Patient Preference Information (PPI) in the HTA decision-making process

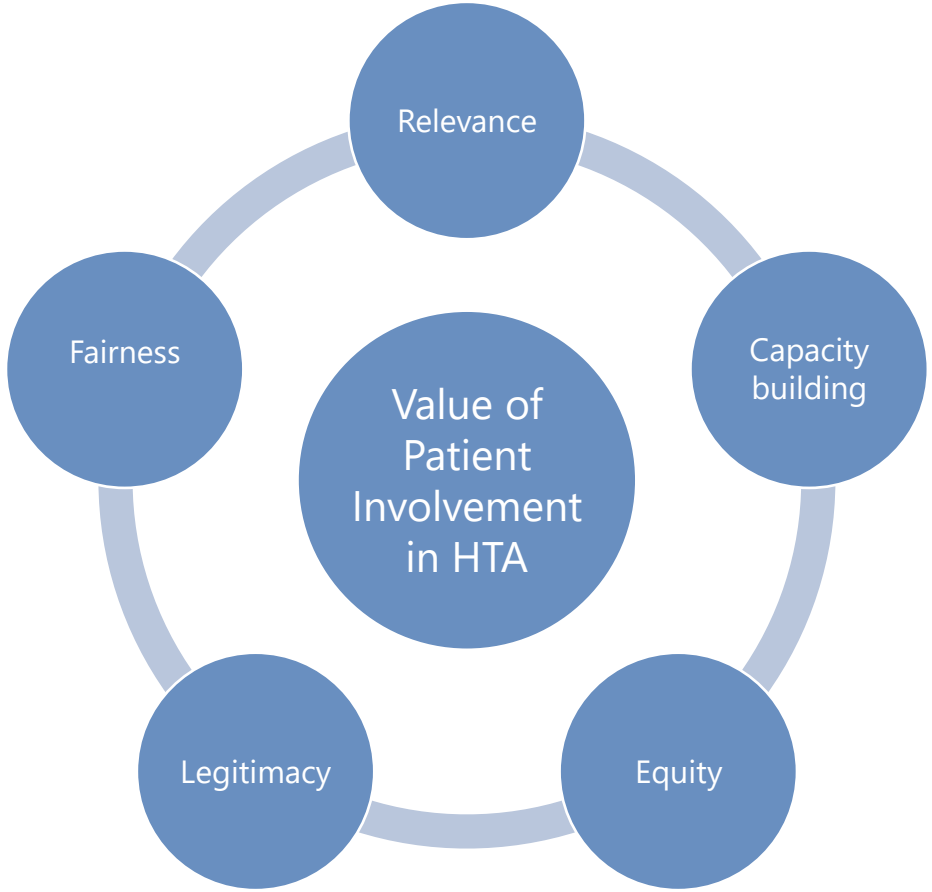
Eugena Stamuli, Msc Health Economics
Founding Partner, Pharmecons Easy Access
eugena.stamuli@pharmecons.com

Μελέτες, Μεθοδολογία και Τεκμηρίωση HTA στην Ελλάδα
Διαδικτυακή Εκδήλωση
22 Απριλίου 2021 | 16:00-19:00

HTA process & Patient Involvement

- "***Health technology assessment*** *(HTA) is a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the formulation of safe, effective, health policies that are* ***PATIENT FOCUSED*** *and seek to achieve best value. Despite its policy goals, HTA must always be firmly rooted in research and the scientific method*" (EunetHTA definition).

- Growing tendency across HTA bodies, with different assessment approaches, for patient involvement in the decision-making process



Adapted from Hunter A, Facey K, Thomas V, et al. EUPATI Guidance for Patient Involvement in Medicines Research and Development: Health Technology Assessment. Frontiers in Medicine. 2018 ;5:231

Patient involvement in HTA

Procedural

- **Prioritiza**
- Involveme
  patients a
  experienc
- Possibility of **appeal** for patients/patient organizations against the final recommendations of the decision makers

Άρθρο 250
Διαδικασία Αξιολόγηση Τεύχος Α' 5/17.01.2018

7. Η Επιτροπή Αξιολόγησης μπορεί να καλεί εκπροσώπους συλλόγων ασθενών και επιστημονικών σωματείων ή εταιρειών ιατρικών ειδικοτήτων για να εκφράσουν τις απόψεις τους.

