



## Methods and Preliminary Results of the ISPOR Oncology Health Economic Modeling Special Interest Group



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## Presenters



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- **Hena Qureshi, BSc BA**, Student, Community Health Sciences, University of Calgary, Calgary, AB, Canada



## Leadership Group

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- **Kathi Apostolidis**, Vice President, European Cancer Patient Coalition (ECPC), Brussels, Belgium
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3



## Student Volunteers

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4



## Why Oncology Modeling?

- Increased focus on the assessment of the value of oncology drugs
  - Cancer Drugs Fund in the UK - Revised
  - Value frameworks in oncology
    - National Comprehensive Cancer Network (NCCN) Evidence Blocks (23 indications completed)
    - American Society of Clinical Oncology (ASCO) Value Framework - Revised
    - European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) – In revision
- New challenges in the assessment of value as standard methods are not applicable to immuno-oncology treatments
- Methods development questions standard methods used in economic modeling

5



## Aims of the Working Group

- Advance knowledge and understanding around oncology economic modeling
- Provide education and resources for researchers interested in the health economic modeling of oncology products
- Stimulate debate and encourage research
- Develop best practices in selected aspects of economic modeling, specific to oncology
- Foster discussions among researchers working in the field in different organizations
- Foster communication and collaboration between health economists and medical organizations and patient representatives (ISPOR Patient Representatives Roundtable)

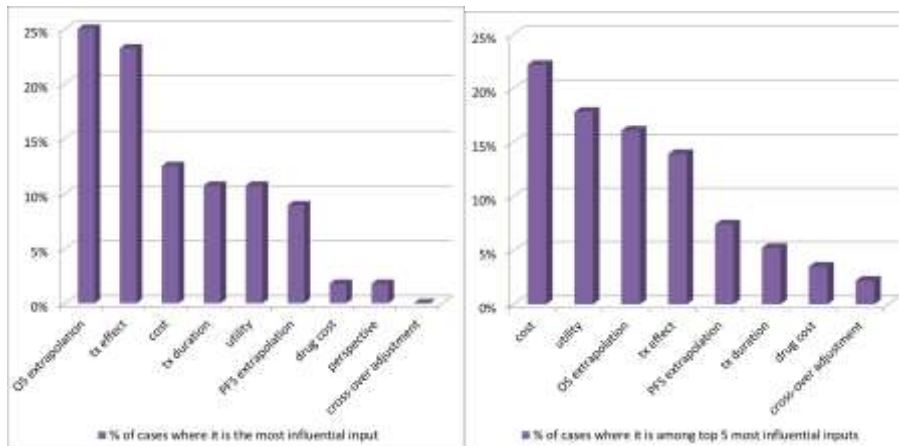
6

# Importance of Utilities and Costs in Oncology



- Utilities are one of the most influential parameters in cost-utility analyses for advanced tumors

Most influential inputs in NICE TAs (2011-2015)



Source: BenedickMuszbek 2015

7

# Modeling Utilities and Costs After Disease Progression or Towards the End of Life in Advanced Oncology



- It is essential that data reflect the decision question and are appropriately elicited/collected/analyzed and implemented
- Traditionally: Many models include a single post-progression/post-response utility/cost data-point
- Are often sourced from previously conducted literature reviews and potentially are not directly applicable to decision question
- This might be due to limited high quality data
- However can influence cost-effectiveness, the pricing and reimbursement decisions



- It is important to assess this data gap in order to provide high quality economic evaluations to inform these decisions

8



## Overview of SIG Project

- Aims:
  - To review methods and availability of data describing health utilities and costs in advanced cancer after disease progression or towards the end of life in oncology
  - To identify current data gaps, issues with data quality
  - To highlight examples of high quality studies
  - To assess challenges in eliciting/collecting high quality data and analyzing and implementing inputs in economic evaluations
  - To discuss and suggest topics for future research and best practices
- A two-step approach:
  - Systematic literature review
  - Case study

9



## Systematic Review Process

### Predefined Protocol

- Study objectives
- Search strategy
  - Sources (databases, grey literature sources)
  - Search terms & combinations
  - Publication date range, language and other limits
- Selection strategy
  - Inclusion and exclusion criteria
  - Screening methods, quality control
- Qualitative synthesis methods
  - Summarize findings by cancer type
  - Economic modeling methods / health-utility data / resource use & costs

10



## Search Strategy – Sources & Limits

### Peer-reviewed indexed literature databases

- Medline (via PubMed)
- Embase (via embase.com)

### Publication date range

- Past 3 years (April 2013 to May 2016)
- Aim is to identify contemporary methods and data (methods & study designs evolving rapidly)

