Assessing the appropriateness of existing model adaptation methods for low and middle income countries (LMICs)

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Acknowledgment of funding/ conflicts of interest

- The study is an independent work funded by the White Rose University Consortium (UK).
- https://www.whiterose.ac.uk/
- No personal conflicts to declare

White Rose university consortium
Universities of Leeds, Sheffield & York

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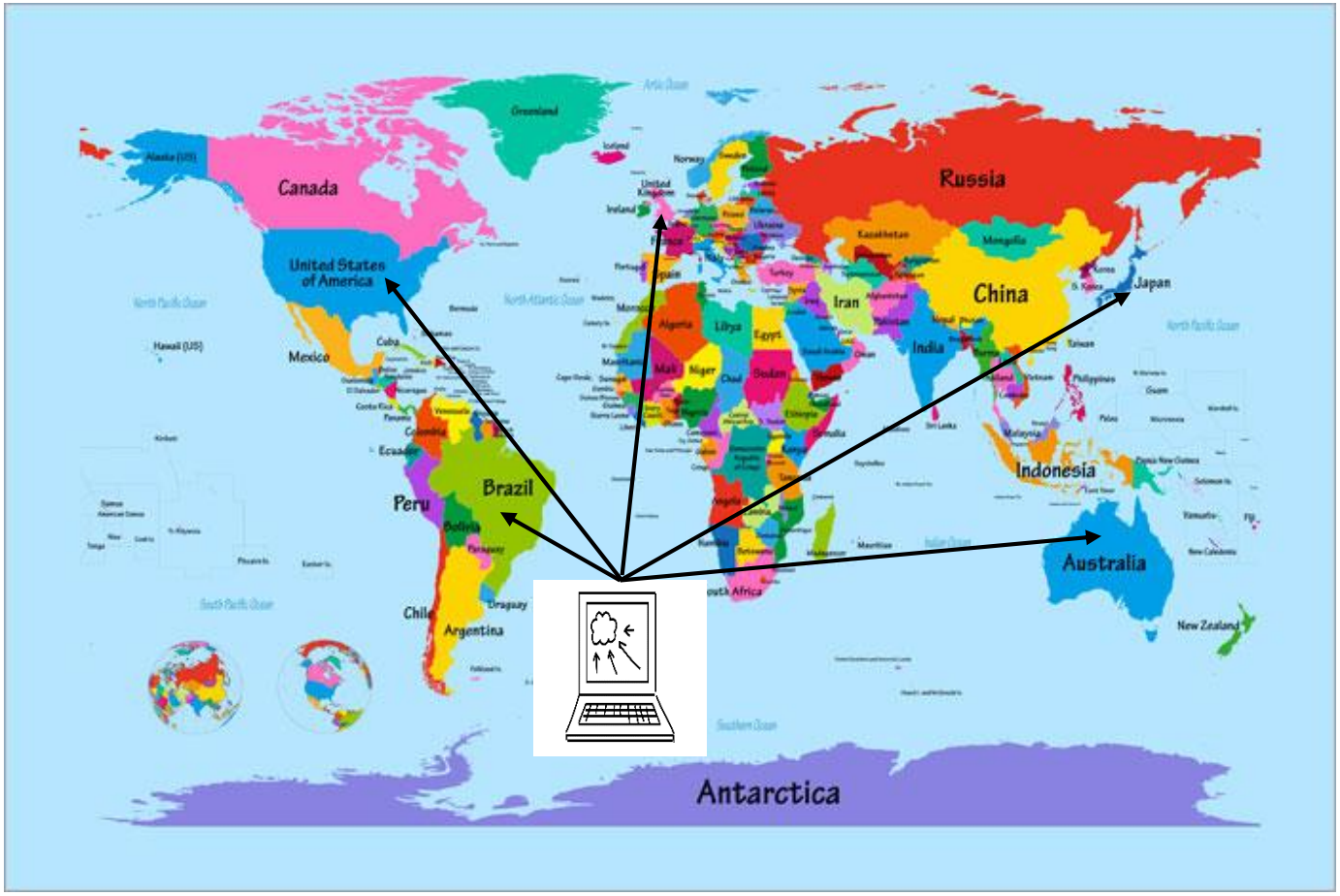
The inefficient way to generate economic evidence for use in local HTA

- Everybody develops their own model
- 'n' countries = 'n' models
- All could be somewhat different
- Confused messaging
- Not every country has the expertise to do it

The efficient way to generate economic evidence for use in local HTA



- One “core” model commissioned by the global parent company
- “Core” model adapted to local needs
- All of slightly different
- Consistent messaging across the globe

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Advantages of the efficient evidence generation approach to LMICs

- Speed
- Cost
- Overcomes the issues of “technical capacity” and other resource constraints

But…..

