Issue Panel 18

HOW TO DEAL WITH MODEL UNCERTAINTY AT THE PLANNING STAGE OF COST-EFFECTIVENESS ANALYSIS?: TIPS FROM GLOBAL EXPERIENCES

Part 1: Issues with model uncertainty

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Healthcare to All

AGENDA

- Problem with model uncertainty at the trial HTA in Japan
- Academic instruction and HTA guidelines
- Practical challenges at model development

Result of the trial HTA 2016-2018 _ Drugs

Product	Disease	Comparator	Result	Ethical/Societal consideration*	Re-analysis
Sovaldi® [Gilead]	HCV	Interferon etc.	Equal or less than ¥5mil./QALY	Infectious control	No
Harvoni® [Gilead]	HCV	Direct acting antivirals etc.	(inconsistent)	Infectious control	Yes
Viekirax® [Abbvie]	HCV	Direct acting antivirals etc.	(inconsistent)	Infectious control	Yes
Daklinza®, Sunvepra® [BMS]	HCV	Interferon etc.	(inconsistent)	Infectious control	Yes
Optivo® [Ono]	Malignant melanoma, NSCLC	Chemotherapy	(inconsistent)	Extending life year	Yes
Kadcyla® [Chugai]	HER2+ Breast Cancer	Chemotherapy	Equal or more than ¥10mil./QALY	Extending life year	No

The CEA committee 7th March, 2018 (translated by Emiko Yoshida)

*When meet any of the four: 1. Infectious control (societal benefit), 2. Additional cost in broader perspective, 3. Extending life year for critical condition, 4. Stand alone treatment, ICER would be further discounted; One item = 5%

Key model concepts were agreed before starting re-analysis

Product	Population	Comparator
Harvoni® [Gilead]	Chronic HCV	NS5A sensitive; Daclatasvir and Asunaprevir
	Compensated cirrhosis	NS5A resistant; No treatment
Viekirax® [Abbvie]	Chronic HCV	Y93 change negative and L31 positive; No treatment
	Compensated cirrhosis	Y93 change negative and L31 negative; Daclatasvir and Asunaprevir
Daklinza®, Sunvepra® [BMS]	Chronic HCV	No treatment
	Compensated cirrhosis	
Optivo® *4 [Ono]	Malignant melanoma	Dacarbazine
	Renal cell cancer	Everolimus
	Non-small-cell Lung Cancer	Non-squamous NSCLC; Docetaxel Squamous NSCLC; Docetaxel
Sapien® XT *5 [Edwards]	Aortic stenosis	High risk for open surgery; Open surgery Not tolerant to open surgery; Conventional (drug) therapy

Chuikyo 13th June, 2018 (translated by Emiko Yoshida)

*4; Maximum length of treatment. Time horizon to be changed in additional analysis
*5; Data source to be continuously discussed

Inconsistency and next steps

What was the decision at the trial HTA implementation?

- Basic rule is to choose the one most appropriately done
- However when it is not obvious which analysis/result is more appropriate, take both in consideration, as long as they follow 2015 HTA guideline
  - Results are different because of the differences in choosing hypothesis and data selection

Future suggestions

- Invite clinical experts to the review committee
  - The trial review committee members including only payers and economists
- Discussion and agreements prior to start anlaysis
  - Outline (population, comparator, cost, method) to be agreed prior to start analysis
- Detailed HTA guideline which covers different disease areas would be needed?

Next step

- Re-analysis by September 2018

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Uncertainties (ref. NICE glossary)

Parameter Uncertainty

- Uncertainty about the mean values of parameters (for example, health outcomes, utilities and resource use) included in the model.

Model Uncertainty

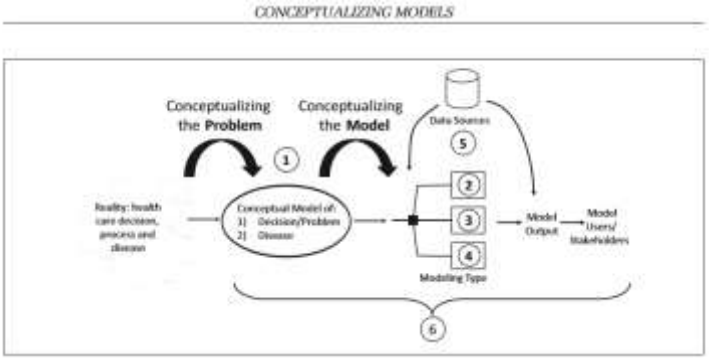
- Uncertainty relating to the range of assumptions and judgements necessary in constructing a model. This can include design features of the model (for example, the assumed standard pathway of care) as well as judgements about the relevance of evidence, assumptions about appropriate distributions for parameters and alternative methods of estimation.

Recommendations

> “ Of greater concern is the degree of freedom that the modeler has in deciding upon the model inputs and assumptions. … Performing extensive sensitivity analysis…, can help to address those concerns of bias of the base case analysis. ”
>
> Drummond Red Book

> “ Review the literature for relevant economic references and any additional clinical or epidemiological literature relevant to the model that has not already been presented, and attach copies of studies and original sources of data used in the economic evaluation (Section 3A.2.1) ”
>
> PBAC Section 3A.2.1

ISPOR Task Force and Drummond Blue Book



Roberts et al., Med Decis Making. 2012 Sep-Oct;32(5):678-89.

"It is important to have a complete picture of the problem, regardless of data availability"

Roberts et al., 2012

"…the ultimate objective in selecting an appropriate structure for a decision model is to make the model no more complex than it has to be to address the policy questions appropriately."

Drummond et al., 2013

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A strong preference in RCT

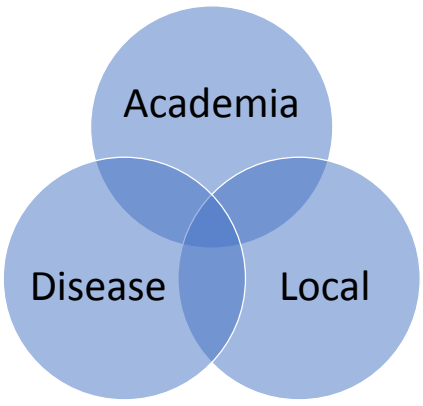
Japanese HTA guideline in 2015 is developed in the similar manner to the NICE reference case (methodological guideline); Chapter 9 explains data source,

> “ Prioritise the data source which maintains good study quality, evidence level and represent clinical practice ”

People often start designing CEA by considering available dataset, and end up with partial analysis, e.g. too short time horizon where RCT is available, wrong comparator which direct comparison available, and small patchy subgroup analysis where RCT is available

Internal pressure to use/apply ‘global model’

What would be a good model?



MSc. Dissertation, E. Yoshida, 2010

- Local HEOR representatives are often requested to use ‘global model’ to start with.
- Local practice/treatment path could be different
- Local effectiveness could be different
- Local cost structure is different
- Available comparator could be different
- Lastly, local HTA guideline is different