### Limits

- Published in English language
- Items with abstracts, human subjects
- Not a case report, commentary, editorial or conference abstract

### Grey literature

- Reports with sufficient detail (e.g., NICE appraisal documentation)

NICE = National Institute for Health and Care Excellence

11



## Search Strategy – Search Terms

Topic	#	MEDLINE Search Algorithm (Adapted for EMBASE)
Cancer	1	"Neoplasms"[MeSH Major Topic] OR oncology[ti] OR cancer[ti] OR carcinoma[ti] OR neoplasm[ti] OR tumor[ti] OR tumour[ti] OR leukemia[ti] OR leukaemia[ti] OR lymphoma[ti] OR malignant[ti]
Post-progression/relapse	2	#1 AND (progress*[tiab] OR fail*[tiab] OR relapse*[tiab] OR recurr*[tiab] OR refractory[tiab] OR metasta*[tiab] OR advanced[tiab] OR "stage IV"[tiab] OR end-of-life[tiab] OR palliative[tiab] OR incurable[tiab] OR non-curative[tiab] OR noncurative[tiab] OR terminal[tiab] OR "supportive care"[tiab])
Limits	3	#2 AND English[lang] AND hasabstract[text] AND ("2013/04/04"[PDAT] : "2016/12/31"[PDAT]) NOT ("animals"[MeSH Terms] OR Case Reports[ptyp] OR Congresses[ptyp])
Utilities	4	#3 AND (utility[tiab] OR EQ-5D*[tiab] OR euroqol[tiab] OR EORTC-8D[tiab] OR "standard gamble"[tiab] OR "time trade-off"[tiab] OR "hui"[tiab] OR "SF-6D"[tiab])
Costs and resource use	5	#3 AND ("Health Care Costs"[MeSH Major Topic] OR cost[tiab] OR costs[tiab] OR charge*[tiab] OR budget*[tiab] OR expenditure*[tiab] OR "resource utilization"[tiab] OR "resource utilisation"[tiab] OR "resource use"[tiab] OR "length of stay"[tiab] OR "length-of-stay"[tiab] OR hospital*[tiab] OR readmission*[tiab] OR admission*[tiab])
Economic evaluations	6	#3 AND ("Cost-Benefit Analysis"[MeSH Major Topic] OR ((cost[tiab] OR costs[tiab] OR cost*[ti]) AND (benefit*[tiab] OR effectiveness[tiab] OR utilit*[tiab] OR analys*[tiab] OR QALY*[tiab])) OR ((economic*[tiab] OR pharmacoeconomic*[tiab]) AND (analys*[tiab] OR assessment*[tiab] OR evaluat*[tiab] OR model*[tiab])))
Total	7	#4 OR #5 OR #6

12



## Study Screening – Eligibility Criteria

		Inclusion criteria	Exclusion criteria
P	Population	<ul style="list-style-type: none"> <li>Metastatic or locally advanced disease: TNM stage IIIb/IV or equivalent, regional (N2+) or distant metastases (M1)</li> <li>Receiving palliative care or progressed on prior treatment</li> </ul>	<ul style="list-style-type: none"> <li>Non-advanced stages of cancer, e.g. on adjuvant therapy, intermediate or early stage such as TNM I-IIIa, local or locoregional metastasis</li> </ul>
I	Investigational Interventions & Comparators		
O	Outcomes		
S	Study Design		

N = node; M = metastasis; TNM = tumor, node, metastasis

13



## Study Screening – Eligibility Criteria

		Inclusion criteria	Exclusion criteria
P	Population		
I	Investigational Interventions / Comparators	<ul style="list-style-type: none"> <li>Any systemic pharmacotherapy for treatment or palliative care</li> <li>Observational studies not evaluating specific therapies</li> </ul>	<ul style="list-style-type: none"> <li>Adjuvant therapy</li> <li>Non-pharmacologic therapy (surgery, radiotherapy), diagnostic tests, quality of care</li> </ul>
O	Outcomes		
S	Study Design		

14



## Study Screening – Eligibility Criteria

		Inclusion criteria	Exclusion criteria
P	Population		
I C	Investigational Interventions & Comparators		
O	Outcomes	<p><b>Primary studies &amp; non-model based economic evaluations:</b></p> <ul style="list-style-type: none"> <li>Health-care after disease progression/ response to treatment (resource use or costs, direct or indirect)</li> <li>Health utility estimates</li> </ul> <p><b>Model based economic evaluations:</b></p> <ul style="list-style-type: none"> <li>Comparison of at least two interventions for costs and health benefits (LY, QALY, progression-free LY)</li> </ul>	<ul style="list-style-type: none"> <li>No reported outcomes of interest</li> <li>No numerical data for the outcomes of interest</li> <li>Documents from health technology assessment websites that do not provide detail of the outcomes of interest for a population of interest</li> </ul>
S	Study Design		