- Data availability may be a large issue in LMICs
- Substantive local KOL/ stakeholder engagement may be required
- LMIC health care systems may be very different to that used in the core model
- Local HTA landscape may be very different in each LMIC

What methodologies/ checklists exist for LMIC model adaptation?

Eight approaches were identified via a systematic review:

1. Heyland's generalisability criteria (1996)
2. Spath's transferability indicators (1999)
3. Welte's transferability decision chart (2004)
4. Boulenger's transferability information checklist (2005)
5. ISPOR (Drummond) application algorithm (2009)
6. EUNetHTA (Turner's) transferability checklist (2009)
7. Antonanza's transferability index (2009)
8. Mullins' model adaptation strategies (2014)

We developed a simple list of criteria by which to formally compare the identified approaches

1. Relevance (need to be specifically about model adaptation)
2. Endorsement from respected organisation (e.g. ISPOR, iHEA)
3. Compatibility with the International Decision Support Initiative's (iDSI) Reference Case i.e. the "Gates" reference case
4. Is there any explanation of how the method was developed?
5. Was the method to develop the checklist comprehensive? (automatically "no" if no explanation given)
6. Practicality – length (shorter is better)
7. External validity - Tested in case studies (any)
8. External validity - Tested in case studies (LMIC)

An appraisal of all eight methods against our criteria

	Heyland's generalisability criteria	Spath's transferability indicators	Welte's transferability decision chart	Boulenger's transferability information checklist	ISPOR (Drummond) application algorithm	EUNetHTA (Turner's) transferability checklist	Antonanza's transferability index	Mullins' model adaption strategies
Relevance (specifically about model adaptation)	generalisability of economic evaluations	transferability of economic evaluations	models included specifically	transferability of economic evaluations	models included specifically	transferability of HTA reports	transferability of economic evaluations	Specific to model adaption
Endorsed by respected organisation (e.g. ISPOR)					ISPOR	Focusses on HTA reports and not models. Hence not relevant		
Compatible with the Gates reference Case	See Table 2	See Table 2		See Table 2			See Table 2	
The paper explains the process used to develop the checklist							explains development of indices not checklist items	
A comprehensive development process was used to develop the checklist			Transferability factors identified from 1) systematic identification, 2) literature search. Factors short listed and grouped for checklist.	Developed using NHS EED and CODECS templates, piloted and modified. Final version tested and validated by EURON-HEEDS.	Monthly/bimonthly teleconferences to develop core assumptions. Peer review of draft report. Updated based on comments from 50 groups.		as above	Developed by a working group based on a systematic review of applied studies and stake holder interviews.
Practicality - length (shorter is better)	6 criteria if studies met minimum methodological standards	5 indicators if methodological standards are met	knock-out criteria, plus transferability factors-14	42 item checklist	4 step algorithm, 3 criteria to assess whether transferable		doesn't explain what to do with result	16 item checklist, 10 key principles
External validity - tested in case studies (any)	reported in paper - not successful	reported in the paper	reported in the paper, plus 2 identified from citation search	reported in the paper - to validate the method			reported in paper - apply to 27 studies	Informally used - Minerva group.
External validity - tested in case studies (LMIC)								

Green = yes, Orange = Partial, Red = No

A comparison of the eight identified methods against the Gates reference case

	Heyland's generalisability criteria	Spath's transferability indicators	Welte's transferability decision chart	Boulenger's transferability information checklist	ISPOR (Drummond) application algorithm	EUNetHTA (Turner's) transferability checklist	Antonanza's transferability index	Mullins' model adaption strategies
1. communicated transparently						Focusses on HTA reports and not models. Hence not relevant		
2. relevant comparators								
3. consider all available evidence								
4. appropriate health outcome								
5. resource use & costs differences								
6. time horizon and discount rate							discount rate is non-critical	
7. non-health effects and costs	not mentioned	not mentioned		not mentioned			not mentioned	
8. costs & effects on sub populations	not mentioned	not mentioned		not mentioned			not mentioned	
9. uncertainty characterised								
10. implementation impacts identified								
11. equity impacts explored	not mentioned	not mentioned		not mentioned			not mentioned	

