Early Dialogue in HTA
Yes, but how to bridge the gap?

EUNetHTA, September 14, 2017

Dr. h.c. Cees Smit,

Patient expert, EGAN/VSOP

Dept. Clin. Epidemiology, LUMC, Leiden

My experience

Hemophiliac, 66 years

Complex patient with comorbidities

Patient Expert, 45 years

Member Study Group ‘Hemophilia in the Netherlands, 1978 – 2017, Leiden University

Member of HTA Platform, RGO, 1999-2005

Member Appraisal Committee ZIN, 2008-2015

This presentation

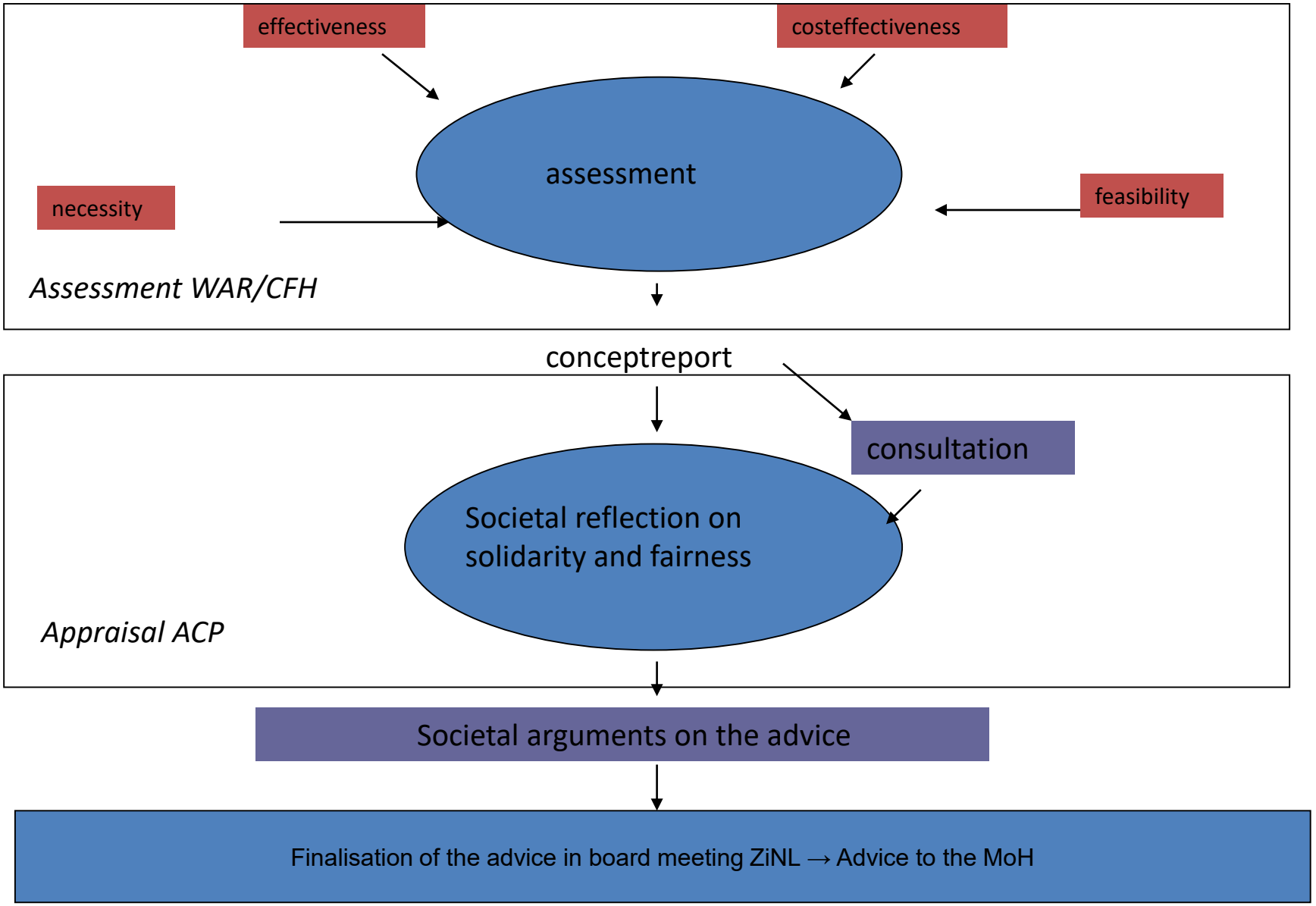
Member Appraisal Committee ZIN, 2008-2015

Lack of an effective dialogue:

HTA, hemophilia & physiotherapy

HTA and Bladder Flushing

Early Dialogue, yes but how to bridge the gap?


effectiveness
costeffectiveness
assessment
necessity
feasibility
Assessment WAR/CFH
conceptreport
consultation
Societal reflection on solidarity and fairness
Appraisal ACP
Societal arguments on the advice
Finalisation of the advice in board meeting ZiNL → Advice to the MoH

Patient (2015) 8:5–10
DOI 10.1007/s40271-014-0086-8

COMMENTARY

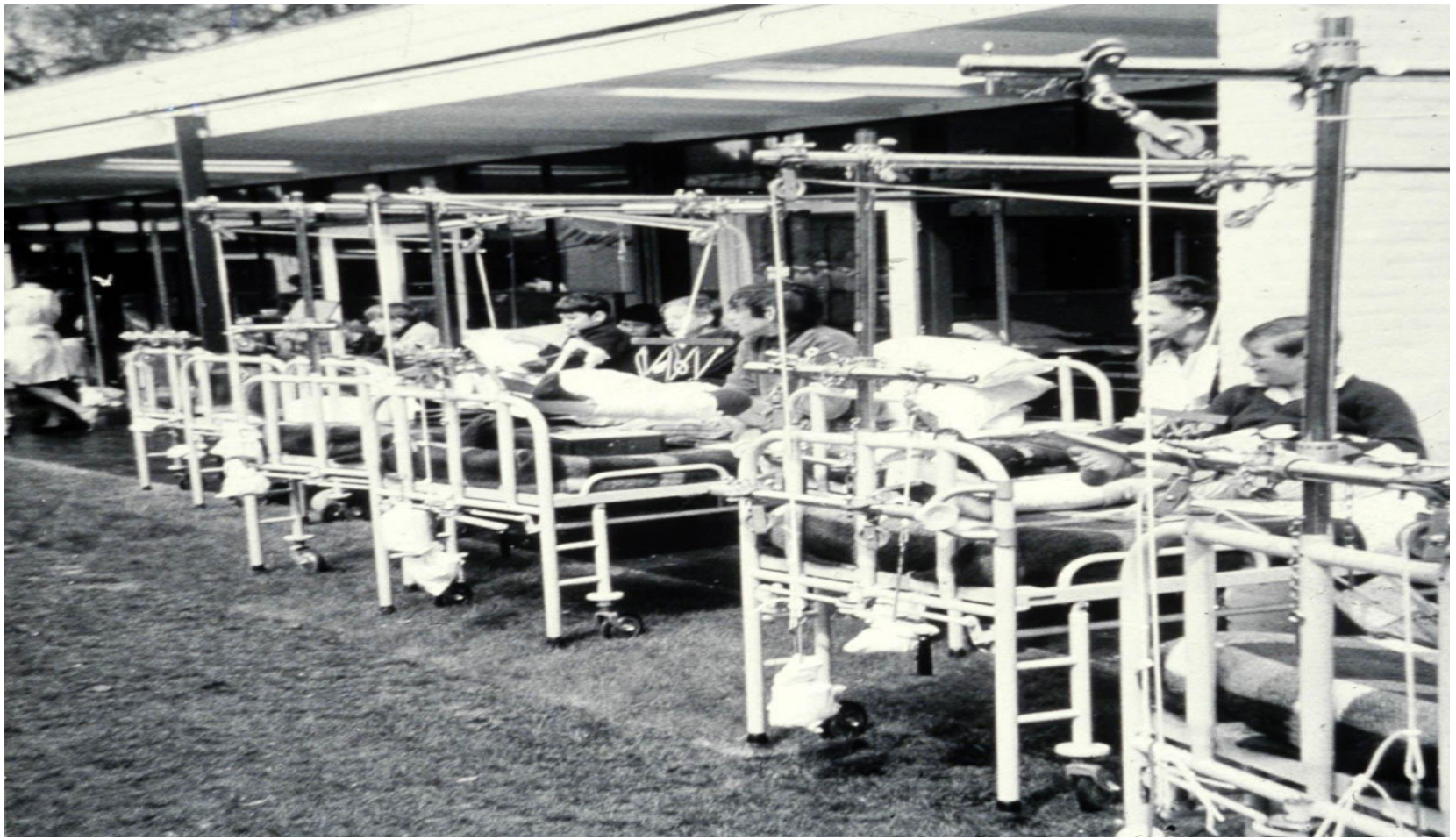
Personal Reflections of a Patient Representative in an Appraisal Committee

