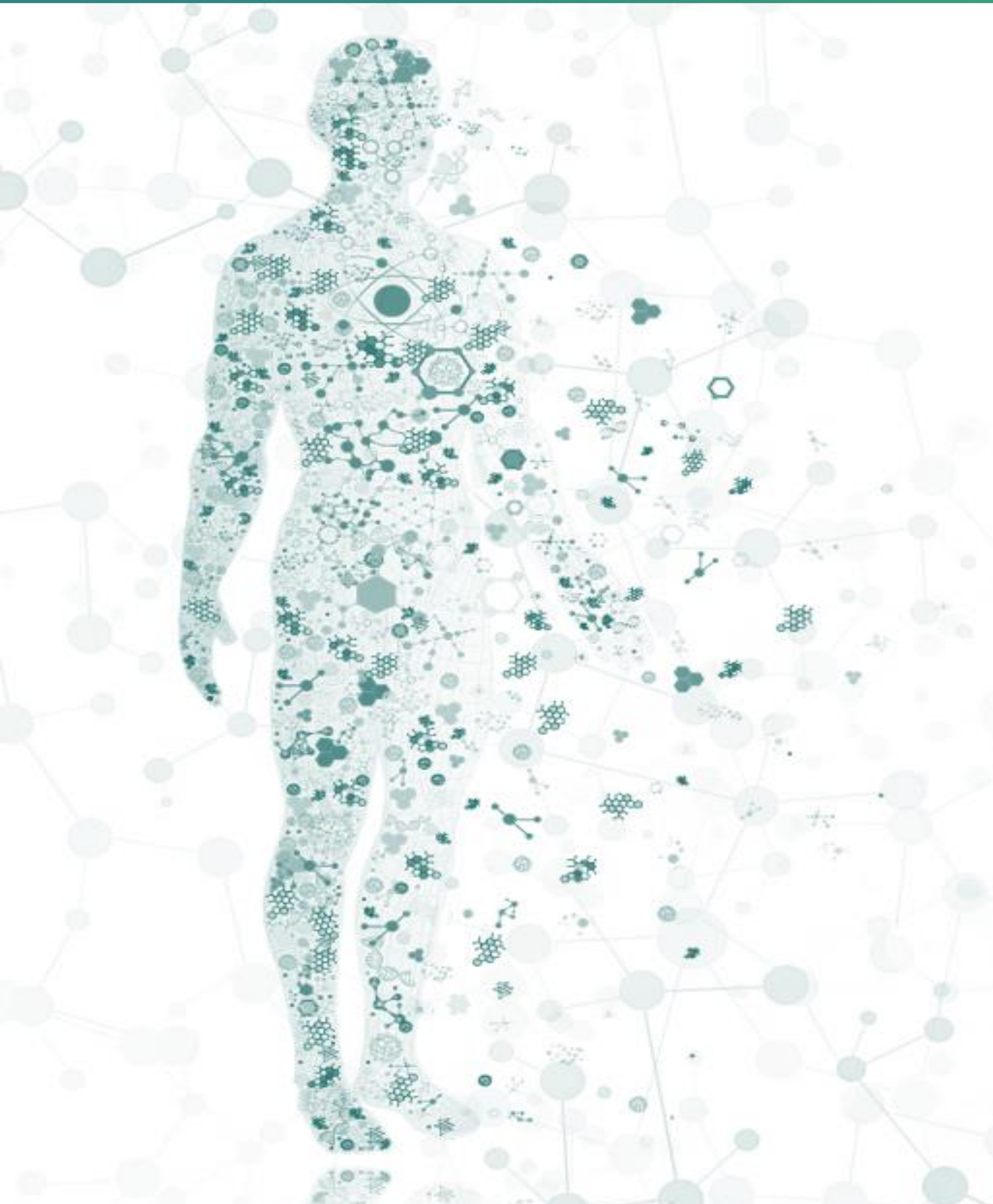

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Health Economic Modelling – Europe & North America

Personal experiences, Johanna Lister

9 October 2019

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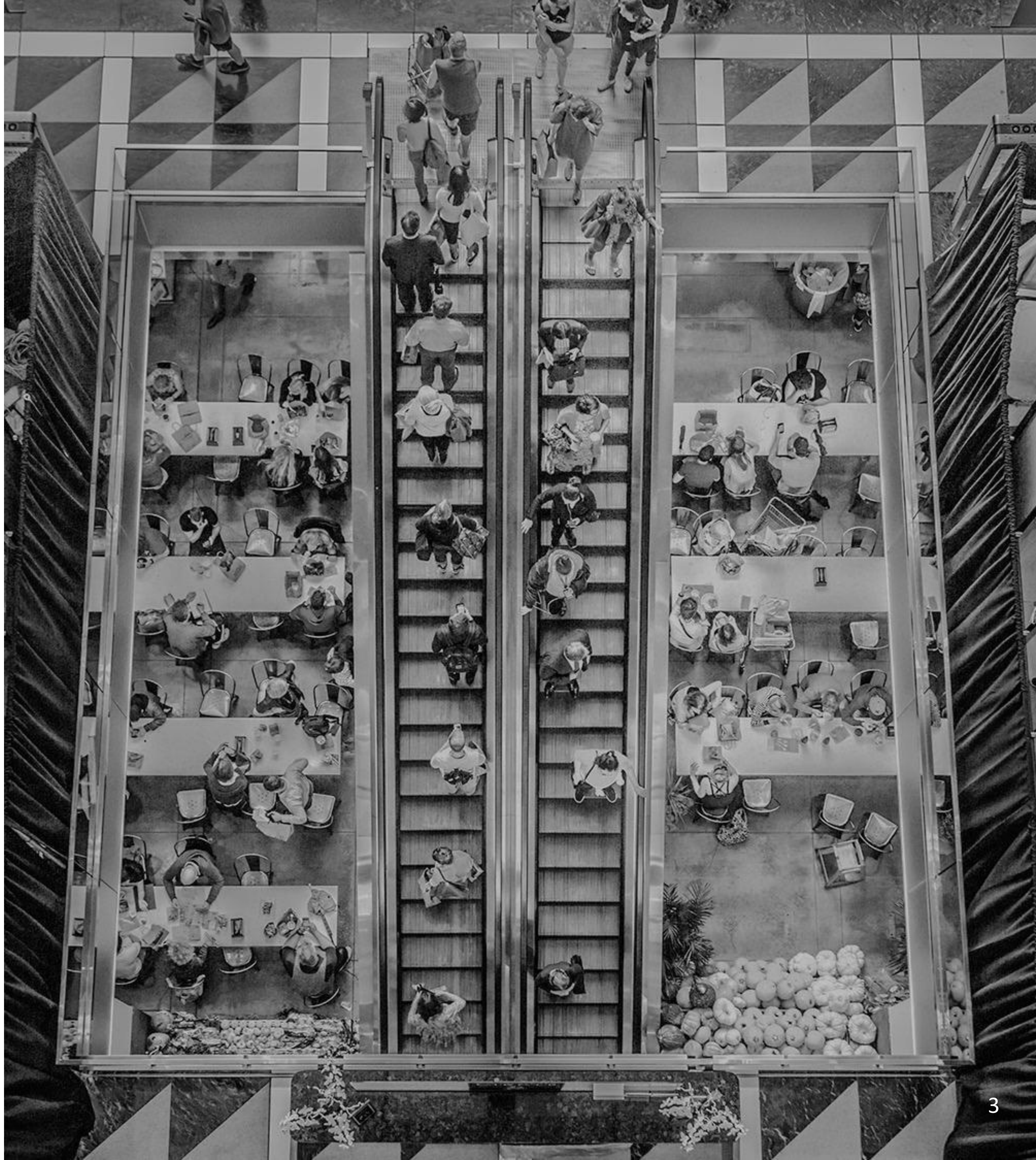
CONTENT

