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Characterizing the Economic Analysis of Technology Appraisal in Global Health Systems

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Comparative Effectiveness Research, Pharmacoeconomics, Health Technology Assessment, cost-effective analysis, outcomes research

Disciplines
Business | Econometrics | Health Economics

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Characterizing the Economic Analysis of Technology Appraisal in Global Health Systems

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1 Introduction

As the emergence of value based care replaces traditional fee-for-service healthcare delivery models in provider settings, both public and private payers alike are turning to Evidence Based Medicine (EBM) to optimize reimbursement and approval decision making. EBM’s use of formal, analytical methods to align research evidence with medical practice has extended to policy makers in referencing quality and cost efficacy of potential therapeutics. As these payers have limited budgets, it is thus necessary to assess the allocation of resources when reviewing any novel health technology*, despite a common public aversity to ration patient access when considering therapeutic choices. Payer interest in the value of new health technologies is further underpinned in controlling increases in price and health consumption if decision making is transferred to the physician and patient.

The field of Health Technology Assessment (HTA) concerns the investigation and evaluation of novel health technologies from the payer standpoint when market access requests are submitted for approval. HTA bodies, created in nations worldwide in the 1970s, reflected the emergence and advancement of biological technologies challenging conventional social, ethical, and political status quo (e.g. artificial organs, genetic therapy, stem cell research)\(^1\). HTA techniques are wide in scope in order to most-holistically examine the character of a novel health technology before decision making occurs. Many components exist to its multidisciplinary evaluation including societal, economic, and organization implications of the therapy in appraisal. This paper concerns the particular economic approach of HTA, Cost Effective

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*A health technology is defined by the World Health Organization as “the application of organized knowledge and skills in the form of devices, medicines, vaccines, procedures and systems developed to solve a health problem and improve quality of lives.”*
Analysis (CEA), that countries conduct in the decision making process as HTA bodies across different countries use different CEA modeling strategies in the evaluation of a novel health technology. By understanding how variability among CEA approach characteristics affect country health outcomes including health spending and health quality, we are better able to model the impact of critical economic decision making factors in policy guidelines of country health cost containment and health quality improvement.

2 Background

2.1 Cost Effective Analysis (CEA)

Under HTA, the economic analysis of the technology is carried out through a cost effective analysis (CEA). The objective of CEA is notably summed up through a health equity lens: a quasi-utilitarian approach to maximize the total health of a population given limited resources. A CEA measures the cost per outcome unit gained of a treatment against a comparator:

\[
\frac{Cost}{Outcome} = \frac{\Delta C}{\Delta E}
\]

(1)

where costs are presented in monetary units and outcomes are described using quantitative non-monetary metrics of health quality\(^2\). Most commonly, the quality-adjusted life year (QALY) has been recognized as an internationally used metric when referencing measurements of disease burden\(^3\). The QALY measures the health outcome of a patient through an index combining the length of life and the patient’s health related quality of life (HRQoL) based on surveys and various patient reported outcomes\(^4\). By standardizing such weights, payers are able to apply quantitative value to assess the cost-per-QALY of a given health technology, using the incremental cost-effectiveness ratio (ICER):
which shows the quantitative benefit of the new treatment against the comparator. Through measuring the cost-effectiveness of a novel technology using an ICER, health systems are able to recognize optimal treatments for patients and enhance the delivery of care based on therapies that offer maximum incremental value. CEA has potential to both identify and validate potentially less-complex or cheaper therapies than current standard of care, bringing novel recommendations to health care payers and providers.

\[
ICER = \frac{C_{new} - C_{old}}{E_{new} - E_{old}}
\]

Figure 1: A cost-effectiveness matrix organizing the potential outcomes for a novel technology against a comparator. Novel health treatments as points that fall past the threshold are deemed overall more cost-effective.

2.2 Willingness to Pay Thresholds

The ICER value forms the guiding metric for payers in the CEA evaluation of the novel technology, often times referenced against a threshold, k. This threshold value is the public payer’s maximum acceptable cost per QALY (or other health measure), often termed a country’s willingness-to-pay (WTP). On average, if the CEA value given by the ICER does not exceed the
threshold, the health technology has a stronger likelihood of payer approval reluctance. This threshold value, however, is often times nondisclosed, as the metric grants incentives for pharmaceutical and biotechnology companies to tailor ICER estimates given by

\[ p^{max} = p_{old} + k\Delta E - \Delta C \]  

in which companies are thus able to compute the max price at which the technology will be approved, triggering funding. The above maximum price value would thus be a private and societal gain fully captured, subsequently negotiated down in the healthcare supply chain.