Qualitative evidence

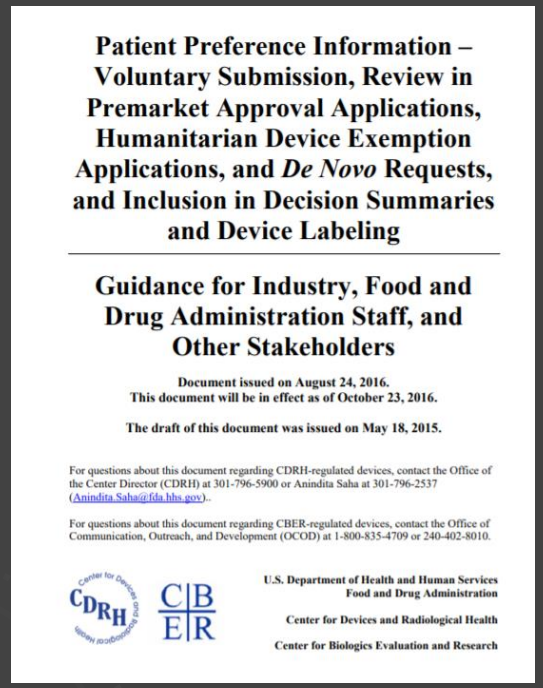
- Patient interviews/focus groups/advisory boards **on burden/experience of disease/treatment**
- **Patient journey**
- Patient perceived **benefit-harm trade-off**
- Trial entry/exit **interviews**
- Patient **forums/social** medial listening

Quantitative evidence

- Patient Reported Outcomes (Symptoms, impact on daily life, HRQoL, treatment satisfaction)
- **Patient Preference Information (PPI)**: Revealed and Stated Preference studies
  (TTO, DCE, WTP, SG, BWS).

Incorporating PPI in Regulatory environment

U.S. FOOD & DRUG ADMINISTRATION



Patient Preference Information – Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and *De Novo* Requests, and Inclusion in Decision Summaries and Device Labeling

Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

Document issued on August 24, 2016.
This document will be in effect as of October 23, 2016.

The draft of this document was issued on May 18, 2015.

For questions about this document regarding CDRH-regulated devices, contact the Office of the Center Director (CDRH) at 301-796-5900 or Anindita Saha at 301-796-2537 (Anindita.Saha@fda.hhs.gov)..

For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration

Center for Devices and Radiological Health

Center for Biologics Evaluation and Research

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

January 2021
EMA/97615/20212021
Stakeholders & Communication Division

Pilot phase for CHMP early contact with patient / consumer organisations

Background and rationale

Patients and their representatives are involved in many activities at EMA and the added value of including their perspectives within committee evaluations has been well demonstrated.

They are currently involved at various timepoints during the medicines' lifecycle, including CHMP evaluations. However, requests for patient input generally come at a later stage of the evaluation, often once major objections have been identified (e.g. expert meeting, oral explanation). Experience shows that late input may lead to missed opportunities to properly incorporate patient perspectives into the assessment process. Therefore in order to make current engagement practices more efficient and enhance timely participation, it is proposed to establish contact with relevant patient / consumer organisations at the start of new medicines assessment. This will enable patients to share aspects such as quality of life, treatment options and unmet medical needs so that the CHMP is well-aware of all aspects from the beginning. This is also expected to facilitate further interactions with patients as the procedure progresses.

This proposed action and process improvement is in line with both the CHMP work plan objective to: 'Incorporate additional and regular processes to capture and include patients' views and preferences in the benefit/risk evaluations', and EMA's Regulatory Science Strategy recommendations which highlight the need to enhance methods to systematically incorporate patient data in regulatory decision-making.

Legal basis

Article 78 of Regulation (EC) Nº 726/2004 allows EMA scientific committees to establish contacts on an

US Food and Drug Administration (FDA) - Center for Devices and Radiological Health & Center for Biologics Evaluation and Research

- Guidance on how to collect patient preference
- Recommendation on incorporating data into a benefit-risk assessment framework
- Recommendation on including preferences information in labelling
- Voluntary submission of preference data
- **Discrete Choice Experiments, the most suitable methods for eliciting PPI**

….this proposed action and process improvement is in line with both the CHMP work plan objective to: 'Incorporate additional and regular processes to **capture and include patients' views and preferences in the benefit/risk evaluations',** and EMA's Regulatory Science Strategy recommendations which highlight the need to **enhance methods to systematically incorporate patient data in regulatory decision-making.**

HTA bodies working towards integrating PPI into decision making processes

- In Europe payers are interested in inclusion of patient preference information
- Belgium, England, Finland, France, Germany, the Netherlands, Sweden and Scotland.

NICE provides advice on patient preference study design

February 2019

"We are delighted to be able to shape our offering to suit the requirements of Pharma Offering advice and guidance on their patient preference study should help it to generate the data required to help future products meet the needs of COPD patients."