Content

- Health economic modelling
- Guidelines and methods
  - BIM, CEM
- Case studies:
  - Typical global health economic modelling project
  - Cancer model
- Conclusions



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HEALTH ECONOMIC MODELLING

ANALYTICS AND MODELING SERVICES ACROSS THE PRODUCT LIFECYCLE

PHASE I

PHASE II

REGISTRATION

ACCESS

EXPANSION

R&D

+ Drug positioning
+ Optimal design and planning
+ Pipeline prioritization

PRE-MARKETING

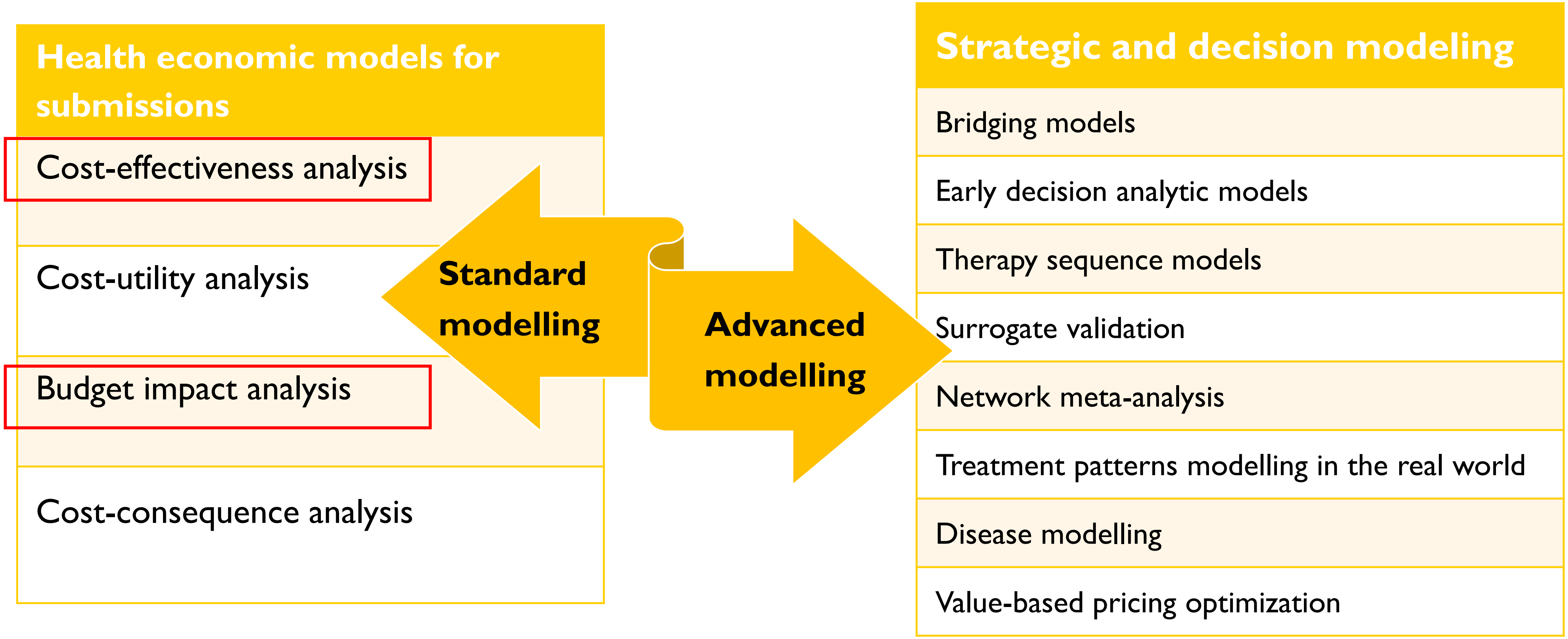
+ Launch strategy
+ Pragmatic trial design
+ Payer-relevant evidence and value development

POST MARKETING

+ Risk sharing strategy
+ Performance plan models
+ Predicting comparative effectiveness
+ Real world cost effectiveness models

Certara has contributed to advance the methodological development in MTC and Bayesian meta-analysis and in large IMI/EU funded research projects on benefit/risk characterization and communication.

