### Is My Global Health Intervention Worth the Investment?

**An Overview of Tools and Techniques** 

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Floating Hospital for Children at Tufts Medical Center

### **Today's presenters**



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- CEA and cross-sectoral applications
- Sources of data on CEA
- Tools for identifying relevant evidence
- Using CEA to address equity concerns
- Transferability of economic evidence: a case study

# **Cost-Effectiveness Analysis (CEA)**

- Compares the costs and benefits of two interventions
- Prioritize interventions that produce the greatest benefit for the funding available
- COVID-19 (before vaccines):
  - Spend limited funds on antiviral treatment, steroids, or oxygen?

### **Measures of Benefit**

- Quality-adjusted life year (QALY)
  - Weights time spent in a given state of health by quality of life in that state
- Disability-adjusted life year (DALY)
  - Measures impact of premature death and years lived with disability
- Standardized measures that permit comparisons across disease areas

### **Incremental Cost-Effectiveness Ratio (ICER)**

### Cost A - Cost B

### Effect A – Effect B

**Incremental Cost-Effectiveness Ratio (ICER)** 

### **Costs** \$150,000 - \$100,000

### QALYs 1-0.5

### **Incremental Cost-Effectiveness Ratio (ICER)**

# \$100,000 per QALY gained

# What is "Cost-Effective"?

- A threshold for decision-making
- Typically based on society's willingness to pay for one additional QALY (or one less DALY)
- Countries apply different thresholds
  - E.g., \$50,000 -- \$100,000 per QALY (US)
  - 1-3x GDP per capita
  - Country-specific criteria

# **Using CEA to Address Health Equity**



Cookson Value Health 2017

# What About Other Sectors?

- Education: level/program completion, test scores
- **Transportation**: km of new road, increase in vehicle capacity
- **Defense**: combat success, training milestones
- More commonly, costs and benefits both expressed in monetary terms ("benefit-cost analysis")

### **Sources of Data on CEA**









REGISTRY

### **Cost-per-QALY Studies**



### **Cost-per-DALY Studies**



# Growth of Cost-per-DALY and Cost-per-QALY Studies in LMICs



### **Tools for Identifying Relevant Evidence**

# **Example: Ranking interventions**

- Scenario: Bangladesh Ministry of Health
- Need: Identify most cost-effective interventions for pregnant women
- Regionally appropriate







#### Welcome to the Global Health Cost-Effectiveness Analysis Registry

Funded by a grant from the Bill and Melinda Gates Foundation, The Center for the Evaluation of Value and Risk in Health (CEVR) at Tufts Medical Center created the CEVR Global Health CEA (GH CEA) registry, a database of cost-effectiveness analysis (CEA) studies that evaluate health interventions from around the world. The Global Health CEA registry focuses on those interventions designed to mitigate disease burden in countries at various stages of industrial development.

The Global Health Cost Effectiveness Analysis (GH CEA) Registry is a free database that compiles research literature on the economic value of global health interventions. Our inclusion criterion for contributing articles is contingent on its application of the "cost-per-DALYaverted" metric, which measures the cost-effectiveness of an intervention.

The GH CEA Registry is a repository of all peer-reviewed cost-per-DALY studies stratified by methods, cost-per-DALY ratios, and disability weights published since the 1990s.

Global health organizations acknowledge the importance of prioritizing limited health care resources, but the question remains: are we spending our money wisely? Cost-effectiveness analysis can help stakeholders gain a better understanding of the return on investment of global health interventions and has the potential to inform smart investments and maximize the impact on population health.

#### Methods

WHO WE ARE

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DOWNLOAD

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SEARCH THE

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Data Visualization

- Global Burden of Disease
- Classification & ICD-10
- Primary, Secondary & Tertiary Prevention Classification

**GH CEA Registry Overview Brochure** 

- Funding Source
- Study Perspective

#### Cost-Per-DALY Ratios

- Target Population
- Intervention & Comparator
- Source
- Costs & DALYs
- Disease Disability Weight

**Disability Weights** 

 Incremental Cost-Effectiveness Ratio (ICER)

Click here for a downloadable and printer-friendly pdf of the GH CEA Registry Overview Brochure. The brochure provides insight into our cost-per-DALY database, its contents and a succinct "getting started" section.

Bill&Melinda GATES foundation

Tufts Medical

INSTITUTE FOR CLINICAL RESEARCH The Center for the Evaluation AND HEALTH POLICY STUDIES of Value and Risk in Health

### ghcearegistry.org

# **Registry Search Page**

#### Keywords:

Select...

#### Disease:

Begin typing disease...