Importantly, each country has distinct thresholds, which then influences the selection of therapeutics in their respective health system. There exists a threshold either explicitly stated by the public payer, or implicitly based on the payer’s aggregate data on historical approval price patterns in cases when the threshold is nondisclosed. Implicitly, it is thought that if many decisions are observed, it is possible to infer the cost per QALY under which approvals occur, thereby acting as the implicit cost-effectiveness threshold. These differences in WTP are, in recent years, known to correlate to the respective country’s ability-to-pay (ATP) for novel health technologies.

### 2.3 Approaches to CEA

Although international structures exist to country-specific pharmacoeconomic guidelines, the approach to CEA of national HTA bodies vary across countries. The process in which CEA variables are measured require considerations that are varying by nature as shown in the table below.
Figure 2: Potential variations to a CEA in terms of factors in consideration, detailing the key attributes to account for costs and outcomes in a cost-effective analysis.

These attributes are critical in an investigation and evaluation of a CEA given the different methods in which the same technology’s costs and outcomes can be measured. Slight variations in the input attributes can have significant effects on the resulting estimate of a cost-effectiveness ratio, particularly fragile for ICERs near a country’s WTP.

All studies of novel health technologies conducted by national HTA bodies thus make clear their methodology in a CEA approach as to validate an analysis compared to another HTA body. Importantly, while classification of CEA approaches as guided by the International Society for Pharmacoeconomics and Outcomes (ISPOR) are documented across each country’s HTA body, no existing literature comparing approaches to health outcomes and health expenditures. The objective of our research was to investigate the characteristics of cost-effectiveness approaches for each country, identify variability across CEA approaches, and assess the correlation between country-specific approaches to CEA and country health and spending related metrics.

By understanding the role that CEA plays in affecting healthcare spending and quality, we are able to gain insight into the optimal CEA modeling strategies that will guide efficient resource allocation of health interventions. At large, identifying CEA approaches that correlate...
with healthcare outcomes will help inform policy makers and payers on key decisions of therapeutic choice to advance healthcare cost containment and quality improvement.

2.4 Economic Evaluation Implications

It is important to acknowledge the broader framework of a CEA in the HTA decision making process. An ICER value from a CEA alone compared against a country’s cost-effectiveness threshold can only be, at most, an aid in the decision making process. The economic analysis comprises only one component of a larger technology assessment process and thus may not be used as the sole factor in a complete decision-making procedure. There must be careful examinations surrounding the use of threshold values and deriving cost-effectiveness ratios from a CEA, discussed in later sections.

3 Research Methodology

3.1 Data Sources

The data sources used in the study consists of the following:

1. UN Human Development Index spread (2015)
2. OECD healthcare spending (2017)
3. WHO world health statistics (2016)
4. Implicit and explicit ICER threshold values
5. CEA ISPOR country-specific pharmacoeconomic guidelines
6. IMF GDP per capita, World Economic Outlook (2018)

The United Nations Development Programme contains reference information regarding the capital and development of global nations in addition to economic growth. This metric, termed the human development index (HDI), summarizes aggregate dimension indices serving as measurements for a country’s development: life expectancy index, education index, and gross national income (GNI) index.

The HDI spread from the 2015 Human Development Index report thus presents an outline to identify varied countries of interest for further investigation in CEA. Countries for CEA analysis were selected from the list based on spread of development indices as well as feasibility for data collection based on previous data points from literature reviews. The resulting group of selected countries fell within very high human development (VHHD), high human development (HHD), and medium human development (MHD). VHHD countries consisted of the G7 nations: Canada, UK, US, France, Germany, Italy, Japan. HHD countries included China, Brazil, Mexico, and Thailand. MHD countries of analysis included South Africa and India.