ECONOMIC AND PREDICTIVE MODELLING AND SIMULATION



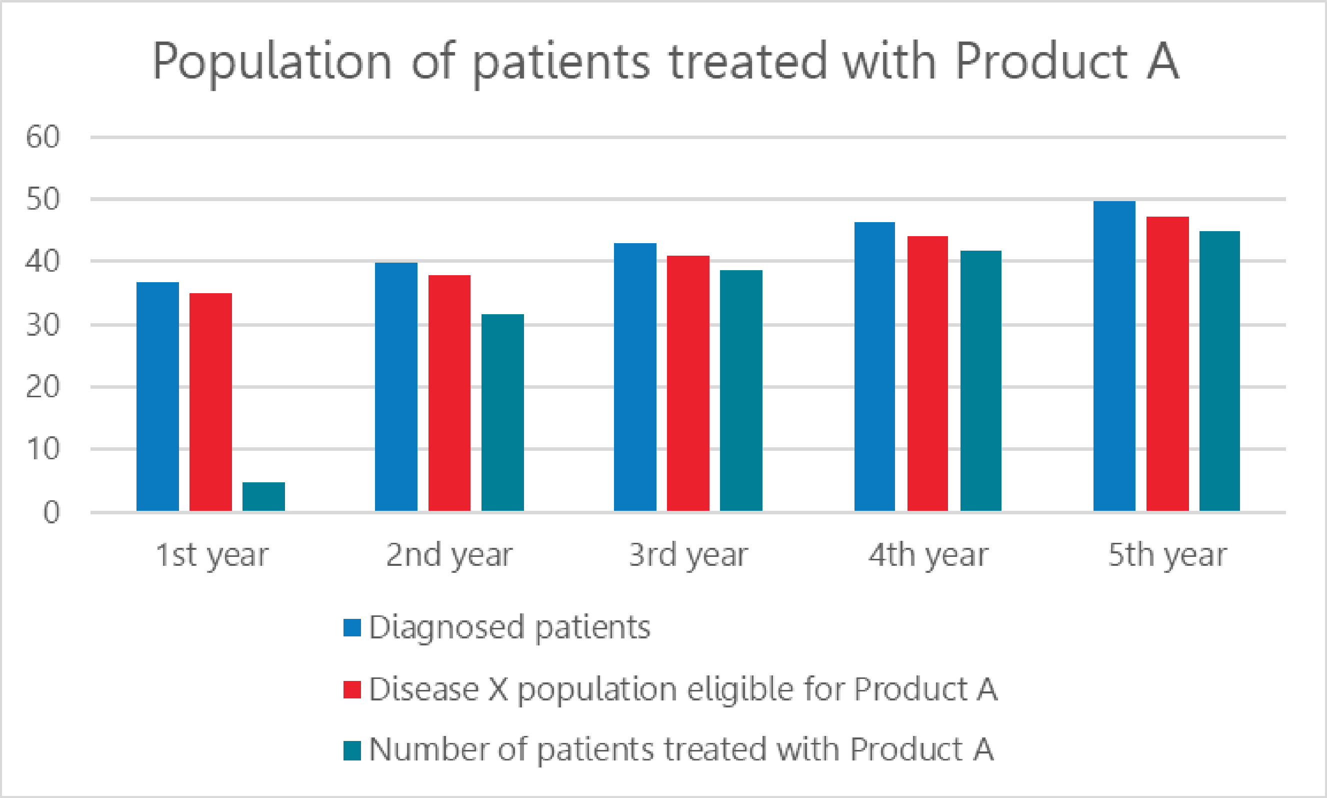
Budget impact models can be used to evaluate financial impact of adding new technology in the healthcare system

- Healthcare **budgets are limited** and under constant pressure from **increasing treatment costs and demand**.
- Payers are therefore increasingly looking to budget impact models to **evaluate the financial impact** of adding new healthcare technologies to their formularies.
- In addition, budget impact models are increasingly being utilised at the regional and local level to inform decision making for access to medicines for **specific local patient populations**.

Current scenario (without PVO)	Future scenario (with PVO)	
Target population	Target population	Incremental budget impact (difference in total costs between scenarios)
x	x	
Current market shares	Future market shares	
x	x	
Annual costs per patient of flare-ups management	Annual costs per patient of flare-ups management	
=	=	
Total costs of flare-ups treatment in target population	Total costs of flare-ups treatment in target population	

Certara has experience developing global budget impact models as well as adapting those for local use

- Certara has carried out a **large number of budget impact analyses** to support national and local payer submissions.
- The models are usually designed to be
  - Fully functional
  - User friendly
  - Interactive
- Certara has experience of developing budget models appropriate to **different countries** and healthcare systems and of adapting models to a variety of situations, including the USA, UK, France, Germany, Italy, Spain, Portugal, Sweden, and Canada.



Cost-effectiveness models can help to assess whether additional clinical benefit is worth the additional cost

New health technology
- Additional health gains
- Additional costs

FUNDS AVAILABLE FOR HEALTH CARE

Health technologies foregone
- Health foregone
- Resources available

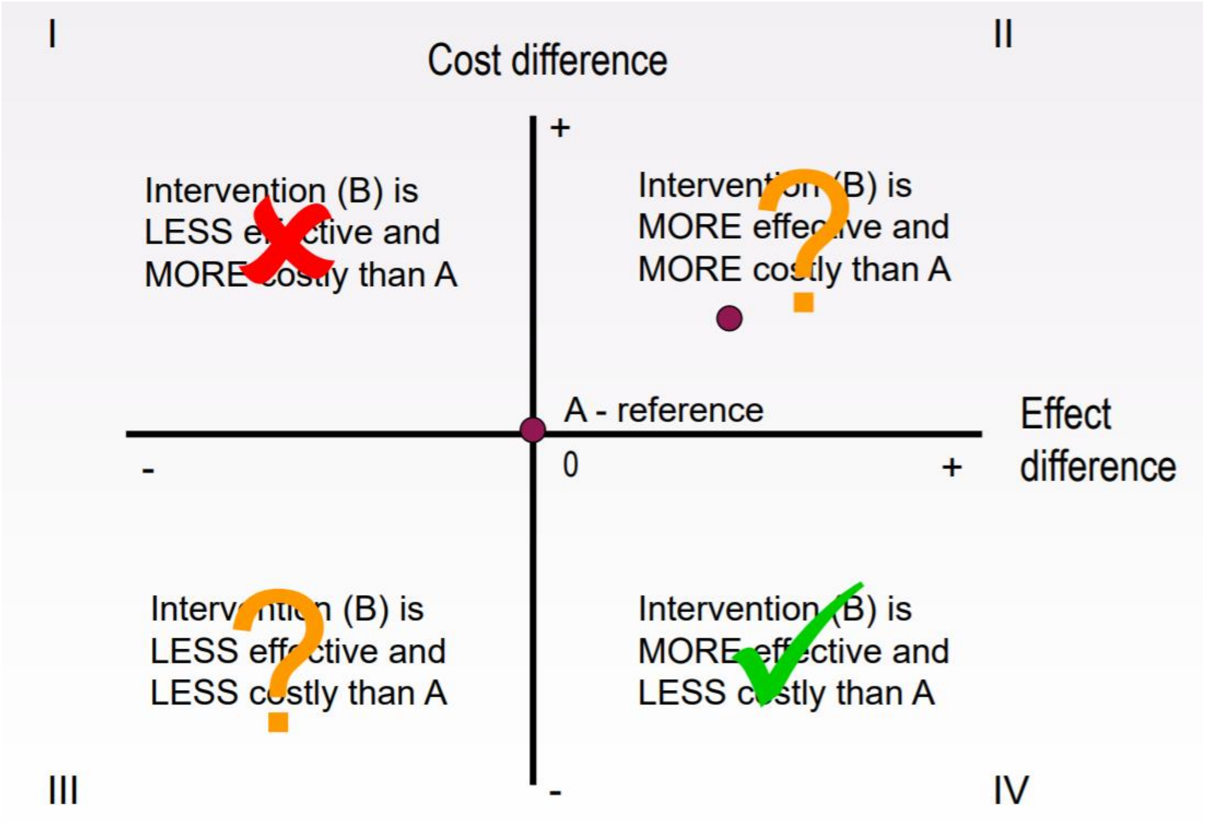
Is the new health technology cost-effective?

