Ελληνική Επιστημονική Εταιρεία Οικονομίας & Πολιτικής της Υγείας

Η Αξιολόγηση της Τεχνολογίας Υγείας: Εμπόδια και Υπερβάσεις

# Η Οπτική των Ιατρών

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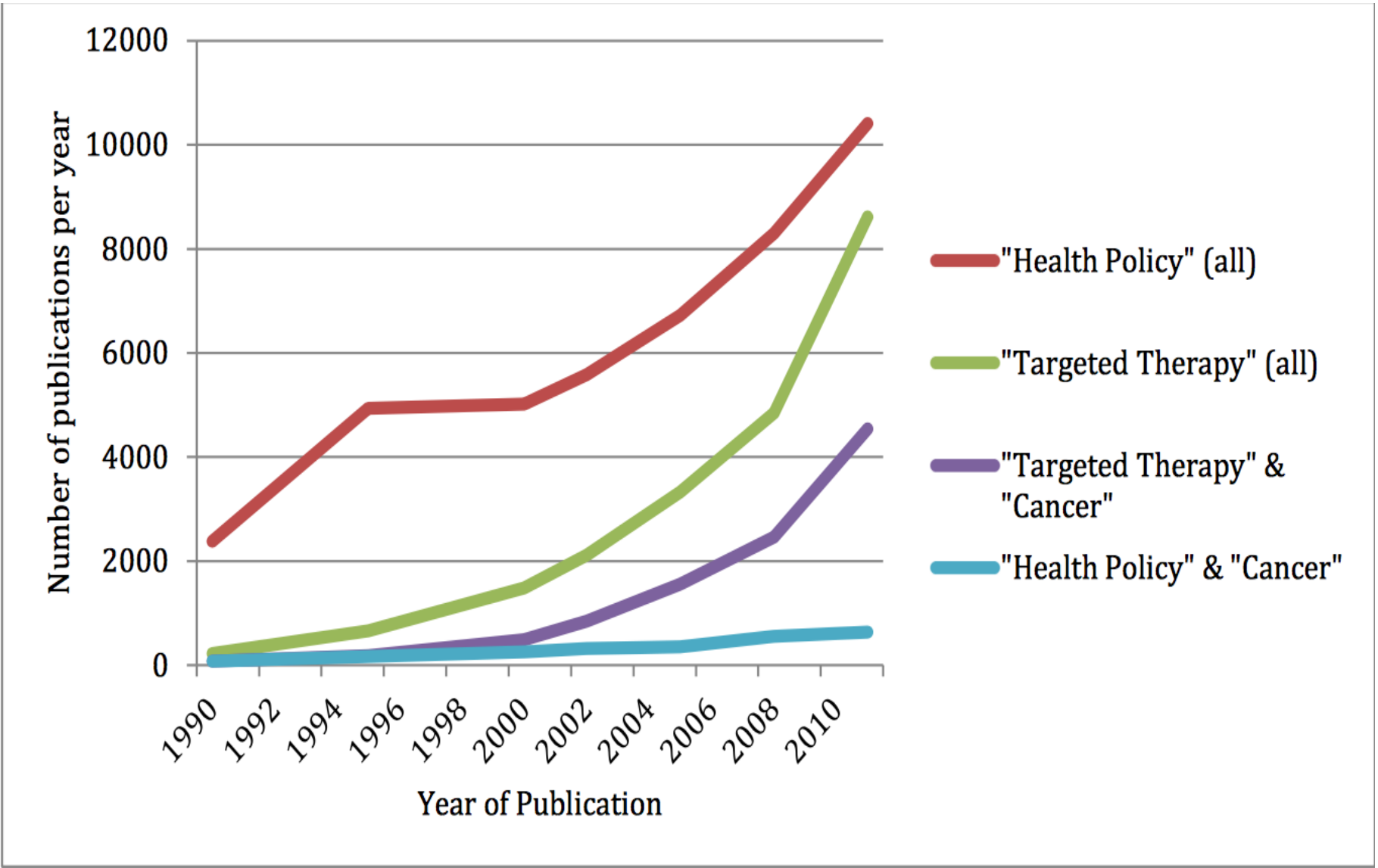
# Targeted Therapies and Health Policy – a Bibliometric Survey Based on PubMed