Cees Smit

Observations & Recommendations

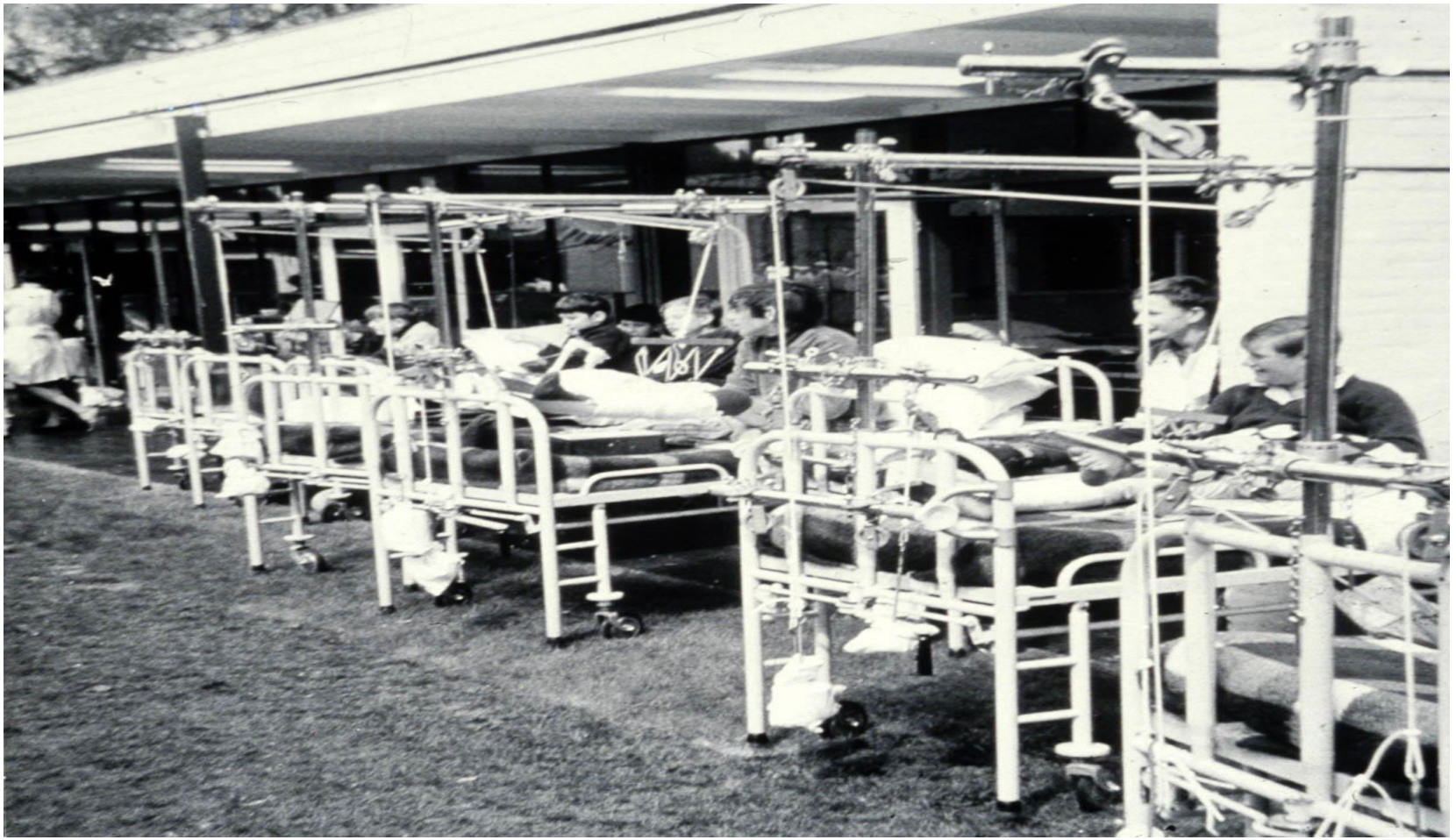
- In 2012 a societal debate on Pompe and Fabry
- No early Dialogue possible
- No possibility to merge the ‘hard’ criteria of HTA assessments with the ‘more soft’ outcome measures of patients and families
- EU Orphan Drug Act (1999) stimulates the research on rare diseases, but there is no clear EU policy how to grant access to orphan drugs within reimbursement procedures (HTA process)

Hemophilia,
an untreatable rare disease in 1965



Hemophilia,
a treatable rare disease in 2015

Hemophilia,
an untreatable rare disease in 1965



The patient group from 1965 to 2015: mobility & comorbidity (hiv & hcv)

Reprinted from the **BRITISH MEDICAL JOURNAL**, *28th January 1989, 298, 235-238*

MIDDLES

Physical condition, longevity, and social performance of Dutch haemophiliacs, 1972-85

C Smit, F R Rosendaal, I Varekamp, A Bröcker-Vriends, H Van Dijck, Th P B M Suurmeijer, E Briët

Abstract

A study was carried out among haemophiliacs in The Netherlands to evaluate the effect of modern substitution treatment (replacing the missing clotting factors) on medical and social performance. Three questionnaires were sent between 1972 and 1985. The use of prophylactic treatment in the group of patients with severe and moderately severe haemophilia increased from 21% (n=242) in 1972 to 36% (n=559) in 1985. Home treatment programmes increased from 4% to 53%. Overall mortality was 2·1 times higher than in the general male population, which leads to a calculated life expectancy of 66 years compared with 74 years in the general male population. Severe joint impairment was prominent in the older age groups, reflecting insufficient treatment in the past. A sharp decrease in the use of inpatient and outpatient hospital facilities was observed as well as much less absence from school and work.

It is concluded that the high costs of modern substitution treatment are fully justified.

employment. Moreover, these studies concerned single treatment networks so that the conclusions may not be generalised.[1-6]

The aim of our study was to evaluate modern haemophilia treatment in The Netherlands. Therefore, we reviewed the medical and social performance of Dutch haemophiliacs by means of questionnaires sent out in 1972, 1978, and 1985.

Methods

We carried out three postal surveys among Dutch haemophiliacs in 1972, 1978, and 1985. The first was based on a haemophilia questionnaire used by the Children's Orthopedic Hospital in Los Angeles, California.[7] The questionnaire was prestructured (multiple choice) and had some open questions. The standardised questionnaires covered a broad range of aspects of haemophilia—for example, type and severity, number of bleedings, transfusion treatment, treatment regimens, orthopaedic state, hospital admissions, education, disability and employment, insurance, social relations, genetic counselling, and so on. Many items were repeated in the second and third

HTA

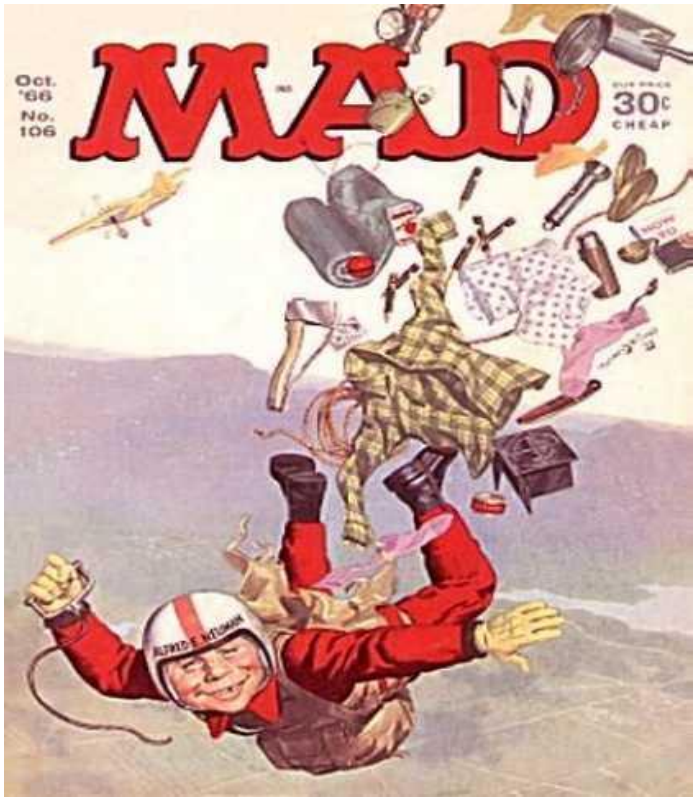
- ***'Prospective well conducted studies on economic issues in hemophilia care are scarce'***