Is the health gain from the new technology likely to be greater than the health foregone?

Incremental cost-effectiveness ratio is a key metrics used in economic evaluation of health technologies

$$\text{ICER} = \frac{\sum \text{Treatment cost} - \sum \text{Comparator cost}}{\sum \text{Treatment QALYs} - \sum \text{Comparator QALYs}}$$

The cost-effectiveness plane is used to visually represent the differences in costs and health outcomes



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GUIDELINES AND METHODS

Many organisations have published health economic modelling recommendations or guidelines

COUNTRY-SPECIFIC PHARMACOECONOMIC GUIDELINES

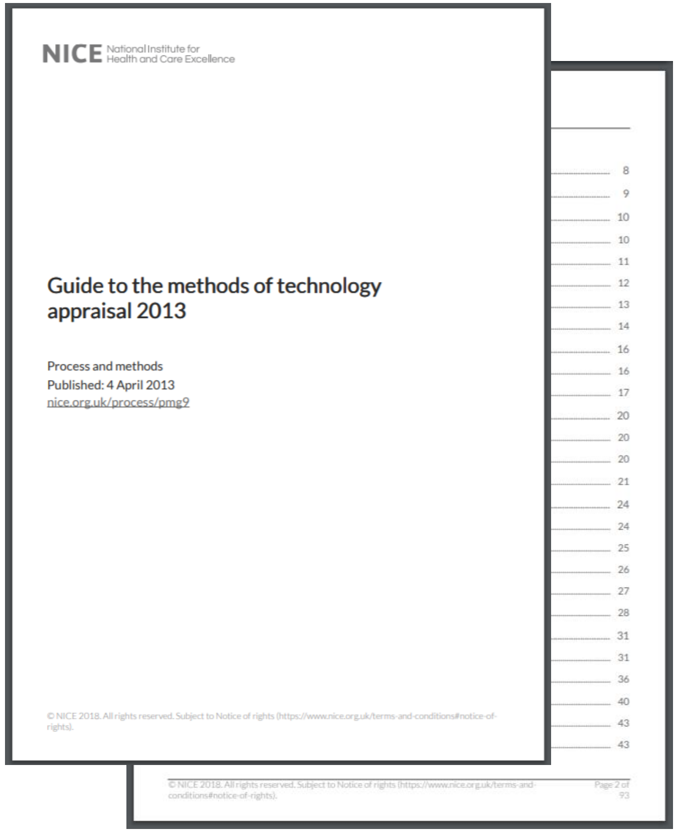
	Published PE Recommendations	PE Guidelines	Submission Guidelines
Africa	South Africa	Egypt	
Latin America		Brazil Colombia Cuba México MERCOSUR (Argentina, Brazil, Paraguay, Uruguay)	
North America	United States	Canada	
Asia	China Mainland	Japan Malaysia Taiwan South Korea	Iran Israel Thailand
Europe	Austria Denmark Hungary Italy Russian Federation Spain Croatia	Baltic (Latvia, Lithuania, Estonia) Belgium France Germany Ireland The Netherlands Norway Portugal Slovak Republic Slovenia Sweden Switzerland	Czech Republic England & Wales Finland Poland Scotland Spain - Regions
Oceania		New Zealand	Australia

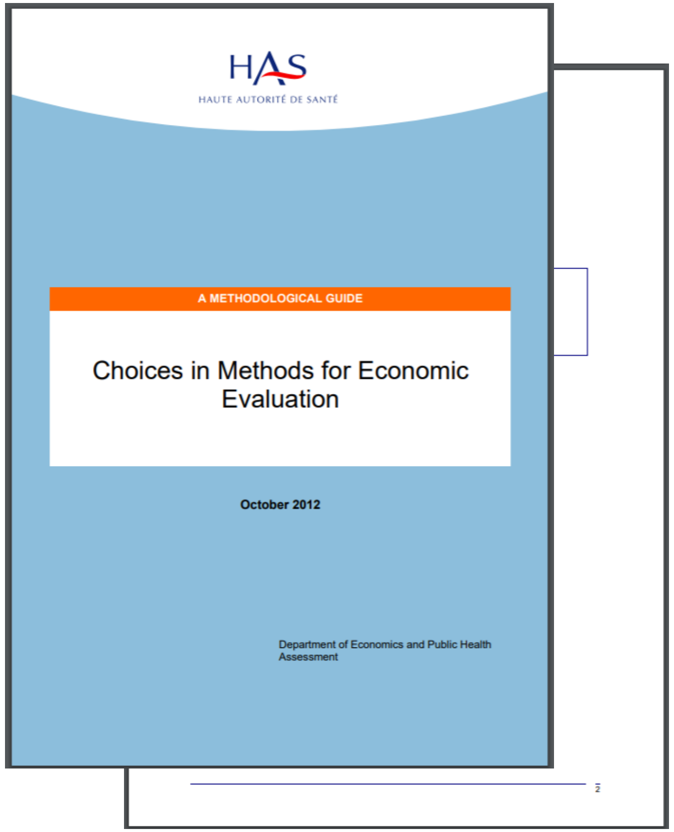
Trans-national guidelines such as those from ISPOR

Source: ISPOR Pharmacoeconomic Guidelines Around the World, https://tools.ispor.org/peguidelines/

Local health economic recommendations/guidelines drive the development of global health economic models

Key differences to take into account?