LY = life-year; QALY = quality-adjusted life-year

15



## Study Screening – Eligibility Criteria

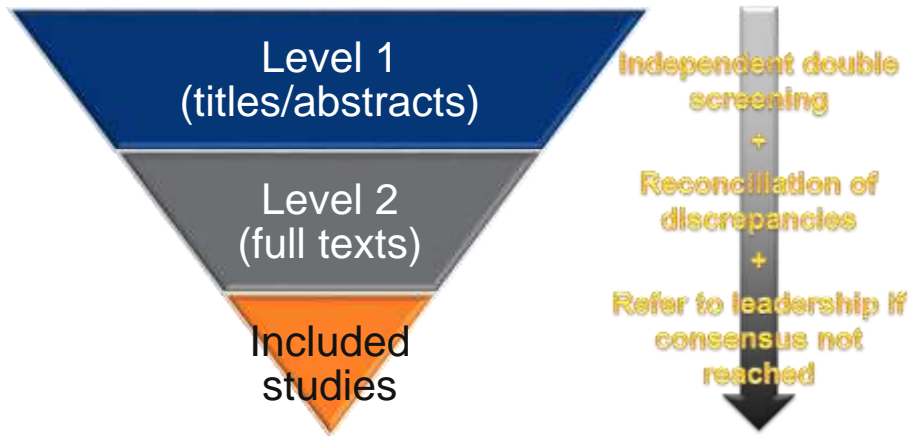
		Inclusion criteria	Exclusion criteria
P	Population		
I C	Investigational Interventions & Comparators		
O	Outcomes		
S	Study Design	<p><b>Primary studies &amp; non-model based economic evaluations:</b></p> <ul style="list-style-type: none"> <li>Observational studies, registries</li> <li>Randomized &amp; non-randomized interventional studies</li> </ul> <p><b>Model based economic evaluations:</b></p> <ul style="list-style-type: none"> <li>Full economic evaluations (CUA, CEA, CMA, cost-consequence analyses) reporting details of methods and/or parameter values used</li> </ul>	<ul style="list-style-type: none"> <li>Literature reviews*, expert opinions, editorials, commentary, or news</li> <li>Case reports or case series</li> <li>In vitro or animal studies</li> </ul>

\*Relevant systematic reviews retrieved to check bibliography for relevant studies  
CEA = cost-effectiveness analysis; CMA = cost-minimization analysis; CUA = cost-utility analysis

16



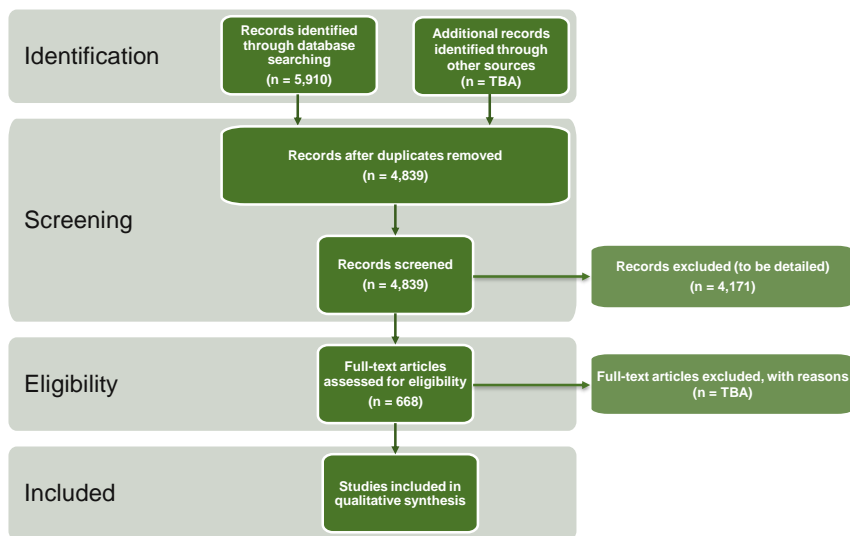
# Study Screening – Methods



Abstracts are tagged according to cancer type

17

# The Flow Diagram of the Systematic Literature Review Process



Based on the PRISMA template: Panic, N., et al., PLoS One, 2013. 8(12): e83138.