  (ref. Swedish Council on Health Technology Assessment. 2011. SBU-Rapports; Band 208E)

- ***'RCT's of hemophilia patients is difficult not only because of low patient numbers'.***

  (ref. IQWiG-Berichte – Nr. 305; 2015)

‘Parachute effect’



HTA, Hemophilia & Physiotherapy

Haemophilia
The Official Journal of the World Federation of Hemophilia,
European Association for Haemophilia and Allied Disorders and
the Hemostasis & Thrombosis Research Society

Haemophilia (2016), 1–6 DOI: 10.1111/hae.13076

ORIGINAL ARTICLE

Evidence for and cost-effectiveness of physiotherapy in haemophilia: a Dutch perspective

P. DE KLEIJN,*¶ E. P. MAUSER-BUNSCHOTEN,† K. FISCHER,† C. SMIT,‡ H. HOLTSLAG§ and C. VEENHOF¶

Van Creveld kliniek, University Medical Center Utrecht; †Van Creveldkliniek, University Medical Center Utrecht, Utrecht, The Netherlands; ‡VSOP, Amsterdam; §AMC, Amsterdam; and ¶Physical Therapy Research, Department of Rehabilitation, Physiotherapy Science and Sports, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht, The Netherlands

HTA, Hemophilia & Physiotherapy

- 2011, physiotherapy out of basic insurance (lack of evidence)
- Assessment procedure within ZIN 2014-2017 (incl. RA/SA)
- In anticipation, we collected evidence levels for hemophilia published in a peer-reviewed journal
- We send two letters and a contribution in public hearing
- No response at all from ZIN on these contributions/letters
- External advice to ZIN: '*Experts agree that exercise, although poorly specified in current guidelines and with a limited evidence base for its effectiveness, is an important element of care for patients with RA. They suggest that future studies should investigate in more detail "what works for whom"….' (ref.: Panaxea, 2016)*

Health Economics, Policy and Law, page 1 of 20
doi:10.1017/S1744133116000281

Contested evidence: a Dutch reimbursement decision taken to court

FLOORTJE MOES*

Department of Health, Ethics and Society, Research School CAPHRI, Maastricht University, Maastricht, the Netherlands

EDDY HOUWAART

Department of Health, Ethics and Society, Research School CAPHRI, Maastricht University, Maastricht, the Netherlands

DIANA DELNOIJ

Tranzo (Scientific Centre for Care and Welfare), Tilburg University, Tilburg, the Netherlands

KLASIEN HORSTMAN

Department of Health, Ethics and Society, Research School CAPHRI, Maastricht University, Maastricht, the Netherlands

HTA & Bladder flushing

- In contrast with hemophilia (≈ 180.000 €/year), rather cheap treatment (≈ 200 € /treatment /twice a month)
- Nevertheless, a reimbursement problem
- Judgement ZIN: no evidence, no RCT's
- Two court cases: first won by patients, second by ZIN
- Still no solution, experts say data collection is possible, but no RCT
- A lot of frustration among urologists & patients
- No stepped care, but now cases of bladder removal (stoma)
- Outcome: more expensive, ↓ QOL Patients/family

Early Dialogue in HTA
How to bridge the gap?

EU Patient Education & Resources

The past 10-15 yrs: Summer School Eurordis,
LSE/HTA, PatientPartner, Value+, material by EUPATI (translations, trainings & webinars)

New handbook: 'Patient involvement in HTA',
presented at the HTAi in Rome, 2017

Patients as partners in HTA, Durhane Wong-Rieger, 2013

So, there is a lot of knowledge and there are capable people within the EU Patient Community to have a dialogue

Possible solutions

- EMA: Patient and Citizen Working Party
- Engagement of patients needs a dedicated structure, with adequate staff and resources
- Early involvement in scoping and scientific advice
- Analyze Patients' Priorities first, see hemophilia: tension new therapies & PUPS
- EUNetHTA should make a time-table when & how to start with what pilots/projects