Source: ISPOR Pharmacoeconomic Guidelines Around the World, https://tools.ispor.org/peguidelines/

There are key considerations to take into consideration when building a global health economic model

Model parameter	Typical consideration across countries
Health Technology	Which health states (or model structure) capture the treatment effect and disease progression so that is can be used across geographies?
Comparator(s)	Which comparators to include? How is efficacy compared to the new health technology (e.g. is ITC/NMA needed/required)?
Adverse events	Do all adverse events need to be included or can a selection be made? If selection can be made, what criteria to use?
Health state utilities	Which patient-reported outcome/instrument is most appropriate for capturing differences in quality of life?
Resource use & cost	Are resource use items (e.g. number of neurologists visits) costs programmed so that they cover needs across different countries and can be easily adjusted?
Technical requirements	How complex/simple should model be? What underlying mathematical techniques may be acceptable? What extrapolation methods are likely to be acceptable?

Source: ISPOR Pharmacoeconomic Guidelines Around the World, https://tools.ispor.org/peguidelines/

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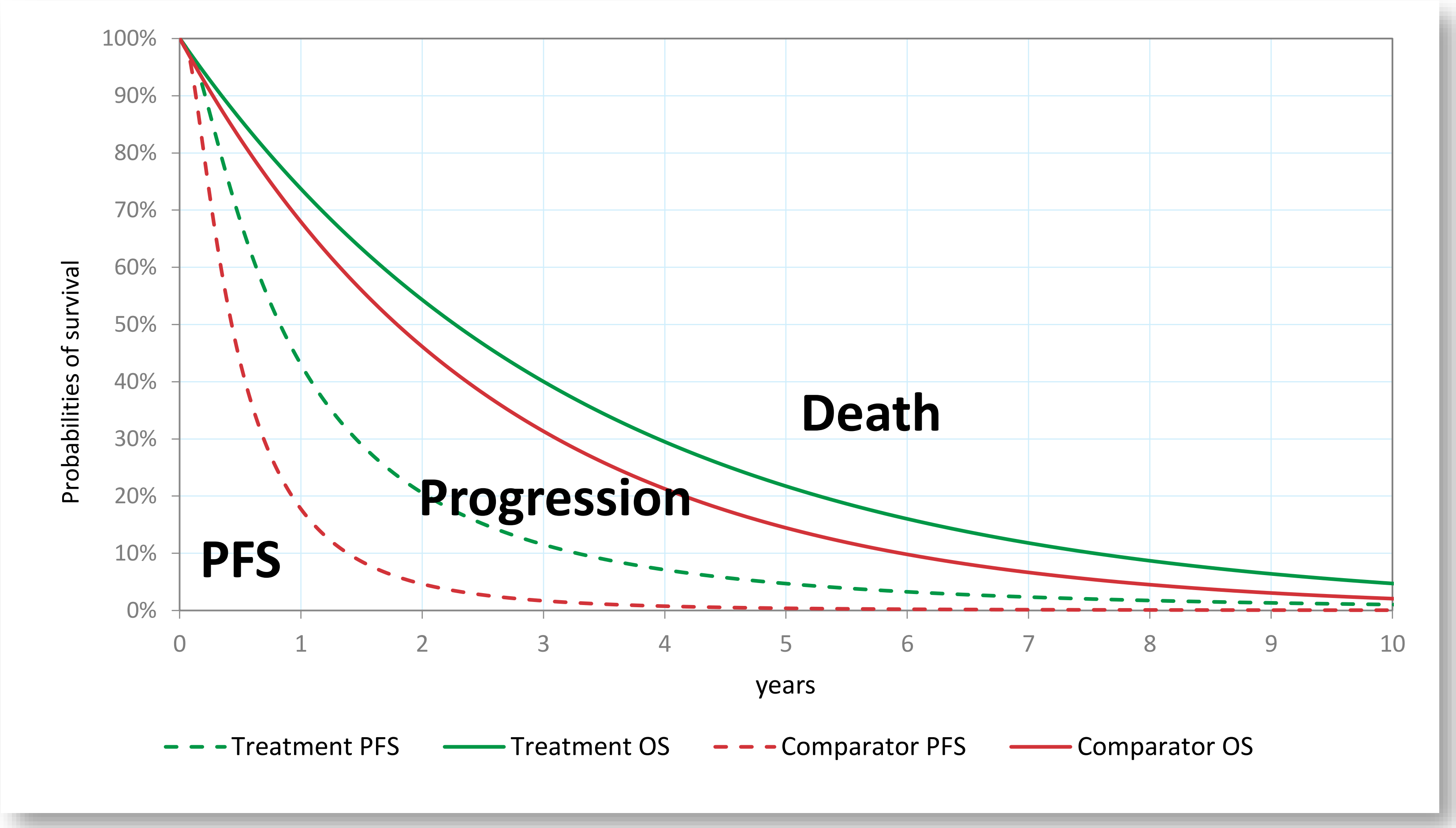
TYPICAL PROJECT – CASE STUDY 1

Health economic modeling

	Cancer Model Structure		
Patient health states	PFS	Progression	Death
Proportion of patients in health states over time	PFS Curve	PFS Curve – OS Curve	OS Curve
Quality of life in a scale 0 to 1	Utility PFS	Utility Progression	0
Cost of being in the health state	Cost of PFS	Cost of Progression	End of life cost

Health economic modeling – Health states



PFS curve details

Median time (months)	
Treatment	10.15
Comparator	5.37
Mean time (months)	
Treatment	17.49
Comparator	7.81

OS curve details

Median time (months)	
Treatment	27.47
Comparator	21.73
Mean time (months)	
Treatment	39.22
Comparator	31.01

Health economic modeling - ICER

Cost PFS | Cost of Progression | End of life cost

$$\text{ICER} = \frac{\sum \text{Treatment cost} - \sum \text{Comparator cost}}{\sum \text{Treatment QALYs} - \sum \text{Comparator QALYs}}$$

Incremental cost-effectiveness ratio

Utility PFS | Utility Progression

QALYs – quality adjusted life years (sum of utilities over time)

Health Economic modeling - Results

Probabilistic results (PSA)