Jeanette Kusel, Director of NICE Scientific Advice

NICE & Myeloma UK collaborate on patient preference report

June 2019

www.myeloma.org.uk/research-and-patient-advocacy/health-services-research-programme/

Belgian HTA body collaborates on 'PREFER' project

February 2017

"The main aim of PREFER is to strengthen patient-centric decision making throughout the life cycle of medicinal treatments by developing expert and evidence-based recommendations on how patient preferences should be assessed and inform decision making."

de Bekker-Grob, E.W., Berlin, C., Levitan, B. et al. Patient (2017) 10: 263.

What are Patient Preferences

Patient preference information (PPI) is defined as: **qualitative** or **quantitative** assessments of the relative desirability or acceptability to patients of specified alternatives or choices among outcomes or other attributes that differ among alternative health interventions (FDA 2015).

- ✓ **Qualitative PPI**… may be useful in identifying **which** outcomes, endpoints or other attributes are valued most by patients and which factors affect patients' perspectives on risk and benefit.
- ✓ **Quantitative PPI** can provide estimates of **how much** different outcomes, endpoints or other attributes are valued by patients, and the **tradeoffs** that patients state or demonstrate they are willing to make among them.

Source: FDA (2016). *Patient Preference Information – Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and De Novo Requests, and Inclusion in Decision Summaries and Device Labeling: Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders*. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health and Center for Biologics Evaluation and Research. https://www.fda.gov/media/92593/download

Patient preferences are not PROs

Differences on….	PPI	PROs
What	Preferences on treatment characteristics, treatment related outcomes and process characteristics	Data on symptom status, physical function, mental health, social function and wellbeing
When	Stated preferences: can be on hypothetical scenarios/treatments Revealed: actual choices, in real-world settings	Before and after an intervention
How	Tailored made questionnaires, informed by the study objectives (i.e. selection of attributes). **Discrete Choice Experiments, widely used method**	Disease-specific questionnaires (e.g.FACT_B) and/or general measures (e.g. EQ-5D)

Use of PPI in different HTA paradigms

QALY-based assessments

- QALY as global measure of health
- Willingness-to-pay threshold per QALY
- UK, Northern European Countries, Australia, Canada

Global scoring

- Assessment of clinical (added) value
  Used for price negotiations
- Efficiency frontier: measures the amount and the probability of gains in patient-relevant outcomes like mortality, morbidity, and QoL
- Germany, France (**and Greece ??? As no WTP value per QALY?)**

NICE's statement on integration of PPI in HTA decision making*

"…patient preference studies could be considered alongside other types of evidence, especially for appraisals that involve **distinctly different treatment options** or are indicated for a **heterogeneous population** or for technologies that have **important non-health benefits**"

IQWiG guidelines on integration of PPI in HTA decision making**

"Efficiency frontiers can be drawn either for an aggregated outcome or for a single outcome criterion such as mortality (death rate), morbidity (symptoms and complaints) or quality of life. However, often data are only available for single outcome criteria. To summarize efficiency frontiers for different patient-relevant outcomes to an overall evaluation, that is, **to aggregate them, the individual results must be weighted. Patient preferences, for example, can be used for this purpose**".

*Bouvy JC et al,. Use of Patient Preference Studies in HTA Decision Making: A NICE Perspective. The Patient-Patient-Centered Outcomes Research. 2020 Apr;13(2):145-9

**IQWIG (2013) How preferences of patients can be determined https://www.iqwig.de/en/press/press-releases/how-preferences-of-patients-can-be-determined.3661.html Accessed April 2021

Application of PPI in HTA decision making

Patient Preferences

✓Attribute trade-offs
✓Relative importance of attributes and levels

Endpoint Selection

- Lack of established Patient-reported outcomes (PROs)
- PPI study is conducted in early phase of drug development

Evidence alongside QALYs

- Elements not captured by QALYs: process utility, different mode of administration (MoA)
- Help HTA committees understand the value of change in MoA

Larger patient population

- Heterogenous patient groups
- Reimbursement for subgroups of patients (e.g., patients with, higher functional limitation, severe end of disease spectrum)

Patients-trade offs

- Very different drug profiles (efficacy, safety, user-friendliness/convenience).
- Minimum acceptable benefit
- Maximum acceptable risk

Overall benefit-risk balance

- **Willingness to pay (society, payor, patient)**
- **Predict treatment uptake (enhance patient compliance / clinicians' uptake & prescription of new intervention)**

Adapted from: Bouvy JC et al,. Use of Patient Preference Studies in HTA Decision Making: A NICE Perspective. The Patient-Patient-Centered Outcomes Research. 2020 Apr;13(2):145-9