For more information

info@smitvisch.nl

www.smitvisch.nl

Presentation of Healthcare providers group

Dr Daniel Widmer, MD

Vice-president UEMO

Healthcare Providers group

EUPHA

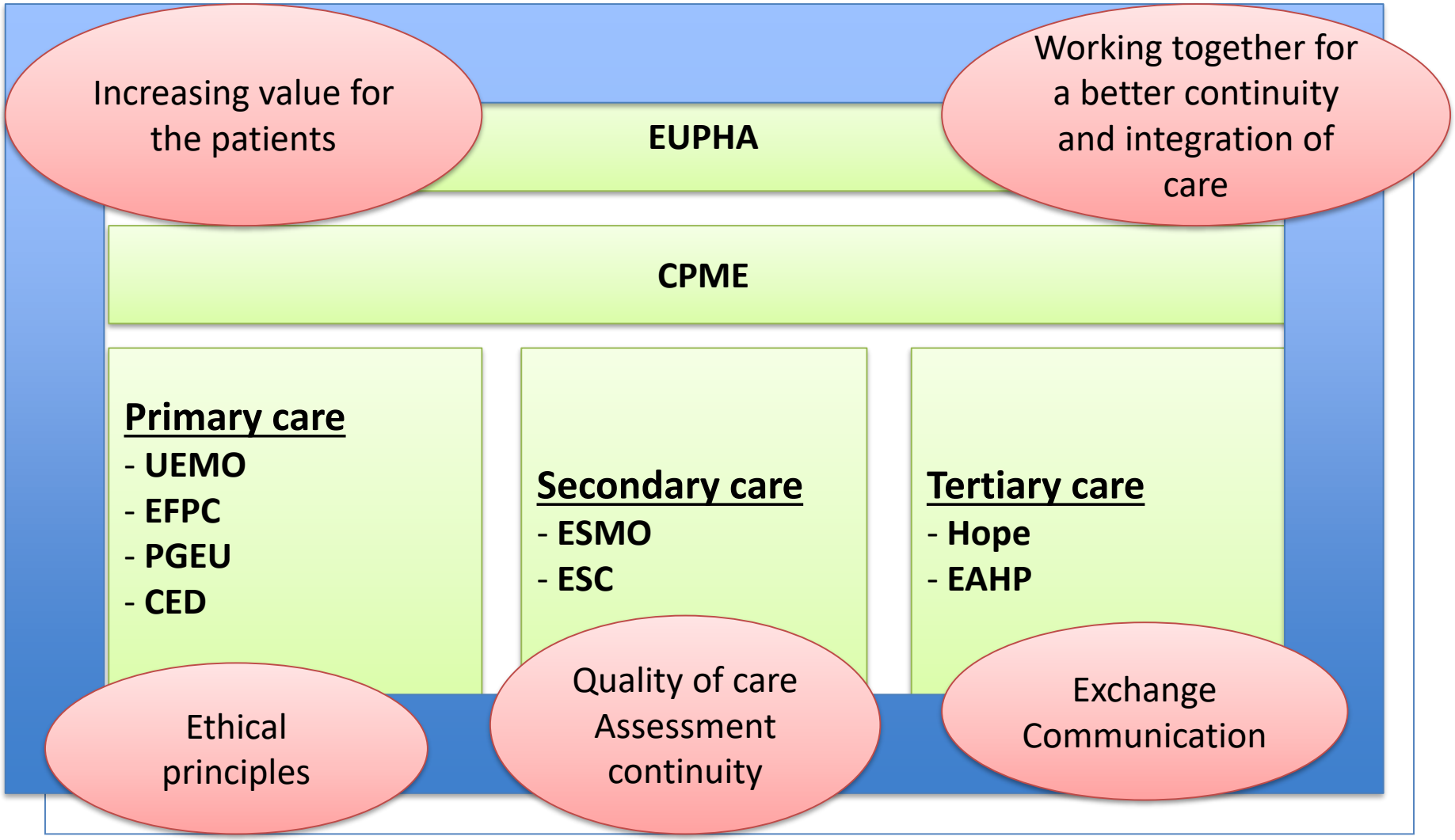
CPME

Primary care
- UEMO
- EFPC
- PGEU
- CED

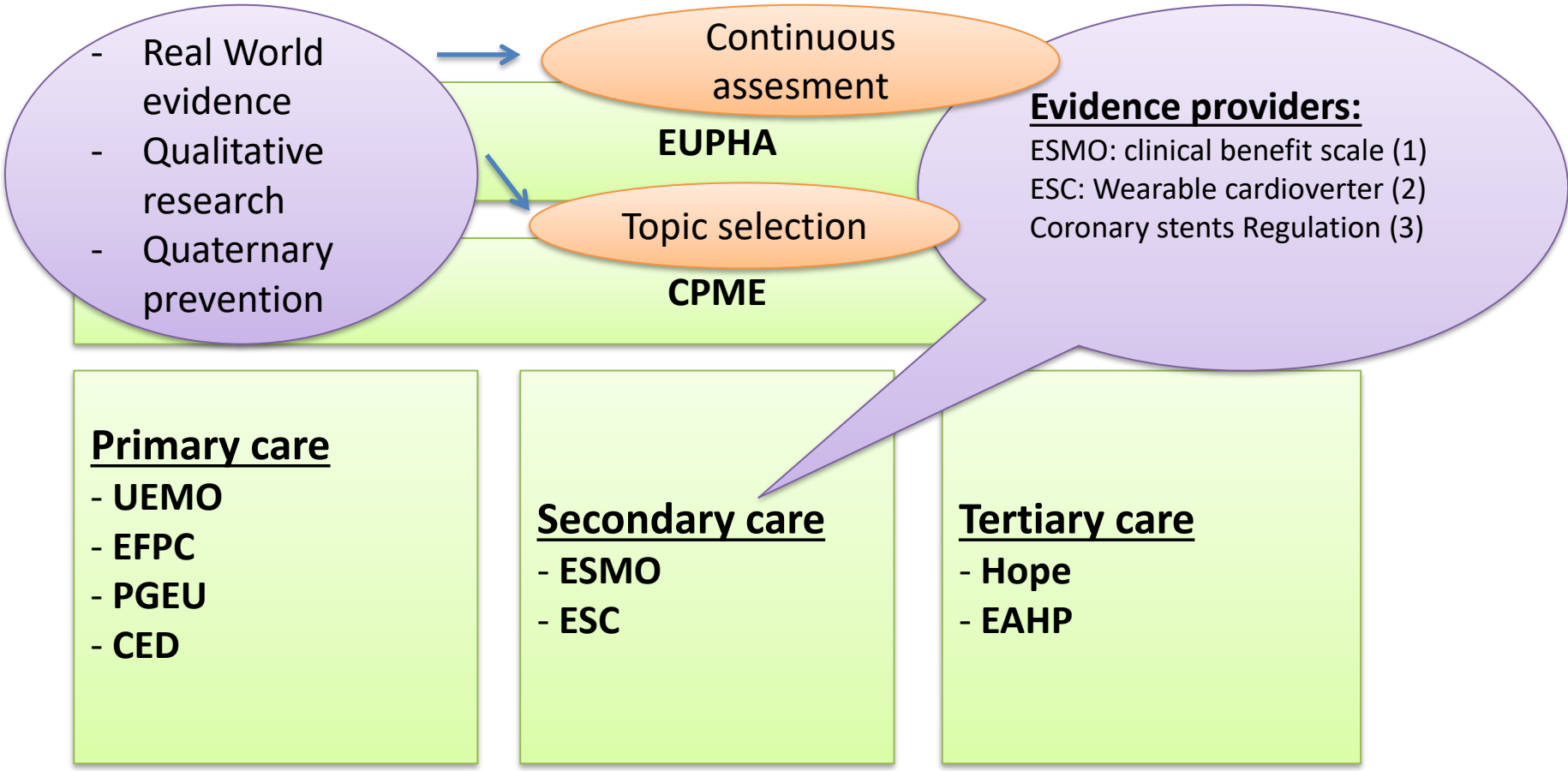
Secondary care
- ESMO
- ESC

Tertiary care
- Hope
- EAHP
- Some hospitals and hospital pharmacists make also I and II care in some countries

Common values



Involvement of HCP



- 1. http://www.esmo.org/Policy/Magnitude-of-Clinical-Benefit-Scale
- 2. http://www.eunethta.eu/outputs/1st-collaborative-assessment-wearable-cardioverter-defibrillator-wcd-therapy-primary-and-sec
- 3 https://www.pcronline.com/eurointervention/111th_issue/volume-12/number-14/275/regulation-of-coronary-stents-physicians-as-stakeholders.html
- 4 Sherman RE, Anderson SA, Dal Pan GJ, Gray GW, Gross T, Hunter NL, et al. Real-World Evidence — What Is It and What Can It Tell Us? New England Journal of Medicine. 2016 Dec 8;375(23):2293–7.

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

THE ESMO-MAGNITUDE OF CLINICAL BENEFIT SCALE

Elisabeth de Vries

University Medical Center Groningen

On behalf of the ESMO-MCBS working group

ESMO in a nutshell

Europe's leading Medical Oncology Society

Working across Europe and around the world to erase boundaries in cancer care and to provide medical oncology education in an integrated approach to cancer care

- A member-based alliance with a network of more than **16,000 oncology professionals**
- Represents over **130 countries**
- Cooperates in partnership with all stakeholder groups to ensure the **highest level of standards** for medical oncology professionals

Reason to develop the ESMO-MCBS

- **2013**: Differences in Europe
  - in cancer outcome
  - in access to anticancer drugs between European countries
  - in access to anticancer drugs within European countries

- **2017:** Novel anticancer drugs not sustainable for all European countries

ESMO-MCBS V1.0

OXFORD ACADEMIC

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EDITOR'S CHOICE

A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS)

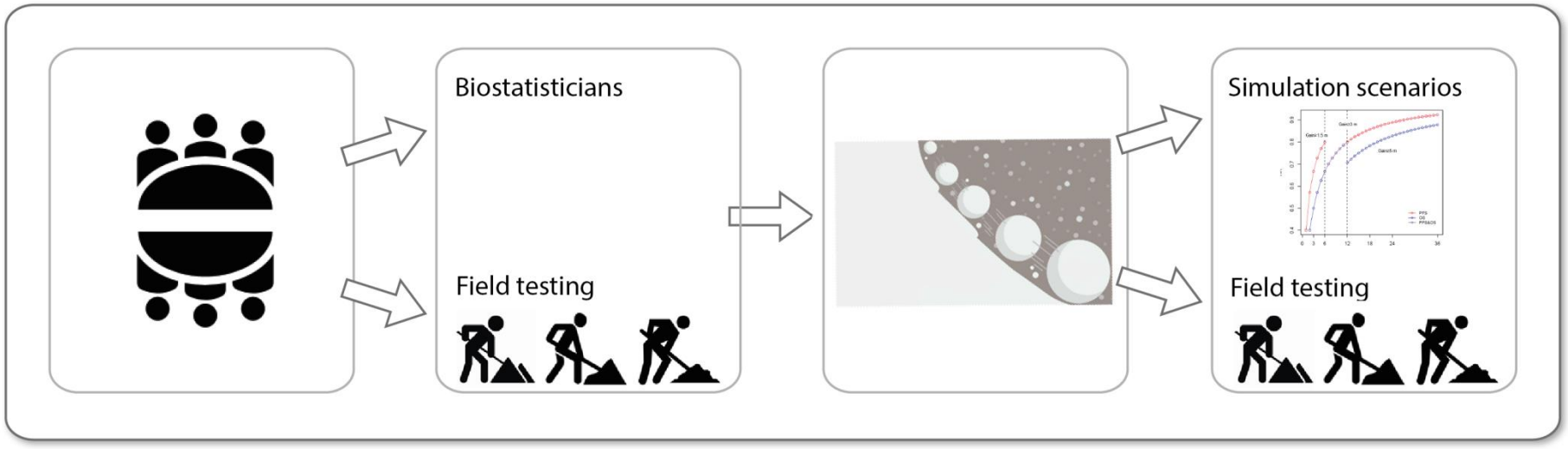
N. I. Cherny, R. Sullivan, U. Dafni, J. M. Kerst, A. Sobrero, C. Zielinski, E. G. E. de Vries, M. J. Piccart