Green = yes, Orange = Partial, Red = No

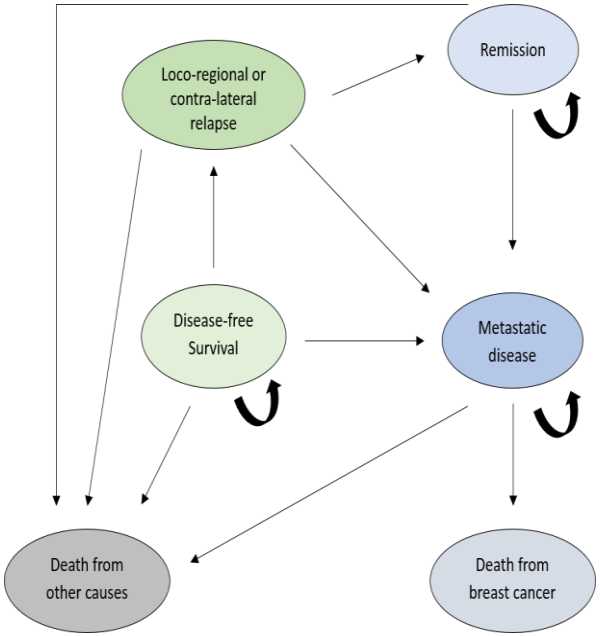
An application of Mullins' checklist of adaptation strategies: Adjuvant docetaxel/ paclitaxel in early breast cancer in South Africa

#	Recommendation	Implementation	Yes	No
1	Conduct good research practice for PE studies	The original model should be vetted for structure and scientific integrity.	✓	
2	Use recommended economic appraisal guidelines & reporting and appraisal standards	Refer to recommended economic appraisal guidelines. If no such guidance exists, consider recruiting a local expert and/or key opinion leader from the region to assure credibility and applicability.	✓	
3	Determine perspective of economic appraisal	In the absence of specific guidance from local decision maker, use both the societal perspective and a narrow focus on direct medical costs only. If desirable, include intermediate perspective	✓	
4	Select available treatment options (comparators)	Use current practice or the most widely used therapy/therapies in the jurisdiction of interest.	✓	
5	Consider the source of cost data	If cost data from the specific country is not available, apply a standard cost per procedure.	✓	
6	Identify and quantify resource use and costs	Include relevant direct and indirect costs associated with the treatment. An activity-based costing method can generate a more accurate product costs.	✓	
7	Consider clinical practice patterns and guidelines	When using decision analytic modelling, incorporate clinical practice patterns/guidelines of the intended country/jurisdiction of interest.	✓	
8	Use country/region specific epidemiologic data	If country/region specific epidemiologic data are not available, use random-effect meta-analysis models and transition probabilities where necessary.		✓

An application of Mullins' checklist of adaptation strategies: Adjuvant docetaxel/ paclitaxel in early breast cancer in South Africa

#	Recommendation	Implementation	Yes	No
9	Explain and justify use of estimated treatment effect	Use the average treatment effect from a multinational trial. Conduct a sensitivity analysis using treatment effect based upon patients from the specific country or region.	✓	
10	Use health state preferences/utilities that are applicable to the region	Use local health state preferences and utilities whenever available; Use the average of published ones if local values not available. If a revalidation is required/desired, include forward translation, back translation, and pretesting of the instrument.		✓
11	Utilize expert opinion sparingly and appropriately	Lower level of evidence. Whenever expert opinion is used, multiple experts should be involved. Delphi method used for consensus.	✓	
12	Use modelling to address non-transferable elements	For data elements that are non-transferable, the model structure, data used as inputs to models, and model validation are important when assessing the quality of models. More info: ISPOR task force reports	✓	
13	Utilize quality-adjusted life years(QALYs)	Determine threshold to enable transfer and applicability of QALYs across jurisdictions unless local guidelines recommend a different metric or approach	✓	
14	Determine and justify discount rate	Use local guidance for discount rate. If none exist, use a "real riskless" discount rate of 3% and conduct sensitivity analysis.	✓	
15	Source/ justification of each data element in PE model	To reflect an evidence-based approach to PE modelling, systematic reviews of the literature should be conducted.		✓
16	Translate findings for the desired perspective	The perspective, the recommendations concerning evaluation of resource use/costs, the choice of the comparator, and the valuation of costs should be considered before considering the transferability and reproducibility.	✓	

An application of Mullins' checklist of adaptation strategies: Adjuvant docetaxel/ paclitaxel in early breast cancer in South Africa



Analysis	Δ Cost (Rand)*	ΔQALYs*	ICER**	Probability CE at R15,630 threshold
Docetaxel based on BCIRG-001 trial	R 6,774	0.238	28,483	0.04
Paclitaxel based on NSABP B-28 trial	- R 578	0.030	Dominant	0.86
Paclitaxel based on CALGB 9344 trial	- R 1,512	0.025	Dominant	0.74

* vs. Standard of care (non-taxane containing chemotherapy); ** Rand per QALY gained

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Conclusions

- Adapting an existing model to the specific needs of a LMIC more preferential than building a local *de novo* model
- A range of transferability methods are available to guide/ inform this localisation process
- One of these methods is Mullins' model adaptation strategy checklist
  - Based on a systematic formal review of the relevant methodologies this is the approach preferred by YHEC
- Use of Mullins' adaptation strategy checklist results in robust models on which to base local HTA decisions
  - See South African case study
  - Substantive local input still required in order to undertake the adaptation

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Thank you!

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