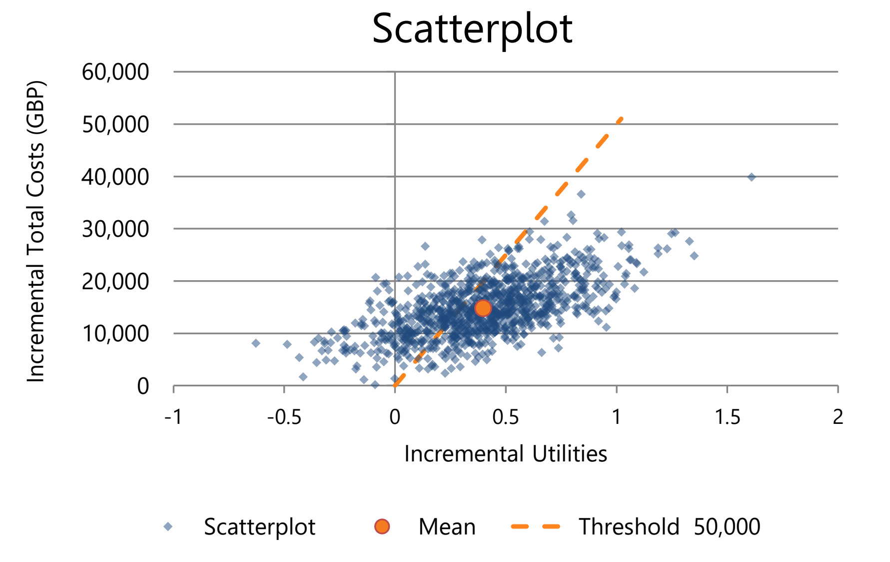
Number of iterations 1000 Run PSA

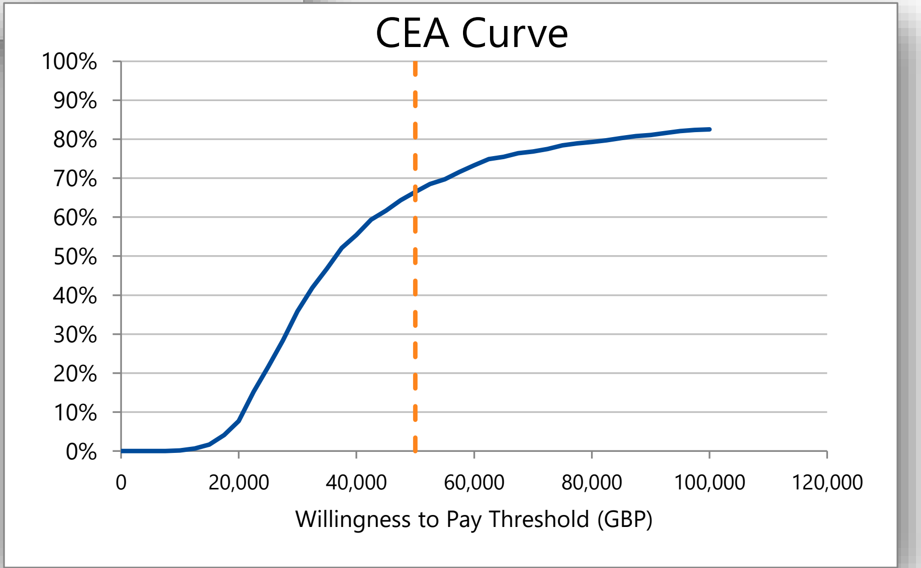
PSA calculation time: 2 min 35.8 sec

	Treatment		Comparator		Incremental		±SD	
Total cost	**53,855**	GBP	**39,058**	GBP	**14,797**	GBP	**5,427**	GBP
Pre-progression cost	31,043	GBP	11,570	GBP	19,473	GBP	5,589	GBP
Post-progression cost	22,812	GBP	27,488	GBP	- 4,676	GBP	3,617	GBP
QALYs	**1.833**		**1.435**		**0.398**		**0.297**	
Life years	2.974		2.319		0.655		0.561	
Progression-free life years	0.950		0.467		0.483		0.167	

ICER *(incremental cost-effectiveness ratio)* **37,134** GBP/QALY

Cost pe





Health Economic modeling - Structure

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- The model structure was built on **sheets**.
- E.g., one oncology model has
  - User interface

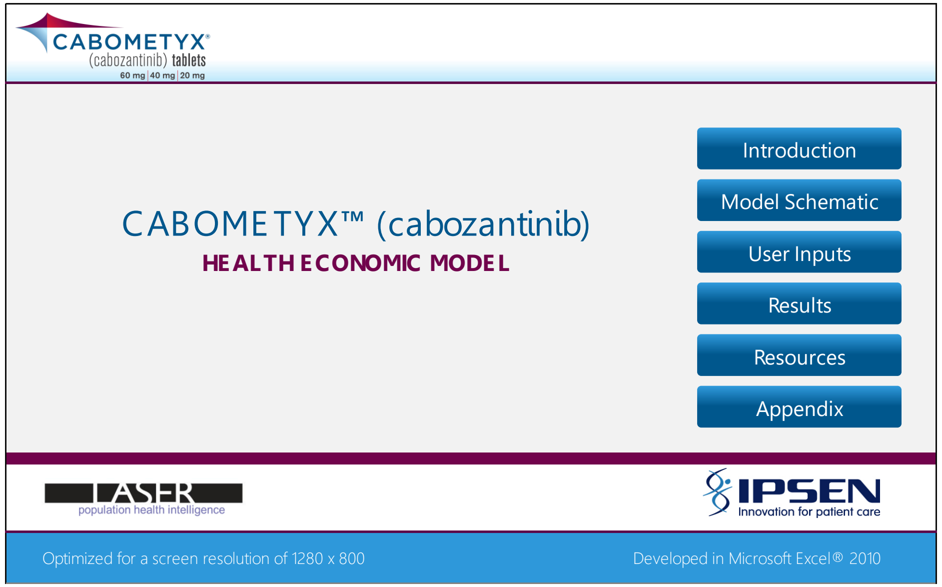
    Home | Introduction | Schematic | User Input | Results | Resources | Appendix

  - Calculation & engine sheets (core of the model)

    Variables | TPs | TPs_NMA | engine_c | engine_e | engine_a | engine_n | engine_b

  - Auxiliary sheet

    PSA | Tornado | Scenario Results | Curve data | UIData



Health Economic modeling – Sheets

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Home

PSA Active

Parametric models

Everolimus (Afinitor®)

Result summary

Total cost	32,200	QALYs (quality-adjusted life years)	1.726
Pre-progression cost	17,598	Life years	2.195
Primary intervention	16,614	Progression-free life years	0.526
Disease Management	862		
Adverse Events	121	QALYs (progression-free state)	0.429
Post-progression cost	14,602	QALYs (post-progression state)	1.297
Subsequent treatments	6,382		
Disease Management	2,667		
End of life costs	5,554		