Ann Oncol (2015) 26 (8): 1547-1573. **DOI:** https://doi.org/10.1093/annonc/mdv249
Published: 30 May 2015 **Article history**

Views PDF Cite Share Tools

ESMO

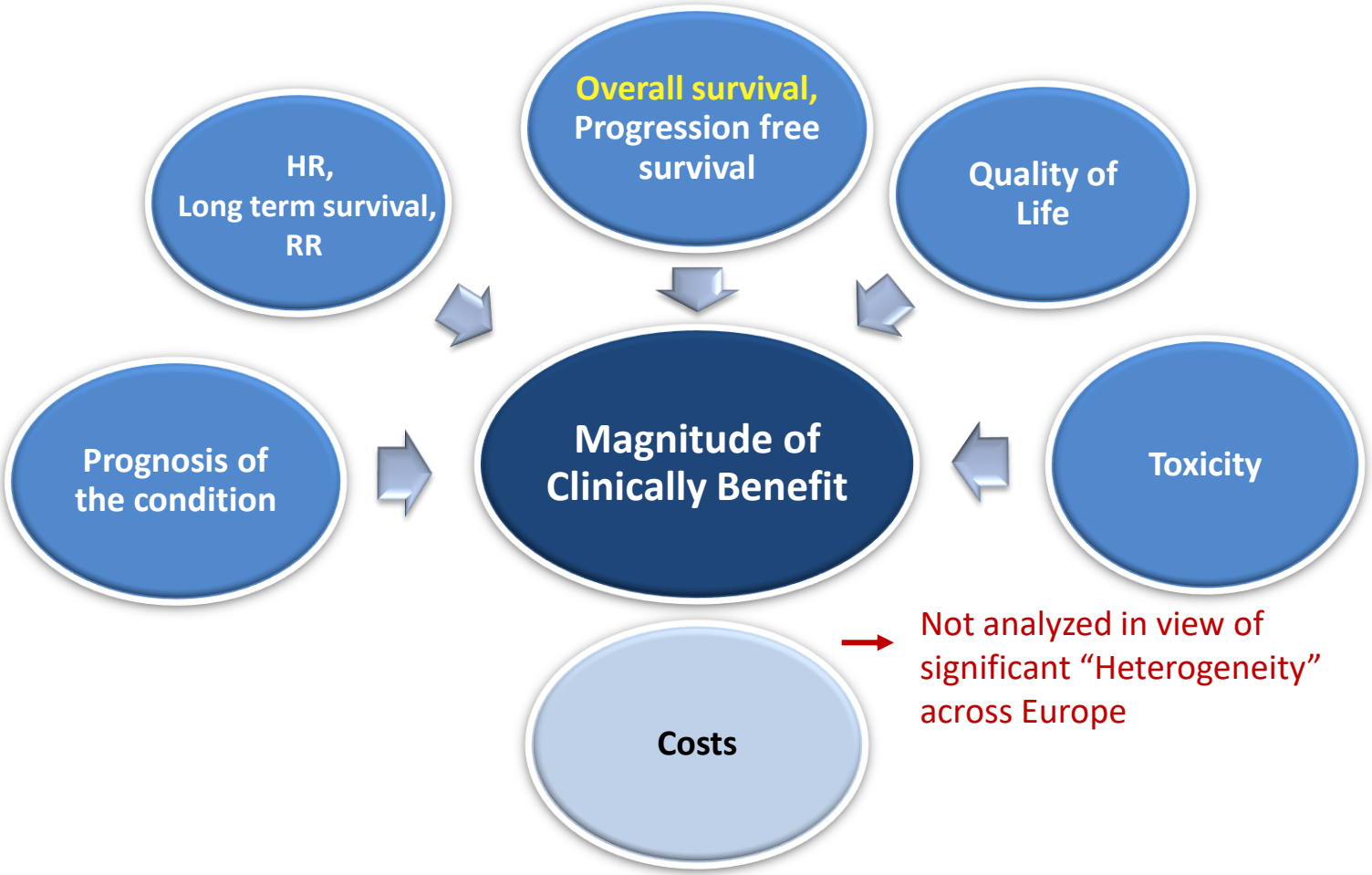
ESMO-MCBS v1.0
developed by task force, field testing & simulation scenarios



Feed back from Pharma and Patients

Cherny et al, Ann Oncol, 2015
Dafni et al, ESMO Open, 2017

Factors taken into account for ESMO-MCBS

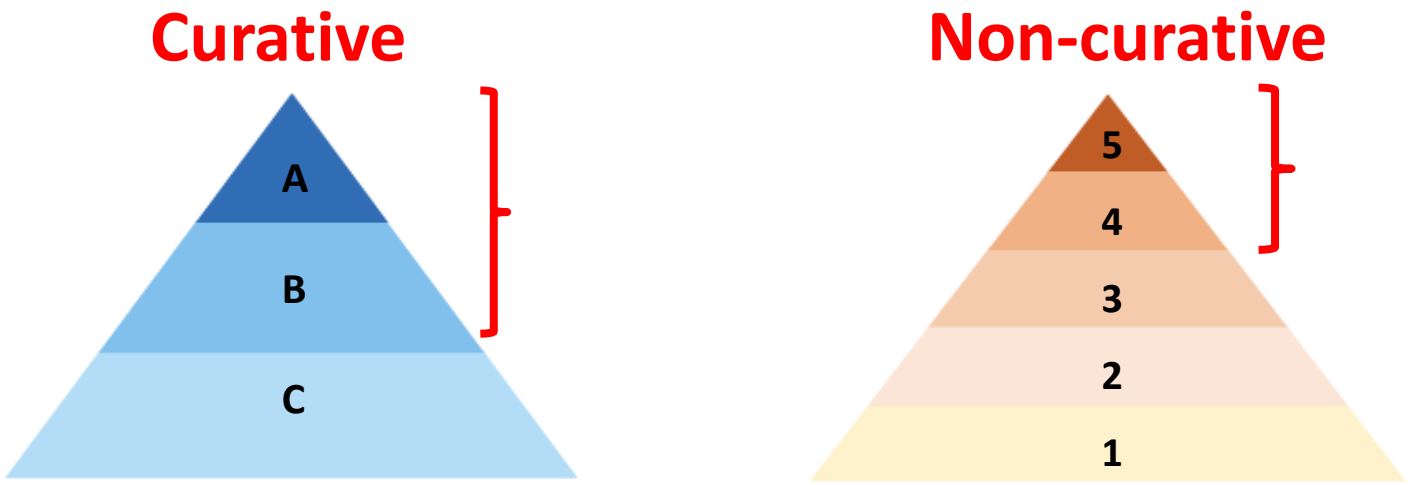


Underlying Premises ESMO-MCBS

1. Cure takes precedence over deferral of death
2. Direct endpoints such as survival and QoL take precedence over surrogates such as PFS or RR
3. DFS in curative disease is a more valid surrogate than PFS or RR in non-curative disease
4. Interpretation of the evidence for benefit derived from surrogate outcomes (such as PFS) may be influenced by secondary outcome data