#### Country:

Begin typing country...

#### Reset filters

#### Intervention type:

Begin typing intervention type...

Region:

Begin typing region...

#### **Comparator:**

Begin typing comparator...

#### Publication year:



Advanced filters

2020

#### Show 10 • entries

GH CEA Registry League Table: Sorted by ICER from lowest to highest. Cost-Saving interventions (green) are considered lowest, Dominated interventions (red) highest.

Article Title (Author)	\$ Year ≑	Sponsor 🍦	Disease 🔶	Country 🖨	Target Population	Intervention	Comparator	ICER (\$/DALY averted)	ICER as % of GDP*	GDP Category <b>♦</b> (2018)^
Implications of scaling up cardiovascular disease treatment in South Africa: a microsimulation and cost-effectiveness analysis. (Basu)	2019	Academic	Ischemic heart disease, Hypertensive heart disease, Diabetes mellitus	South Africa	Both women and men ; Age: Adolescents: 12-18 years, Adults: 19-40 years, Adults: 41-64 years, Older adults: >65 years ; with Cardiovascular diseases and risk factors for CVD	Pharmaceutical: Scale-up of cardiovascular disease treatment based on WHO-PEN guidelines	Standard/Usual Care- Current treatment levels fo chronic cardiovascular conditions	Cost- Saving	NA	Cost-Saving
Implications of scaling up cardiovascular disease treatment in South Africa: a microsimulation and cost-effectiveness analysis. (Basu)	2019	Academic	Ischemic heart disease, Hypertensive heart disease, Diabetes mellitus	South Africa	Both women and men ; Age: Adolescents: 12-18 years, Adults: 19-40 years, Adults: 41-64 years, Older adults: >65 years ; with Cardiovascular diseases and risk factors for CVD	Pharmaceutical: Scale-up of cardiovascular disease treatment based on South Africa's Primary Care 101 guidelines	Standard/Usual Care- Current levels of treatment for cardiovascular disease:	Cost- Saving	NA	Cost-Saving
Cost-effectiveness of dengue vaccination in ten endemic countries. (Zeng)	2018	Industry	Dengue	Brazil	Healthy ; Both women and men ; Age: Children: 6-11 years	Immunization: Routine dengue vaccination only at age 9	None	Cost- Saving	NA	Cost-Saving



### **Example filters:**

#### Keywords:



# Sample output:

Study	Intervention	Country	ICER (\$/DALY averted)
Lohse et al.	Gestational diabetes prevention: screening; lifestyle adjustment	India	Cost-saving
Feldhaus et al.	Pre-eclampsia prevention, supplementations: calcium; magnesium sulfate	Nepal	\$4
Sutherland et al.	Post-partum hemorrhage prevention: misoprostol treatment	India	\$7
Adam et al.	Breast feeding support; tetanus vaccination	Bangladesh, Bhutan, India, North Korea, Maldives, Myanmar, Nepal, Timor Leste	\$12

# **DALY Calculator**

DALY Calculator	Calculate DALYs for an individual	Calculate DALYs for	a population	References	Code			
In Disease:	puts:			(	Outputs	:		
Severe lower respirate	ory infections	Disability weight = 0.133	3					
Country:								
Cameroon	• Y	ears lived with disease	e = 5					
Gender:		ife expectancy at age of	of premature d	eath = 35.67				
Both	·	, , , , , , , , , , , , , , , , , , , ,	,					
Age of onset of diseas	se (years): Y	ears of Life Lost (YLI	Ls),					
30	a	nd total Disability Ad	ity (YLDs), justed Life Ye	ars (DALYs):				
Age of premature dea	th due to disease (years):	Contribution of YLLs	18.85					
35		Contribution of YLDs	0.62					
Discount rate?		Total DALYs	19.47					
Discount rate:								

### **DALY Calculator Case Study**

Country	Cost per HIV Case Averted (\$)	DALYs per Case (95% CI)	Cost per DALY Averted (\$)
Benin	7,183	18.3 (8.9-30.9)	2,075
Cameroon	2,404	18.2 (9.0-30.5)	727
S. Africa	3,153	21.7 (14.1-37.3)	1,035



- Enables "generalized" CEA for optimizing essential intervention or benefit design
- Tools/data available to populate models
  - Allowance for country-specific data as available



# WHO-CHOICE



Joncheere. Priority Setting in Universal Health Coverage. 2014

## HIPtool

- Open-access platform to allow countries to develop evidence-based benefits packages
- Includes optimization algorithm to maximize:
  - Health outcomes
  - Equity
  - Financial risk protection