Το πλαίσιο λειτουργίας της Αξιολόγησης Τεχνολογιών Υγείας (ΑΤΥ – HTA) στην Ελλάδα

1 Έγκριση Κυκλοφορίας από τον Ευρωπαικό Οργανισμό Φαρμάκων

2 Τιμολόγηση με βάση το μέσο όρο των 2 χαμηλότερων χωρών της Ευρωζώνης

3 Υποβολή φακέλου από τον ΚΑΚ προς την ΕΑΦΑΧ. Προϋπόθεση η προηγούμενη έγκριση σε 5 εκ των παρακάτω 11 χωρών (εξωτερικά κριτήρια: Βέλγιο, Αυστρία, Σουηδία, Φινλανδία, Γαλλία, Ισπανία, Ολλανδία, Πορτογαλία, Γερμανία, Ιταλία, Δανία)

Εξαιρέσεις από τα εξωτερικά κριτήρια: Ορφανά Φάρμακα, Φάρμακα για τη Μεσογειακή Αναιμία, Εμβόλια Εθνικού Προγράμματος Εμβολιασμών, Παράγωγα Αίματος, Βιομοειδή, Γενόσημα, Κλώνοι, Συνδυασμοί γνωστών δραστικών ουσιών , φάρμακα καλώς καθιερωμένης χρήσης)

4 Εσωτερικά κριτήρια Αξιολόγησης

Κλινικό Όφελος (σοβαρότητα και φορτίο νόσου, επίπτωση στη θνησιμότητα, νοσηρότητα, Ασφάλεια και Ανεκτικότητα)

Σχετική αποτελεσματικότητα

Αξιοπιστία Κλινικών Δεδομένων

Επίπτωση στον Προϋπολογισμό

Δείκτης Κόστους – Αποτελεσματικότητας

5 Διαδικασία Διαπραγμάτευσης

Συμφωνίες που περιλαμβάνουν εκπτώσεις, κλιμακωτές εκπτώσεις βάσει του όγκου πωλήσεων, συμφωνίες με βάση το αποτέλεσμα, συμφωνίες ανά θεραπευτική ένδειξη, συμφωνίες επιμερισμού κινδύνου και συμφωνίες σε συνάρτηση με θεραπευτικά ορόσημα σε συγκεκριμένες χρονικές περιόδους

Εισήγηση προς ΕΑΑΦΑΧ για την ύπαρξη η μη συμφωνίας

6
- Εισήγηση της ΕΑΑΦΑΧ προς τον ΥΥ
- Πλήρης Ένταξη, Ένταξη με περιορισμούς, Απόρριψη
- Έγκριση Εισήγησης, Δημοσίευση Απόφασης και Ένταξη προϊόντος στη Θετική Λίστα
- Παραπομπή στην Επιτροπή Θεραπευτικών Πρωτοκόλλων

7 Αξιολόγηση ανά τριετία

HTA Conference: Value Driven Healthcare and Shared Decision Making
Αθήνα 18 Φεβρουαρίου 2020

"HTA: An Opportunity for Development" Dimitrios Filippou, President of the National Medicines Organization, President of the Medicines Negotiations Committee, HTA Conference 2020

What is important?

4 **Εσωτερικά κριτήρια Αξιολόγησης**

Κλινικό Όφελος (σοβαρότητα και φορτίο νόσου, επίπτωση στη θνησιμότητα, νοσηρότητα, Ασφάλεια και Ανεκτικότητα)