Definition ESMO-MCBS substantial improvements

- Curative setting A & B or non-curative setting 5 & 4

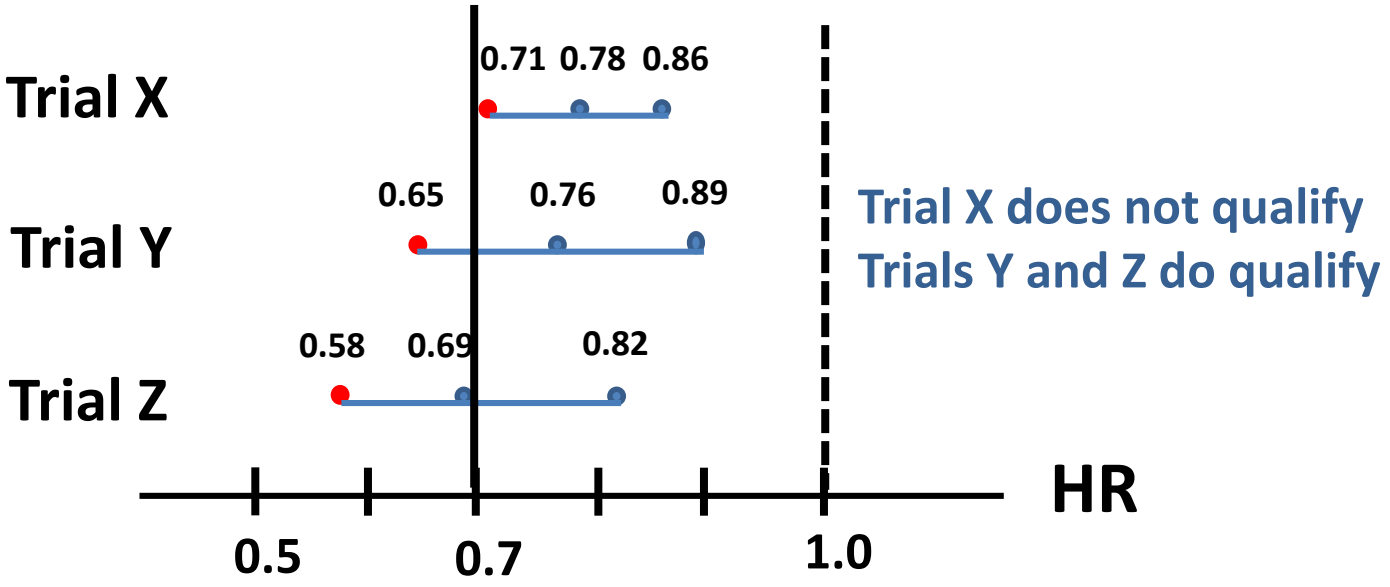


3 Rules, ESMO-MCBS, 1 of them

a. More than one outcome may be applicable
b. For a required HR, not the point estimate but the lower limit of the 95% CI is used to take into account the variability of the estimate

Example: for threshold set at HR ≤ 0.70

it is the lower limit of the 95%CI which has to be ≤ 0.70



Reasons ESMO-MCBS v1.1

- The ESMO-MCBS is a dynamic tool
- v1.0 only scored comparative studies➔ need grade single arm studies
- Further reasons for revision
  - Experience field testing and scoring recent studies
  - Input/queries from clinicians and industry
  - Active internal peer review
- Detailed discussions & field testing
- ESMO-MCBS v1.1 Annals of Oncol, Cherny et al. 2017

Forms ESMO-MCBS V1.1

- **Curative Setting** → Evaluation form 1
  A, B, C
- **Non-curative setting** → Evaluation form 2a
  5, 4, 3, 2, 1
  Evaluation form 2b
  4, 3, 2, 1
  Evaluation form 2c
  4, 3, 2, 1
- **Non-curative setting** → Evaluation form 3
  Single arm studies
  4, 3, 2, 1

Evaluation form 1:
for new approaches to adjuvant therapy or new potentially curative therapies

Grade A	Mark with X if relevant
>5% improvement of survival at ≥3 years follow-up	
Improvements in DFS alone (primary endpoint) (HR <0.65) in studies without mature survival data	

Grade B	
≥ 3% but ≤ 5% improvement at ≥3 years follow-up	
Improvement in DFS alone (primary endpoint) (HR 0.65 - 0.8) without mature survival data	
Non-inferior OS or DFS with reduced treatment toxicity or improved Quality of Life (with validated scales)	
Non-inferior OS or DFS with reduced treatment cost as reported study outcome (with equivalent outcomes and risks)	

Grade C	
<3% improvement of survival at ≥ 3 years follow-up	
Improvement in DFS alone (primary endpoint) (HR >0.8) in studies without mature survival data	
Improvements in pCR alone (primary endpoint) by ≥30% relative AND ≥15% absolute gain in studies without mature survival data	

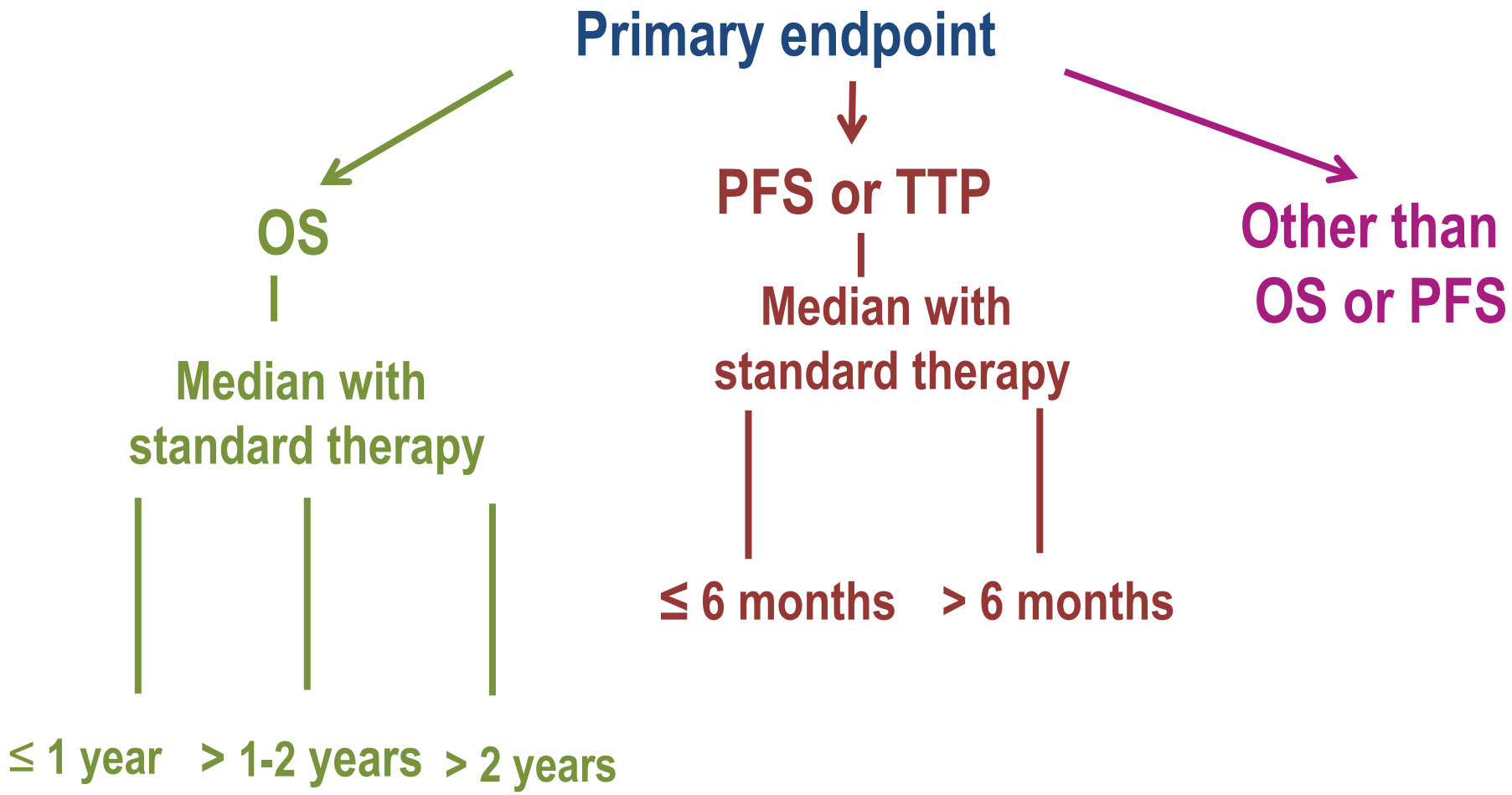
Evaluation form 1: for new approaches to adjuvant therapy or new potentially curative therapies

Magnitude of clinical benefit grade (highest grade scored)

A	B	C

ESMO-MCBS distinctions v1.1:

for treatment with non-curative intent



Evaluation form 2a: for therapies that are not likely to be curative with primary endpoint OS

IF median OS with the standard treatment ≤12 months

Grade 4	Mark with X if relevant
HR ≤0.65 AND Gain ≥3 months	
Increase in 2 year survival alone ≥10%	

Grade 3	
HR ≤0.65 AND Gain ≥2.0 - <3 months	

Grade 2	
HR ≤0.65 AND Gain ≥1.5 - <2 months	
HR >0.65-0.70 AND Gain ≥1.5 months	

Grade 1	
HR > 0.70 OR Gain <1.5 months	

Evaluation form 2a: for therapies that are not likely to be curative with primary endpoint OS