### **HIPtool**





health interventions prioritization tool

### **Using CEA to Address Equity Concerns**

# **Community Women's Groups to Address Perinatal Mortality**

- Perinatal mortality reduced 16%
- \$79 per DALY averted vs. usual care
- Meta-analysis of community women's groups
  - Neonatal mortality rate reduction in "most marginalized": 60%



Malawi

### **Transferring Economic Evidence Between Settings**

Model adaptation methods: a case study on Taxanes for adjuvant treatment of early breast cancer in South Africa

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# Outline

- Background
  - Description of the CEA model
  - Factors to consider
- Mullin's Checklist/Recommendations for model adaptation
- Potential use for adapting equity-informed CEA

# Background

- Formal structures and processes for the systematic utilization of economic evidence in LMICs unclear.
- Steady growth in the number of economic evaluation studies in LMICs.
- Context-specific challenges for undertaking EE
  - quality of data
  - limited local technical capacities
- Furthermore, the development of de novo models for economic evaluations both time-consuming and expensive.
- Adapting economic evaluation models may be one way of circumventing some of these challenges.

# Background

- An economic evaluation is considered to be transferable if it can be appropriately adapted for application in another setting,
- Distinct from a generalizable evaluation where results can be applied to other settings without adjustment.
- To transfer economic models across settings, first determine which part(s) of the model needs to be adapted
- A range of approaches have been proposed for judging which parts of the model need adaptation
- These approaches mostly used in HIC but limited evidence on their application in LMIC settings
- In our case study we documented methodology, feasibility and the empirical challenges of adapting EE models from one setting to another

# Background

- We undertook a case study on the transferability of an economic evaluation model developed in the UK to South Africa.
  - Taxanes "Docetaxel and Paclitaxel" for the adjuvant treatment of early breast cancer
- The study was based on an existing model built at the University of Sheffield (UK)
- This was a state transition (Markov) model developed in Microsoft Excel.
- The model makes assumptions about clinical practice and disease pathways in the treatment of early breast cancer



# Mullins' recommendations for model adaptation

No	Recommendation	Implementation	yes	no
1	Conduct good research practice for Pharmacoeconomic studies	The original model should be vetted for structure and scientific integrity.	~	
2	Use recommended economic appraisal guidelines and required 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.	~	

No	Recommendation	Implementation	yes	no
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.		~
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 they are available; Use the average of published ones if local utilities are not available. If a revalidation is required/desired, include forward translation, back translation, and pretesting of the instrument.		~

No	Recommendation	Implementation	yes	no
11	Utilize expert opinion sparingly and appropriately	Expert opinion represents lower levels of evidence. Whenever expert opinion is used, multiple experts should be involved. Use the Delphi method 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. See http://www.ispor.org/taskforces/GRPModelingTf.asp for more information.	*	
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 exists, use a "real riskless" discount rate of 3% and conduct sensitivity analysis.	*	
15	Source and 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.	~	

# Performance against Mullins' Checklist (1/2)

- We used a well-validated model
- Resource use data and unit cost (price) data obtained from South Africa
- However....
- Disease epidemiology partly SA-specific
  - Annual probability of death in patients with metastatic disease not SA-specific
  - Annual probability of metastatic disease in patients with locoregional or contralateral recurrence not SA-specific
  - But the probability of dying for females by age group SA-specific

### Clinical effectiveness not SA-specific

- Clinical effectiveness largely transferable
- But assumption may not hold here- breast cancer prognosis may differ between ethnic groups. Ethnicity of RCT participants different from SA ethnic groups.

# Performance against Mullins' Checklist (2/2)

### Health state utilities not SA-specific

- Based on literature review of utilities from multiple settings
- Difference in preferences and methodologies for eliciting preferences between settings may limit transferability of health state utilities

### • Clinical practice patterns partly SA-specific

- Was accounted for in estimating context-specific costs
- But intervals between treatment cycles different in SA and RCT

# Adapting Equity-Informed CEA

- Current adaptation methods largely focus on conventional CEA models
- But could potentially be useful for adapting equity-informed CEA → 'Equity impact analysis' e.g. Extended CEA, Distributional CEA
  - Considers the health equity impact (distribution of health benefits, financial risk protection benefits and opportunity costs) of alternative policy options



From: Cookson et al 2017 Value in Health, Volume 20, Issue 2, 2017, Pages 206-212 https://doi.org/10.1016/j.jval.2016.11.027.

# Concluding remarks

- Adapting models to LMIC setting doable but...
  - Requires access to the model or comprehensive reports
  - Requires technical expertise
  - Scarcity/unavailability of data in LMICs a limiting factor

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### Thank you!