3.1.2 OECD Health Expenditure and Financing Database (2017)<sup>11</sup> 

Metrics for country health expenditure data were pulled from the Organisation for Economic Co-operation and Development’s health spending database. The OECD defines healthcare expenditure as the “final consumption of health care goods and services” which includes both individual care consumption and collective health administration and public health spending, but excludes spending on investments (e.g. pharmaceutical R&D dollars and bench research). For each country, the aggregate health spending value was taken with respect to voluntary, out-of-pocket, and government/compulsory expenditures.
3.1.3 WHO World Health Statistics

Life expectancy data from the World Health Organization served as a proxy for individual country’s health outcomes. Life expectancy as measured by the average number of years of lifetime survival, applied to both males and females, serves as a reflection of a country’s overall mortality level in its population. Driven by public health and medical interventions, the numerical lifespan acts as a quantitative value representing the quality of care within a country. Thus, mortality and health expenditure data serve as outcome variables of interest when examining correlations with respect to CEA approach.

3.1.3 Implicit and Explicit ICER Threshold Values

In order to locate data on country WTP, often an implicit value, an assessment of both academic literature and country-specific government health insurance programs allowed for source reliability and information cross-checking. Comparative effectiveness thresholds for all countries selected were gathered based on persistent, similar line-item values from secondary sources in academic literature and payer HTA process documents. Final data inputs relied upon an average of upper and lower threshold values (when available) converted to 2017 USD.

Specifically, only the United Kingdom’s and Thailand’s HTA bodies, the National Institute for Health and Care Excellence (NICE) and the Health Intervention and Technology Assessment Program (HITAP) respectively, explicitly mention a threshold value used to guide decision making. These threshold values were sourced directly from online HTA website literature for both the two countries. The remaining countries do not delineate set values for a threshold on official HTA-related released literature; thus requiring further investigation into historic patterns of approval prices to arrive at an implicit WTP threshold. Implicit country threshold values were thus cross checked on multiple sources of academic literature and country-
specific health technology economic assessment bodies to derive repeatable estimates. The articles used are cited in the threshold column of Figure 3 below in the results section. Of particular note is the usage of Wood’s approach\textsuperscript{13} to derive threshold estimates for less developed nations without well-established HTA bodies that lacked detailed cost-effectiveness analysis explanations. Woods creates a predictive model extrapolating from the United Kingdom cost-effectiveness threshold to estimate opportunity-cost-based WTP for low/middle income countries, for which there had previously been no values available.

3.1.4 CEA ISPOR Country-specific Pharmacoeconomic Guidelines\textsuperscript{14}

The International Society for Pharmacoeconomics and Outcomes (ISPOR) specializes in health economics & outcomes research (HEOR) and includes data on variables related to cost-effectiveness approaches in assessing a novel technology. ISPOR’s data system includes information on guidelines used as an “analytical tool used with increasing frequency to assist decision making in the financing and management of pharmaceutical products.” These guidelines for each selected country serve as the regression inputs for comparison against health outcomes of interest. In situations where CEA approach data was not available through ISPOR’s pharmacoeconomic guidelines, academic literature was referenced for specific data points.

3.1.5 IMF GDP Per Capita Prices, World Economic Outlook (2018)\textsuperscript{15}

In order to account for the effect that inherent country development holds on the country’s ATP, GDP per capita and population statistics were gathered from the International Monetary Fund’s World Economic Outlook report for each selected country. The regression is controlled for these other, non-CEA approach-related factors that may impact healthcare spending, effectively isolating the interaction of CEA attributes on outcomes of interest.
3.2 First Round Regression

To examine the role of WTP threshold data in a country’s HTA, univariate linear regression models of WTP were tested against outcomes of interest. Country WTP threshold data is noted to proportionally relate to health expenditure and health quality. By determining the correlation between WTP threshold data and regression outcomes, we are able to determine if such relational factors exist and maintain WTP threshold data in further regression analysis as a controlling variable in later regressions with all CEA approach characters as explanatory variables of interest. This controls for the influence of the threshold variable on outcomes of interest, isolating potential effect of CEA attributes on outcomes further.

Upon confirming WTP relationship, multivariate least squares regression were run on country approach factors against outcomes of interest. This phase two of first round regression gives insight into the strength of the correlation between CEA approach variables and outcomes, modeling both continuous and dummy variable effects on country health expenditure and life expectancy.