18

# Extraction templates



19

# Extraction template



## Extraction of data/methods focusing on post-progression / response or end of life

- Study characteristics:
  - Country, indication(s), objective(s)
- Study description
  - Scope, description of treatments included, study population, time horizon
  - Economic evaluation and model
- Study design
  - Costs: type of costs, resources, methods
  - Utilities: elicitation, valuation, mapping
- Description of results
- Values

## Short quality assessment questionnaire

- Sufficient description:
  - Methods, comparators
- Potential bias
- Uncertainty
- Validation
- For economic evaluations:
  - Consistency of population in data sources
- Use of post-progression / response data
- Key strength and limitations
- Best practice flags

20



Breast cancer  
**PRELIMINARY RESULTS**

**Preliminary Utility Findings: Breast Cancer**



	n/N (%)
Number of utility estimates identified	8
Primary studies	2
Used in economic evaluations	4
Study design	
Post hoc analysis of trial	0
Longitudinal observational study	0
Cross-sectional observational study (clinical setting)	2/6 (33%)
Patient survey	0
Vignette study	4/6 (67%)
Expert opinion	0
Other	0
Unclear	2/6 (33%)
Sample size for the post-progression health state utility estimate	
Mean (SD) range	
<10	0
10 - <20	0
20 - <50	2/6 (33%)
50 - <100	0
100 - <150	2/6 (33%)
150+	0
Unclear	2/6 (33%)
Estimation method	
EQ-5D	1 (13%)
EQRTIC-6D	0
HUI	0
SF-6D	0
Other PBM	1 (13%)
Mapped	0
Vignette	4 (67%)
HCP estimate	0
Other	0
Unclear	2 (25%)

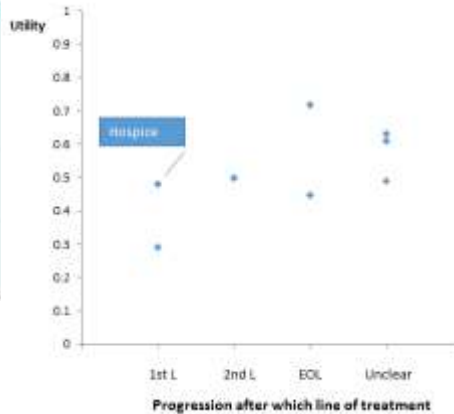
	n/N (%)
Number of assessments post-progression, per patient	
1	1/6 (17%)
2	0
3	0
4	0
5+ or at regular intervals throughout time in health state / remaining lifetime	0
Unclear	1/6 (17%)
NA (vignette study)	4/6 (67%)
Did vignette description adequately represent all times in the health state (if quality of life is expected to change over time within the health state, did the description adequately represent the full spectrum of HRQL)	
Yes	0
partially	0
no	2/6 (33%)
unclear	2/6 (33%)
NA (not vignette study)	1/6 (17%)
Utility estimate for caregiver / family member / friend reported	
Yes	0
No	6/6 (100%)
Were data relaxing for patients too ill to complete an assessment	
Yes	1/6 (17%)
partially	0
no, a proxy respondent was used	0
no, other	0
unclear	1/6 (17%)
NA (vignette study)	4/6 (67%)

PBM = preference-based measure; HCP = healthcare professional; NA = not applicable

# Preliminary Utility Findings: Breast Cancer



All EU	
Were the characteristics of the patient sample informing the utility estimate representative of the model population in the post-progression health state (e.g. for age, phase of disease, or other variables likely to impact utility)?	
Yes	0
Partially	0
No	0
Unclear	4/6 (67%)
NA (not used in an economic evaluation)	
	2/6 (33%)
Were there other sources of bias in the estimate?	
Yes	2/6 (33%)
Possibly	1/6 (17%)
No (none identified)	0
Unclear	3/6 (50%)
Was an estimate of uncertainty reported (e.g. standard deviation, 95% CI, range)?	
Yes	3/6 (50%)
Range only	0
No	3/6 (50%)



PBM = preference-based measure; HCP = healthcare professional; NA = not applicable

23

## Examples of Strengths and Limitations



Example strengths	Example limitations
Relationship between time from death and utility was reported. Factors associated with low utility were identified (e.g. fatigue, pain, depression)	The progressive state in the vignette study was intended to describe an average patient who was not receiving active treatment and was in palliative care; the model health state included subsequent active treatment
	Small sample size for the post-progression utility estimate (25-57 respondents)
	Low response rate; patient characteristics (e.g. site of metastasis) may not be typical of all patients and patients with poorer health status may be less likely to respond - could result in upward bias of utility estimates
	During patient interviews to develop vignettes, there was quite substantial idiosyncratic variation between women, and their responses provided information that was different from what was identified from the literature. Due to these differences, the health states may not be entirely representative of advanced breast cancer as experienced by women in each country
	Utility estimates used in models were referenced to other model publications and insufficient detail were reported to determine whether utility data are relevant for the model population or to assess data quality

