What is needed to be successful? Health Policy. 2015 Feb 7.
- Completeness and Changes in Registered Data and Reporting Bias of Randomized Controlled Trials in ICMJE Journals after Trial Registration Policy. PLoS ONE. 2011;6(9): e25258.
Where we are?

Croatian process of decision-making; HTA process and main HTA users in Croatia
Croatian process of decision-making and HTA process

Industry submission files

Croatian Health Insurance Fund (CHIF)
“Drugs Committee” and “Medical Devices Committee” “APPRAISAL”

Agency for Quality and Accreditation in Healthcare and Social Welfare - HTA Department “ASSESSMENT” (Currently not mandatory)

HTA document with recommendation

Croatian Health Insurance Fund (CHIF) Board “DECISION”

CHIF Board “DECISION”

HTA document with recommendation

EUnetHTA and HTA Network (Article 15, CBHC Directive) Full Core HTA and Core HTA for Rapid REA of Pharmaceuticals and other health technologies

Request

National adaptation

Active collaborative production

Hospitals Management “DECISION”

Request

HTA document with recommendation

Agency for Quality and Accreditation in Healthcare and Social Welfare - HTA Department “ASSESSMENT” (Currently not mandatory)

Request

HTA document with recommendation

MoH “DECISION”

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National adaptation

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Hospitals Management “DECISION”

Request

HTA document with recommendation

Agency for Quality and Accreditation in Healthcare and Social Welfare - HTA Department “ASSESSMENT” (Currently not mandatory)

Request

HTA document with recommendation

MoH “DECISION”

Hospitals Management “DECISION”
Conclusion - the future of HTA in Croatia

- The way for establishing a transparent, scientific, independent evidence-based HTA process in Croatia was not easy and quick process

For further sustainable and mandatory HTA process in Croatia:

- support and commitment of government institutions (political decision)
- appropriate legal framework and funding
- educated permanent staff
- appropriate stakeholders involvement
- further national and international cooperation and collaboration (network)
Thank you for your attention!

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