Step 1

Preliminary magnitude of clinical benefit grade

4	3	2	1

Step 2

Assessment QoL & grade 3-4 toxicities

Does secondary endpoint quality of life show improvement	
Are there statistically significantly less grade 3-4 toxicities impacting on daily well-being*	

Upgrade 1 level if improved QoL or toxicity is shown

If there is a long term plateau in the survival curve, and OS advantage continues to be observed at 5/7 year, <u>also score</u> according to Form 1 (treatments with curative potential) and present both scores i.e. A/4

Step 3

Final adjusted magnitude of clinical benefit grade

5	4	3	2	1

Evaluation form 3: for single-arm studies in "orphan diseases" and for diseases with "high unmet need" when primary outcome is PFS or ORR

Grade 3	Mark with X if relevant
PFS ≥6 months	
ORR (PR+CR) ≥60%	
ORR (PR+CR) ≥20, <60% AND Duration of response ≥9 months	

Grade 2	
PFS ≥3-<6 months	
ORR (PR+CR) ≥40, <60%	
ORR (PR+CR) ≥20, <40% AND Duration of response ≥6 months <9 months	

Grade 1	
PFS 2-<3 months	
ORR (PR+CR) ≥20, <40% AND Duration of response <6 months	
ORR (PR+CR) >10, <20% AND Duration of response ≥6 months	

Evaluation form 3: for single-arm studies in "orphan diseases" and for diseases with "high unmet need" when primary outcome is PFS or ORR

Step 1

Preliminary magnitude of clinical benefit grade

3	2	1

Step 2

Adjustments

1. Downgrade 1 level if there are ≥ 30% grade 3-4 toxicities impacting on daily well being
2. Upgrade 1 level if improved QoL
3. Upgrade 1 level for confirmatory, adequately sized, phase 4 experience

Step 3

Final adjusted magnitude of clinical benefit grade

4	3	2	1

ESMO's efforts to make the scale accessible

- Presentations
- Workshops also for patients
- Support of those who want to use the scale for various reasons
- Will develop a web based infographics tool
- Website with information about ESMO-MCBS

http://www.esmo.org/Policy/Magnitude-of-Clinical-Benefit-Scale

AWARENESS AND UTILISATION SURVEY

What do you know about the ESMO-MCBS?

The survey results will be presented during ESMO 2017

News & Editorials

News and editorial coverage about the scale

ANNALS OF ONCOLOGY

Articles

The ESMO Magnitude of Clinical Benefit Scale was published in *Annals of Oncology*

Scale Evaluation Forms v1.0 & v1.1

Download your copies of version 1.0 and 1.1 evaluation forms

Q&A

Questions & Answers

Published on *ESMO Open*: questions regarding the development, structure and potential applications of the scale

Presentations

The scale has been presented on several occassions. Access the session webcasts here

Clinical Practice Guidelines News

The latest news about ESMO Guidelines with MCBS grading

Magnitude of Clinical Benefit Scale Working Group

Annals of Oncology 0: 1–27, 2017
doi:10.1093/annonc/mdx310

SPECIAL ARTICLE

ESMO-Magnitude of Clinical Benefit Scale version 1.1

N. I. Cherny[1*], U. Dafni[2], J. Bogaerts[3], N. J. Latino[4], G. Pentheroudakis[5], J.-Y. Douillard[4], J. Tabernero[6], C. Zielinski[7], M. J. Piccart[8] & E. G. E. de Vries[9]

[1]Cancer Pain and Palliative Medicine Service, Department of Medical Oncology, Shaare Zedek Medical Center, Jerusalem, Israel; [2]Laboratory of Biostatistics, School of Health Sciences, National and Kapodistrian University of Athens & Frontier Science Foundation-Hellas, Athens, Greece; [3]Methodology Direction, EORTC Headquarters, Brussels, Belgium; [4]ESMO Head Office, Lugano, Switzerland; [5]Medical Oncology Department, Ioannina University Hospital, Ioannina, Greece; [6]Medical Oncology Department, Vall d'Hebron University Hospital, Barcelona, Spain; [7]Division of Oncology, Medical University Vienna, Vienna, Austria; [8]Jules Bordet Institute, Universite Libre de Bruxelles, Brussels, Belgium; [9]Department of Medical Oncology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

*Correspondence to: Prof. Nathan I. Cherny, Norman Levan Chair of Humanistic Medicine, Medicine (BGU), Cancer Pain and Palliative Medicine Sevice, Department of Medical Oncology, Shaare Zedek Medical Center, Jerusalem 91031, Israel. Tel: +972-508-685780; E-mail: mcbs@esmo.org

Background: The ESMO Magnitude of Clinical Benefit Scale (ESMO-MCBS) version 1.0 (v1.0) was published in May 2015 and was the first version of a validated and reproducible tool to assess the magnitude of clinical benefit from new cancer therapies. The ESMO-MCBS was designed to be a dynamic tool with planned revisions and updates based upon recognition of expanding needs and shortcomings identified since the last review.

Methods: The revision process for the ESMO-MCBS incorporates a nine-step process: Careful review of critiques and suggestions, and identification of problems in the application of v1.0; Identification of shortcomings for revision in the upcoming version; Proposal and evaluation of solutions to address identified shortcomings; Field testing of solutions; Preparation of a near-final revised version for peer review for reasonableness by members of the ESMO Faculty and Guidelines Committee; Amendments based on peer review for reasonableness; Near-final review by members of the ESMO-MCBS Working Group and the ESMO Executive Board; Final amendments; Final review and approval by members of the ESMO-MCBS Working Group and the ESMO Executive Board.

Results: Twelve issues for revision or amendment were proposed for consideration; proposed amendments were formulated for eight identified shortcomings. The proposed amendments are classified as either structural, technical, immunotherapy triggered or nuanced. All amendments were field tested in a wide range of studies comparing scores generated with ESMO-MCBS v1.0 and version 1.1 (v1.1).

Conclusions: ESMO-MCBS v1.1 incorporates 10 revisions and will allow for scoring of single-arm studies. Scoring remains very

Implementation ESMO-MCBS Information based on:

- Interviews of people
  - asking ESMO for information
  - with known expertise with regards to implementation
- Publications
- Survey of ESMO-members and on website about scale implementation
  - 288 completed from 64 countries
    - 181 aware of the ESMO-MCBS from 49 countries

Implementation ESMO-MCBS by:

1. ESMO organisation
2. Doctors in patient care
3. Teaching
4. Academic groups
5. Industry
6. Organisations and countries using the scale as a policy tool
7. Groups looking to application in other settings