# Good Practice Example

## Cross-sectional observational study

- Respondents were 114 palliative care patients (27 breast cancer, 30 prostate cancer, and 57 colorectal cancer)
- Time to death followed up for all respondents
- Utility presented with time from death
- Factors associated with lower HRQoL included fatigue, pain and depression

### Limitations

- Potential selection bias (small patient sample in each cancer and low response rate)

### Potential improvements

- Larger sample size
- Proxy respondent for patients too ill to complete questionnaires (with investigation of potential bias in proxy responses)
- Longitudinal design to characterise utility changes over time
- Collect caregiver's own utility

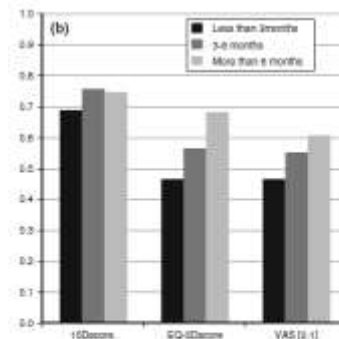


Fig. 1 a Mean health utility scores by cancer type, b Mean health utility scores by time from response to death. EQ-5Dvex (0 being best, 1 = full health); EQ-5D (-0.594 = worst health; 0 being best, 1 = full health); VAS, visual-analogue (0 worst imaginable health state, 1 best imaginable health state)

Farkkila et al., 2014

25

## Preliminary Findings from Cost Studies: Breast Cancer

<b>Number of Cost Studies Identified</b>	7
- Post-progression state	4 (57.1%)
- Pre-/Post-progression state	1 (14.3%)
- Not clear	2 (28.6%)
<b>Treatment</b>	
- First line	2 (28.6%)
- End of life/Palliative Care	1 (14.3%)
- Not clear	4 (57.1%)
<b>Initial Treatment - Chemotherapy</b>	3 (42.9%)
<b>Mean Age of Patients</b>	59.6 yrs (49.6 yrs - 77.1 yrs)
<b>Average Study Time Horizon</b>	4.62 yrs (1 yr - 7 yrs)
<b>Type of Study – Observational Studies</b>	6 (85.7%)
<b>Country for Resource Use</b>	
- USA	4 (57.1%)
- Canada	2 (28.6%)

26

## Preliminary Findings from Cost Studies: Breast Cancer

<b>Cost Categories</b>	
- Adverse Event	1 (14.3%)
- End of Life	1 (14.3%)
- Indirect Costs	1 (14.3%)
<b>Types of Resources Included</b>	
- Drugs	2 (28.6%)
- Hospitalizations	2 (28.6%)
- Procedures	1 (14.3%)
- Imaging	1 (14.3%)
- Social Care	1 (14.3%)

27

## Preliminary Findings from Cost Studies: Breast Cancer

### Strengths

- Resource use mostly reported for post-progression period
- Patients reported to be in the metastatic stage

### Limitations

- Studies focused on the utilization of resources
- Cost of resources were not included or the factors that influenced costs
- Small sample sizes and generally limited to one center

28

# Examples of Strengths and Limitations



Example strengths	Example limitations
Resource use mostly reported for post-progression period	Studies focused on the utilization of resources
	Cost of resources were not included or the factors that influenced costs
	Small sample sizes and generally limited to one center

29

## Preliminary Findings from Economic Evaluations: Breast Cancer

<b>Number of Studies Identified</b>	8
<b>Model</b>	
- Yes	7 (87.5%)
- No	1 (12.5%)
<b>Treatment</b>	
- First line	4 (50.0%)
- 2 <sup>nd</sup> line	1 (12.5%)
- 3+ line	1 (12.5%)
- Not clear	2 (25.0%)
<b>Type of analyses- Cost-utility</b>	8 (100.0%)
<b>Perspective</b>	
- Societal	2 (25.0%)
- 3rd party payer	5 (62.5%)
- Provider	1 (12.5%)

30

## Preliminary Findings from Economic Evaluations: Breast Cancer

<b>Post-progression/response period modeled with constant cost per cycle?</b> - Yes - No - NA	5 (62.5%) 2 (25.0%) 1 (12.5%)
<b>Post-progression/response period modeled with constant utility per cycle?</b> - Yes - Partially - NA/Not clear	5 (62.5%) 1 (12.5%) 2 (25.0%)
<b>Country for Resource Use</b> - USA - UK - China - Canada	3 (37.5%) 3 (37.5%) 1 (12.5%) 1 (12.5%)