Σχετική αποτελεσματικότητα

Αξιοπιστία Κλινικών Δεδομένων

Επίπτωση στον Προϋπολογισμό

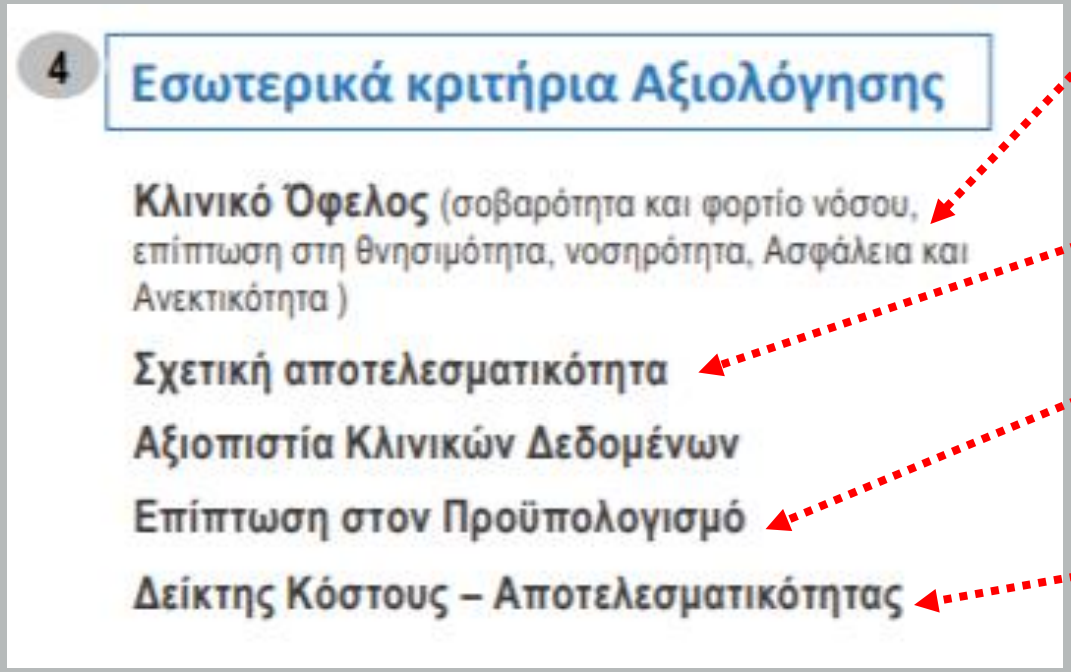
Δείκτης Κόστους – Αποτελεσματικότητας

Methods: Discrete Choice experiment

Factors	Treatment A	Treatment B	Neither of these treatments
Average overall survival	7 years (1 year, 3 years, 5 years, **7 years**, 9 years)	3 years (1 year, **3 years**, 5 years, 7 years, 9 years)	
Average remission period	5 years 3 months (1 year, 3 years, 5 years, 7 years, 9 years)	9 months (1 year, 3 years, 5 years, 7 years, 9 years)	
Mild or Moderate side-effects	60 out of 100 (60%) risk; Lasting up to 2 mths	20 out of 100 (20%) risk; Lasting up to 2 mths	
Severe side-effects	5 out of 100 (5%) risk; Lasting longer than 2 mths	10 out of 100 (10%) risk; Lasting up to 2 mths	
How treatment is taken	Intravenous drip (Hospital / clinic) Time: 2-3 hours	Subcutaneous Injection (Hospital / clinic) Time: 15 mins	
Frequency of taking treatment	Fortnightly	Weekly	
Average out of pocket costs to you over a year	£0	£0	
I would choose	○ Treatment A	○ Treatment B	○ Neither

Fifer S, Galinsky J, Richard S. Myeloma Patient Value Mapping: A Discrete Choice Experiment on Myeloma Treatment Preferences in the UK. Patient Prefer Adherence. 2020 Jul 28;14:1283-1293.

The perspective of HTA & negotiation committees: the case of rare vs. common disease



Adapted from : Mentzakis E et al, Health Econ Policy Law. 2011 Jul;6(3):405-33.

Methods: Discrete Choice experiment

Example Choice Problem	Drug A to treat common disease	Drug B to treat a Rare Disease
The severity of the disease	Serious impact	Moderate impact
The impact of treatment on a patients health	Gain of 1 year	Gain of 10 years
The total budget to treat affected population	20 million to fund	100 million to fund
The cost of treating a single patient	€ 10,000 per patient	€ 12,000 per patient
WHICH PROGRAMME WOULD YOU PREFER?	Prefer to fund drug A	Prefer to fund drug B

Ερωτήσεις προς συζήτηση

- Ποιος θεωρείτε ότι πρέπει να είναι ο ρόλος και η συμμετοχή των ασθενών/ενώσεων ασθενών στη διαδικασία ΑΤΥ;
- Πως θα βλέπατε ένα ιδανικό σενάριο συνεργασίας ανάμεσα σε

  ασθενείς - φαρμακευτικές - επιτροπές ΑΤΥ/διαπραγμάτευσης τιμών φαρμάκων;
- Ποιες είναι οι προκλήσεις και εμπόδια στη συνεργασία αυτή και πως μπορούν να ξεπεραστούν;
- Εκτιμάτε ότι οι προτιμήσεις ασθενών μπορούν να παίξουν ρόλο στις αποφάσεις επιτροπής HTA;

ΕΛ.Ε.Φ.Ι.

ΕΛΛΗΝΙΚΗ ΕΤΑΙΡΕΙΑ
ΦΑΡΜΑΚΕΥΤΙΚΗΣ
ΙΑΤΡΙΚΗΣ

Μαιάνδρου 23, 115 28 Αθήνα

T 210 7211845

E info@elefi.gr

W www.elefi.gr