The NEW ENGLAND JOURNAL of MEDICINE

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# Duration of Adjuvant Chemotherapy for Stage III Colon Cancer

A. Grothey, A.F. Sobrero, A.F. Shields, T. Yoshino, J. Paul, J. Taieb, J. Souglakos, Q. Shi, R. Kerr, R. Labianca, J.A. Meyerhardt, D. Vernerey, T. Yamanaka, I. Boukovinas, J.P. Meyers, L.A. Renfro, D. Niedzwiecki, T. Watanabe,* V. Torri, M. Saunders, D.J. Sargent,* T. Andre, and T. Iveson

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# Are there any clinical implications and for whom?

**For patients: YES!**

**IDEA: Adverse events 3 vs 6 months**

- **NEUROTOXICITY 2 to 6 times lower**
- **DIARRHEA 20% to 30% lower**
- **MUCOSITIS 2 times lower**
- **HAND AND FOOT SYNDROME 2 to 3 times lower**

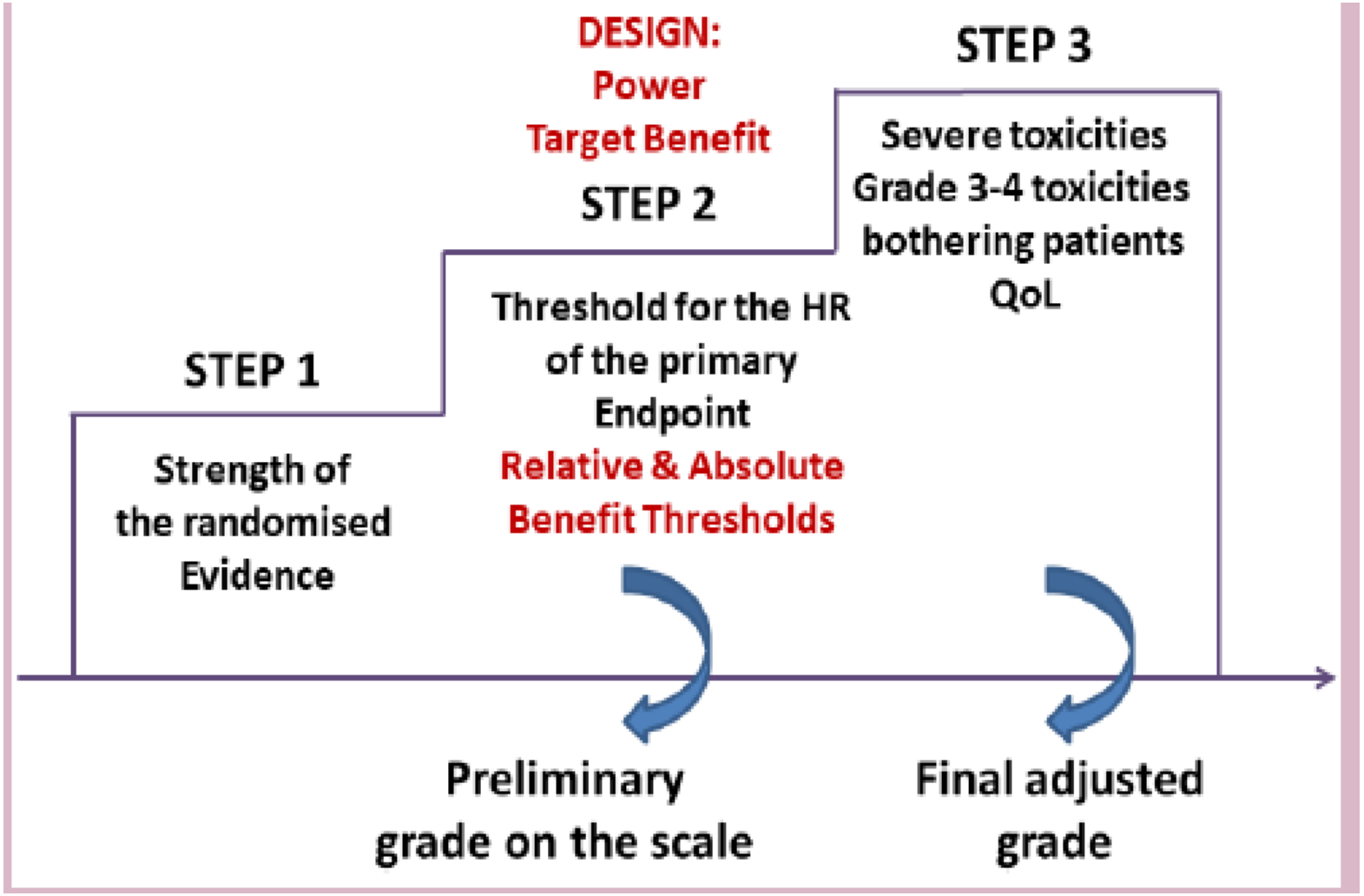
# Are there any clinical implications and for whom?