Cycle	Year	Month	Cost Discount	Effect Discount	Alive	Dead	Died current cycle	PFS	Progressed this cycle	Total progressed	PFS	OS	OS TP	On treatment	Check 1	Check 2	Check 3
Total					2.4030			0.5300							0	0	0
0	0	0.0	1.000	1.000	1.0000	0.0000	0.0000	1.0000	0.0000	0.0000	1.0000	1.0000	1.0000	1.0000	TRUE	TRUE	TRUE
1	0	0.9	1.000	1.000	0.9981	0.0019	0.0019	0.9830	0.0151	0.0151	0.9830	0.9981	0.9981	0.9853	TRUE	TRUE	TRUE
2	0	1.8	1.000	1.000	0.9874	0.0126	0.0107	0.9056	0.0668	0.0818	0.9056	0.9874	0.9893	0.9190	TRUE	TRUE	TRUE
3	0	2.8	1.000	1.000	0.9646	0.0354	0.0229	0.7761	0.1086	0.1885	0.7761	0.9646	0.9769	0.8060	TRUE	TRUE	TRUE
4	0	3.7	1.000	1.000	0.9335	0.0665	0.0310	0.6447	0.1064	0.2888	0.6447	0.9335	0.9679	0.6881	TRUE	TRUE	TRUE
5	0	4.6	1.000	1.000	0.8984	0.1016	0.0352	0.5311	0.0893	0.3672	0.5311	0.8984	0.9623	0.5827	TRUE	TRUE	TRUE
6	0	5.5	1.000	1.000	0.8615	0.1385	0.0369	0.4378	0.0716	0.4237	0.4378	0.8615	0.9590	0.4932	TRUE	TRUE	TRUE
7	1	6.4	1.000	1.000	0.8244	0.1756	0.0371	0.3624	0.0566	0.4621	0.3624	0.8244	0.9570	0.4187	TRUE	TRUE	TRUE
8	1	7.4	1.000	1.000	0.7881	0.2119	0.0364	0.3017	0.0447	0.4864	0.3017	0.7881	0.9559	0.3571	TRUE	TRUE	TRUE
9	1	8.3	1.000	1.000	0.7529	0.2471	0.0352	0.2527	0.0355	0.5002	0.2527	0.7529	0.9554	0.3060	TRUE	TRUE	TRUE
10	1	9.2	1.000	1.000	0.7192	0.2808	0.0337	0.2130	0.0284	0.5062	0.2130	0.7192	0.9552	0.2636	TRUE	TRUE	TRUE
11	1	10.1	1.000	1.000	0.6870	0.3130	0.0321	0.1806	0.0229	0.5065	0.1806	0.6870	0.9553	0.2281	TRUE	TRUE	TRUE
12	1	11.0	1.000	1.000	0.6565	0.3435	0.0305	0.1540	0.0186	0.5025	0.1540	0.6565	0.9556	0.1984	TRUE	TRUE	TRUE

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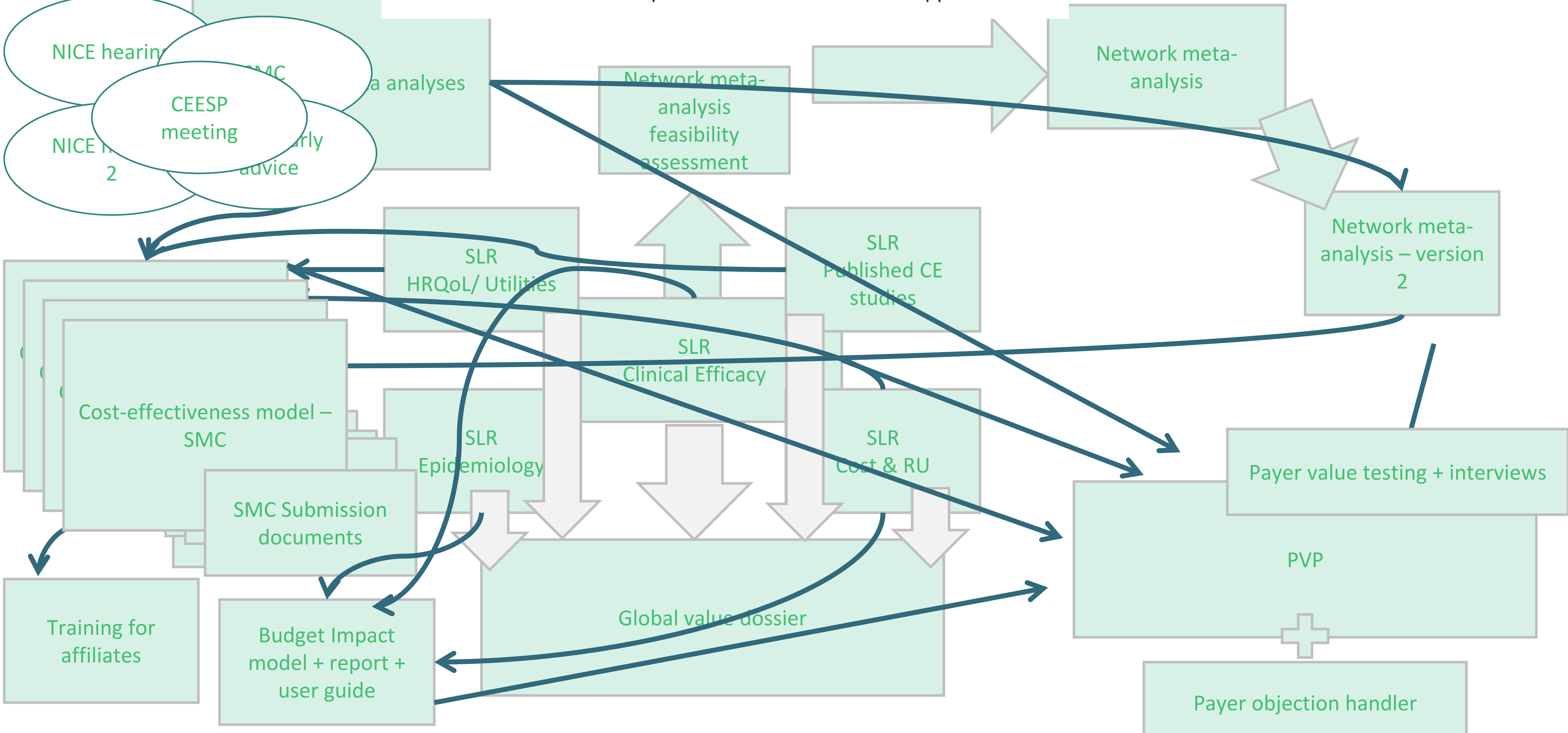
TYPICAL PROJECT – CASE STUDY 2

- Number of team members involved: ~35
- Number of countries helped to with reimbursement application: 14



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All done?