ESMO-MCBS – inclusion of scores in Guidelines

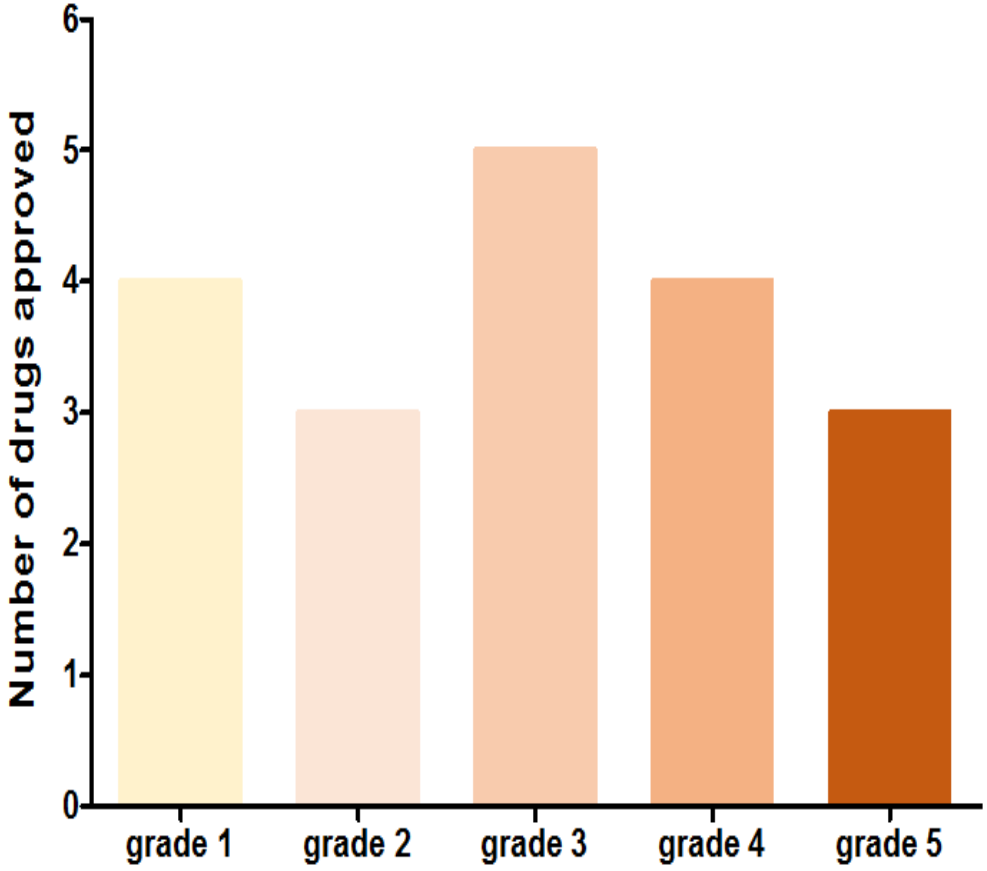
Example: Metastatic NSCLC

Therapy	Disease setting	Trial	Control	Absolute survival gain	HR (95% CI)	QoL/ toxicity	MCBS score[b]
Nivolumab	Advanced	Nivolumab versus docetaxel in advanced squamous-cell NSCLC [98] Phase III	Docetaxel in patients with advanced SCC who have disease progression during or after 1st-line chemotherapy. Control OS 6 months	OS gain: 3.2 months. 2-year survival gain 15%	OS: HR for death 0.59 (0.44-0.79)	Improved toxicity profile	**5 (Form 2a)[c]**
Nivolumab	Advanced					Improved toxicity profile	**5 (Form 2a)**
Ramucirumab	Advanced					Deteriorated toxicity profile	**1 (Form 2a)**
Pembrolizumab	Advanced	Pembrolizumab vs docetaxel for previously treated, PD-L1-positive, advanced NSCLC (KEYNOTE-010): a randomised controlled trial [96] Phase III NCT01905657	Docetaxel in patients with previously treated, PD-L1-positive, advanced NSCLC. Control OS 8.5 months	In PD-L1 >1%:[d] OS gain: 1.9 months In PD- L1 >50%:[d] OS gain: 6.7 months	In PD-L1 >1%:[d] OS: HR for death 0.71 (0.58–0.88) In PD-L1 >50%:[d] OS: HR for death 0.54	Improved toxicity profile	**In PD-L1 >1%: 3 (Form 2a)** **In PD-L1 >50%: 5 (Form 2a)**

EMA approved since 2016 scored with ESMO-MCBS 1.0

Tumor type	Drug	ESMO-MCBS score
NSCLC	Nivolumab	**5**
NSCLC	Pembrolizumab	**5** in PD-1 > 50%
Renal cell carcinoma	Nivolumab	**5**
Melanoma	Nivolumab	**4** nivolumab alone
Renal cell carcinoma	Lenvatinib	**4**
Soft tissue sarcoma	Olaratumab	**4** olaratumab + doxorubicin
Breast cancer	Palbociclib	**4** palbociclib + fulvestrant
		3 palbociclib + letrozole
NSCLC	Pembrolizumab	**3** in PD-L1 > 1%
Colorectal cancer	Ramucirumab	**3**
Neuroendocrine tumor	Everolimus	**3**
Renal cell carcinoma	Cabozantinib	**3**
NSCLC	Bevacizumab	**2**
Colorectal cancer	Trifluridine/tipiracil	**2**
Melanoma	Nivolumab	**2** nivolumab + ipilimumab
NSCLC	Afatinib	**1**
NSCLC	Necitumumab	**1**
NSCLC change to existing indication	Erlotinib	**1**
NSCLC	Ramucirumab	**1**

Distribution ESMO-MCBS 1.0 grades EMA approved solid tumor drugs since 2016



Implementation of the ESMO-MCBS

1. ESMO organisation
2. Doctors in patient care
3. Teaching
4. Academic groups
5. Industry
6. Organisations and countries using the scale as a policy tool
    1. Doctors to convince insurance companies or ministry of health
    2. WHO appreciates the ESMO-MCBS as an important tool to use globally
    3. Countries/National HTA agencies use it for decision making

Medical oncologists in Czech Republic evaluated solid cancer drugs

- Medical oncologists evaluated solid cancer drugs, reimbursed in their Cancer Centres, to be published in Klinicka Onkologie.

- ESMO-MCBS recognised by the Czech Society for Oncology as parameter for drug reimbursement decision-making, in addition to cost-utility analysis

- Not yet known how payers will respond, but in the past they expressed their wish for a similar scoring system

Tomas Buchler

World Health Organization

WHO Essential Medicines List for Solid Tumors 2015

Cytotoxics			Miscellaneous	Hormones
Bleomycin	Docetaxel	Methotrexate	Trastuzumab	Anastrozole
Capecitabine	Doxorubicin	Oxaliplatin	Imatinib	Bicalutamide
Carboplatin	Etoposide	Paclitaxel	Filgrastim	Dexamethasone
Cisplatin	Fluorouracil	Vinblastine	Calcium folinate	Leuprorelin
Cyclophosphamide	Gemcitabine	Vincristine		Tamoxifen
Dacarbazine	Ifosfamide + mesna	Vinorelbine		
Dactinomycin	Irinotecan			

http://www.who.int/medicines/publications/essentialmedicines/EML2015_8-May-15.pdf

WHO Essential Medicines List for Solid Tumors 2015

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World Health Organization

WHO appreciates the ESMO-MCBS as important tool to use globally

ESMO is a NGO in official collaboration with WHO

1. WHO considers the ESMO-MCBS methodology has potential to review current and future anti-cancer medicines for the Essential Medicine List

2. Multiple countries asked WHO for guidance on how to prioritize cancer drugs to be used in their country
   - WHO takes holistic approach: therefore analysis of disease burden, costs, but sees ESMO-MCBS also a tool of interest

Other countries

- **India's** National Cancer Grid of >100 centers is looking to adopt / adapt ESMO-MCBS as they start to create HTA processes for cancer drugs

- **Chile, Zambia and Malaysia** are trialling at policy level - using ESMO-MCBS as a go/no go prior to conducting a 'proper' cost effectiveness and / or pricing negotiation
  - likely ≥ 5 other countries are doing the same

- **Germany's** Institute for Quality and Efficiency in Health Care (IQWiG), assesses added benefit of drugs to appropriate comparator to inform drug price negotiations
  - High correlation between IQWiG and ESMO-MCBS analyses
  - Further collaboration between IQWiG and ESMO

Implementation of the ESMO-MCBS

1. ESMO organisation
2. Doctors in patient care
3. Teaching
4. Academic groups
5. Industry
6. Organisations and country(s) using the scale as a policy tool
7. Groups looking to application in other settings

Groups looking at application in other settings

1. EHA is currently performing field testing of the ESMO-MCBS for hematological anticancer drugs

EUROPEAN HEMATOLOGY ASSOCIATION

2. Value Based Heathcare assessment in the non-pharmaceutical domain

ECCO EUROPEAN CANCER ORGANISATION

ESMO-MCBS and ASCO Value Framework

Extensive analysis by comparing the two scales, leading to next steps

Converging on the value of value frameworks.
Schnipper and Schilsky. J Clin Oncol 2017

Conclusion ESMO-MCBS

- Used worldwide
  1. ESMO
  2. In patient care
  3. Teaching
  4. Academic groups
  5. Industry
  6. As a policy tool
  7. Potential application in other settings

- ESMO-MCBS is valuable tool to:
  - rationalise use and allocation of resources
  - focus on treatments with higher anticipated benefit

ESMO-MCBS working group & important people who provided information

ESMO-MCBS working group

- Jan Bogaerts, Belgium
- Nathan Cherny, Israel
- Urania Dafni, Greece
- George Pentheroudakis, Greece
- Martine Piccart, Belgium
- Josep Tabernero, Spain
- Christoph Zielinski, Austria

ESMO office: Nicola Latino, Keith McGregor, Jean Yves Douillard

ESMO EXC board

ESMO-MCBS Guideline Committee

ESMO-MCBS numerous field testers

Important people who provided information

- Richard Sullivan, André Ilbawi, Tomas Buchler, Alexandru Eniu