**For healthcare resource allocation: Yes!**

- Savings from 3 months rather than 6 months chemo: **More than half a billion Euros saving per annum if every stage 3 CRC patient in Europe has 3 months CAPOX rather than 6 months chemotherapy**
- **In Greece a rough estimation is 750 patients stage III/annum x 5000 Euros=3.500.000Euros savings/year**

The cost of 6 months therapy using CAPOX was £10,514 per patient versus £11,461 for FOLFOX. (NICE)
446,800 CRC pts diagnosed in 2012 in Europe, worldwide 1,360,602 (globocan)
25% stage 3: 111,700 in EU, @ £5257 saving per case = £587,206,900 per annum saving to health care system

# The three critical evaluation steps of ESMO-MCBS



# ESMO MCBS - Ranking of 1st-line mCRC treatment options in ESMO-MCBS field testing

| Medication | Trial | Setting | 1° out-come | PFS control | PFS gain | PFS (HR) | OS control | OS gain | OS (HR) | QoL | Tox-icity | ESMO-MCBS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| FOLFOX4 ± pmab | PRIME | 1st-line mCRC (post hoc WT *KRAS, NRAS, BRAF*†) | PFS | 7.9 mo | 2.3 mo | 0.72 (0.58–0.90) | 20.2 mo | 5.8 mo | 0.78 (0.62–0.99) | - | - | **4** |
| Pmab + mFOLFOX6 vs bev + mFOLFOX6 | PEAK | 1st-line mCRC WT *KRAS* | PFS | - | - | NS | 24.3 mo | 9.9 mo | 0.62 (0.44–0.89) | - | - | **4‡** |
| FOLFIRI ± cmab | CRYSTAL | 1st-line mCRC stratified for WT KRAS (post hoc WT *KRAS*, *NRAS*) | PFS | 8.4 mo | 3.0 mo | 0.56 (0.41–0.76) | 20.2 mo | 8.2 mo | 0.69 (0.54–0.88) | - | - | **4** |
| Cmab vs Best Supportive Care | | Refractory metastatic KRAS-WT | OS | 1.9 mo | 1.8 mo | 0.4 (0.30–0.54) | 4.8 mo | 4.7 mo | 0.55 (0.41–0.740 | - | - | **4** |
| FOLFOX4 ± pmab | PRIME | 1st-line mCRC WT *KRAS* | PFS | 8.0 mo | 1.6 mo | 0.80 (0.66–0.97) | 19.4 mo | 4.4 mo | 0.83 (0.70–0.98) | - | - | **3** |
| FOLFIRI ± cmab | CRYSTAL | 1st-line mCRC stratified for WT *KRAS* | PFS | 8.4 mo | 1.5 mo | 0.70 (0.56–0.87) | 20.0 mo | 3.5 mo | 0.80 (0.67–0.95) | - | - | **3** |
| IFL ± bev | | 1st-line mCRC | OS | - | - | - | 15.6 mo | 4.7 mo | 0.66 (0.54–0.81) | - | - | **3** |
| FOLFIRI ± panitumumab | | 2nd line metastatic KRAS-WT | PFS | 3.9 mo | 2 mo | 0.73 (0.59–0.90) | - | - | - | - | - | **3** |

†Note: data presented in the table are in fact for the WT *RAS* (i.e. WT *KRAS* and *NRAS* exons 2/3/4) subgroup of PRIME and not the WT *KRAS*/*NRAS*/*BRAF* subgroup as stated here and in the original Cherny NI, et al paper;
‡Unbalanced crossover.
Bev, bevacizumab; BSC, best supportive care; cmab, cetuximab.