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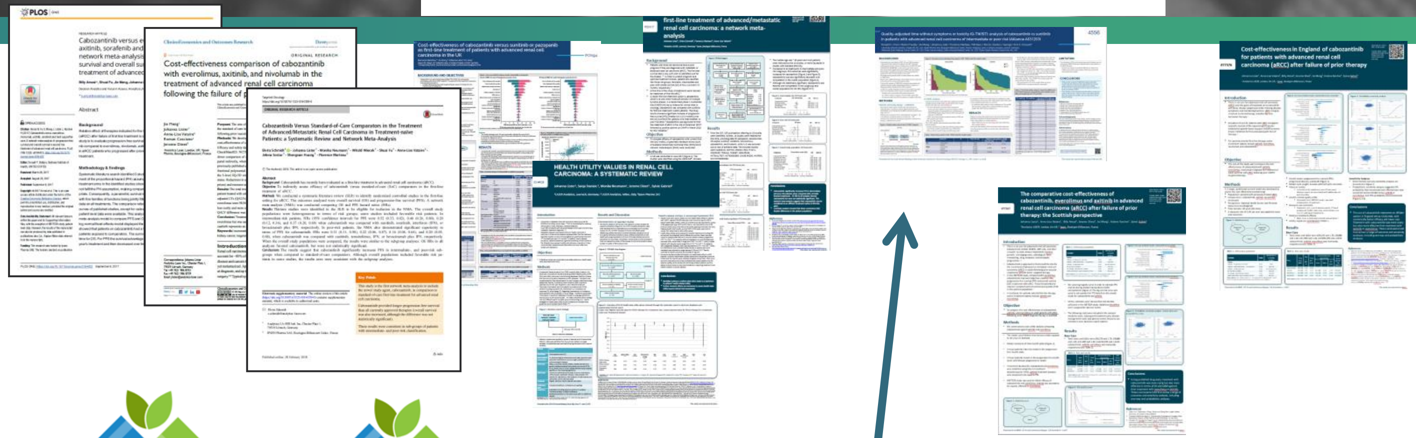
Eleven accepted publications



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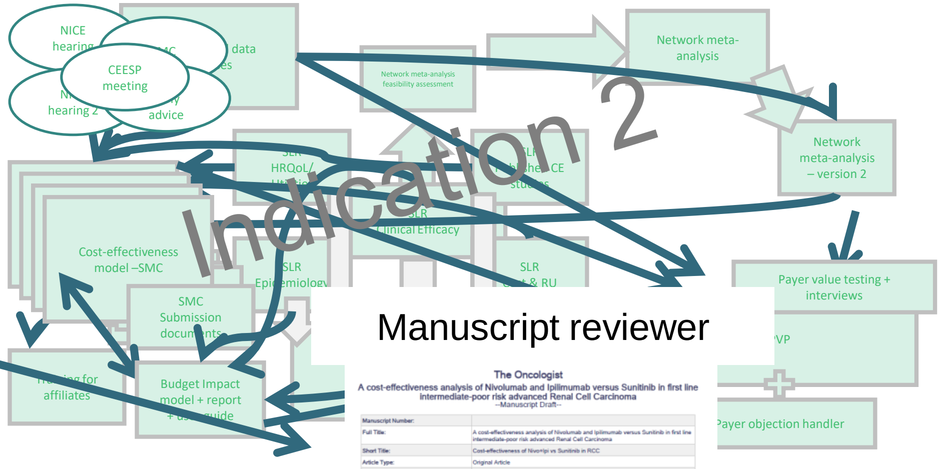
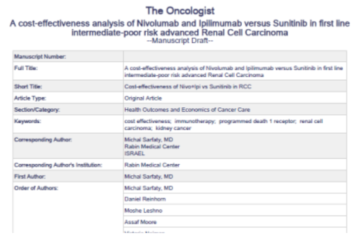
European market access strategy & evidence generation



Manuscript reviewer



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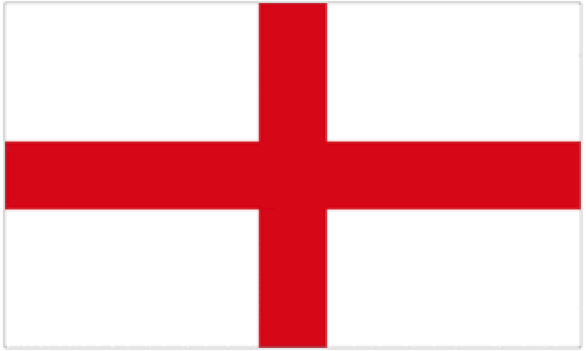
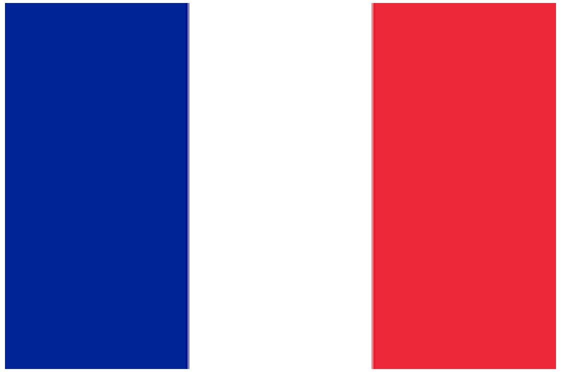
Were there differences in how the health economic models were used (or not) in decision-making?







CONCLUSIONS

Policy decisions needs to be made with insufficient information – can health economic modelling contribute to the debate?

Why use modelling?

- Policy decisions need to be made with **insufficient information**; trial data is said to provide "*a very precise answer to the wrong question*" (Buxton 1997).
- What is the **real life effectiveness** in a different population, dosages, and over time?
- Health economic models do not only provide an economic assessment but also a framework for integrating evidence from **multiple sources** and making **assumptions explicit**.

Important aspects of modelling

- **Timing**: models cannot be validated for a long time (e.g. 20 years), and need to be built with current evidence and updated later on.
- **Transparency**: it should be possible to see what assumptions were made and how inputs were selected.
- **Long term effect**: No-one knows what happens in 10 or 20 or 30 years time. However, this highlights the importance of making judgement on this issue.

Considerations

- **Surrogate measures**: are health states based on clinical events that are meaningful for the patients?
- **Bias**: errors in equations or in assumptions, such as what data to use in case of data gap (e.g. proxy utility values).
- **Complexity**: maybe difficult to review, validate or just to understand.
- **Trustworthiness**: Conservative assumptions versus those that favour the health technology in order to achieve cost-effectiveness

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