Adapted from Cherny NI, et al. Ann Oncol 2015 [Epub ahead of print] (Table 6 – Colorectal Cancer).

ESMO-MCBS, European Society for Medical Oncology Magnitude of Clinical Benefit Scale.

# Barriers

- Implementation
- Timelines
- Transfer of results to target groups
- Credibility of the messenger and the message

# Scientific, technical, logistic and cultural barriers

- "Cancer" not a single disease but hundreds of diseases undergoing constant evolution
- Heterogeneity in pathophysiology and treatment effects, and challenge of identifying molecular targets/pathways with limited adverse effects
- Lack of consensus on surrogate endpoints
- In the absence of high-quality evidence there will be a risk that the uptake and diffusion of technologies may be influenced by social, financial and institutional factors that may not generate optimum health outcomes and an efficient use of limited resources
- Competitive grant mechanisms inhibit collaborative efforts (Widespread duplication of efforts)
- Lack of valid and well-defined biomarkers to predict prognosis and treatment response, and lack of accompanying regulatory agency guidance

# Scientific, technical, logistic and cultural barriers(2)

- Clinical trials take too long and focus too much on survival
- Working internationally in HTA, companies are required to develop multiple dossiers and employ multiple analytical approaches
- Different economic measures are applied in different countries, leading to inconsistent results
- Lack of consensus around what constitutes “value” in a new treatment (focus on added therapeutic value rather than on
- economic evaluation of health technology)
- Unaffordable cost of new drugs; lack of transparency about how the price of a drug is calculated
- What’s the procedure in case of further indications are needed
- Prevention, early detection, and palliative care are valued differently in different countries and by different organizations

# Scientific, technical, logistic and cultural barriers(3)

- Patient needs and preferences ignored
- Paternalistic/hierarchical doctor-patient relationship fails to value patient/citizen involvement in treatment decisions
- Governments do not sufficiently value innovation or foster a "can do" culture

# Solutions

- Create multi-stakeholder forum including patients/citizens and develop concrete policy proposal
- Promote dialogue between clinicians, public health entities, patient associations, and companies to get a better sense of priorities
- Establish fund for “high-risk” pilot projects
- Support research to define the “utility” for patients of treatments that can be built into or supplement cost-effectiveness calculations
- Increase international collaboration among stakeholders to define value and innovation
- Increase cross-training among decision makers at different levels of health care

# Actions for researchers and policy-makers

- Improve collaboration and ensure close, personal, two-way communication
- Consolidate mutual trust

# Actions for researchers

- Promote research which includes results on effectiveness ( identifying not only the benefits but also any expected risks and costs of the technology assessed) and highlights the uncertainty of the estimates
- Foster the synthesis of research results and their integration with information of real usefulness to health policy-makers. Translate this to the local context as far as possible
- Incorporate the views of research policy-makers, ensure the research is perceived as timely and of high quality and advocate for it to be relevant to health policy and demands of the public

# Actions for researchers (2)

- Include representatives of the various health system stake-holders in the drawing – up of recommendations in order to enhance their acceptability
- Avoid becoming embroiled in power and budget struggles and be aware of the high turnover of managers and health policy-makers
- Take policy-makers into account in the format, presentation and dissemination of scientific evidence by introducing take-home messages, brief summaries of the research, graphic communication and clear health-policy recommendations

# Actions for policy-makers

- Instigate cultural change and acquire the necessary training and skills in order to introduce scientific evidence into the decision-making process
- Health-care managers and policy-makers should have greater involvement in systematic reviews and be furnished with adequate support to enable health-care staff to participate in these. This would increase the acceptability of the assessment reports and improve their impact

# Actions for policy-makers(2)

- Health managers and policy-makers should make regular assessments of the availability of scientific evidence an integral part of the development of public health policy
- Create health policy networks or observatories that promote the joint efforts of researchers and health-care managers

# Dialogue

- Ongoing dialogue between researchers and policy-makers emerges as one of the key factors
- The question is how to promote appropriate collaboration between scientists and policy-makers, i.e how to favor the facilitators while eliminating ( or at least diminishing) existing barriers

A new, more deliberative, appropriate and cooperative way of working together must be developed by bridging the gap between researchers and policy-makers.