3.3 Second Round Regression

In order to test conditions of correlation between CEA attributes and outcome variables of interest, we construct various multiple regression linear models with stepwise ANOVA trials. To control for other country-specific factors, we include variables with significant effect on outcomes of interest from first round regressions. Through stepwise analysis, multivariate model selection based on a minimum Bayesian Information Criterion (BIC) stopping rule determine CEA attribute effect on outcomes of interest. The stepwise regression fit serves to maximize the likelihood function, $L(\beta)$, through estimating the variable parameters, $\beta$, that maximize the
probability density functions at the observed data points. The BIC perspective to assess stepwise model fit is defined as:

\[
BIC = -2 \log(L(\beta)) + k \ln(n)
\]  

(4)

where \( k \) is the number of estimated parameters and \( n \) is the number of model observations in reframing likelihood maximization as minimizing negative log-likelihood. Thus a BIC stepwise fit maximizes parameter fit of potential multivariable effects on outcomes of interest.

4 Results

4.1 Threshold Values

Both explicit and implicit WTP values were collected for selected countries through identifying data from each country’s established public health economics and outcomes research (HEOR) or HTA body. Final ICER thresholds were based on selected upper and lower threshold values, converted to USD and adjusted for inflation to 2017 prices. Explicit thresholds, consisting of only the United Kingdom and Thailand, were gathered from public government disclosures. Implicit thresholds determined through literature reviews on academic journals and government databases formed the upper and lower threshold bounds, of which the mean formed the threshold value. The thresholds used in the study are listed in Figure 3.

<table>
<thead>
<tr>
<th>Table 1 Established ICER Thresholds by Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>Canada</td>
</tr>
<tr>
<td>UK</td>
</tr>
</tbody>
</table>

12
<table>
<thead>
<tr>
<th>Country</th>
<th>Organization</th>
<th>Level</th>
<th>Low</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>Agency for Healthcare Research and Quality (AHRQ)</td>
<td>Very</td>
<td>$50,000</td>
<td>$150,000</td>
<td>$100,000</td>
</tr>
<tr>
<td>France</td>
<td>Haute Autorité de Santé (HAS)</td>
<td>High</td>
<td>$35,263</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>Institute for Quality and Efficiency in Health Care (IQWiG)</td>
<td>Very High</td>
<td>$133,881</td>
<td>$5,228</td>
<td>$69,554</td>
</tr>
<tr>
<td>Italy</td>
<td>Italian National Health Services (NHS)</td>
<td>Very</td>
<td>$29,363</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td>Central Social Insurance Medical Council</td>
<td>Very</td>
<td>$45,259</td>
<td>$54,311</td>
<td>$49,785</td>
</tr>
<tr>
<td>China</td>
<td>China Ministry of Health (MoH)</td>
<td>High</td>
<td>$4,210</td>
<td>$5,814</td>
<td>$5,012</td>
</tr>
<tr>
<td>Brazil</td>
<td>Brazil Ministry of Health</td>
<td>High</td>
<td>$2,153</td>
<td>$23,016</td>
<td>$12,585</td>
</tr>
<tr>
<td>Mexico</td>
<td>Mexico General Health Council</td>
<td>High</td>
<td>$24,083</td>
<td>$6,953</td>
<td>$15,518</td>
</tr>
<tr>
<td>Thailand</td>
<td>Health Intervention and Technology Assessment Program (HITAP)</td>
<td>High</td>
<td>$4,826</td>
<td></td>
<td>$4,826</td>
</tr>
<tr>
<td>S. Africa</td>
<td>Republic of South Africa Department of Health</td>
<td>Medium</td>
<td>$1,211</td>
<td>$4,857</td>
<td>$3,034</td>
</tr>
<tr>
<td>India</td>
<td>Medical Technology Assessment Board (MTAB)</td>
<td>Medium</td>
<td>$118</td>
<td>$793</td>
<td>$456</td>
</tr>
</tbody>
</table>

*Figure 3: List of collected threshold values by country in inflation adjusted 2018 USD prices.*

### 4.2 CEA Approaches

The following table documents the CEA approach of each country based on Figure 2’s list of attributes on cost-effective variables. Attributes consist of both categorical and numeric data, referring to the methods and perspectives taken in the CEA calculations when assessing value of a novel health technology.
<table>
<thead>
<tr>
<th>Country</th>
<th>Life Expectancy</th>
<th>Health Expenditure</th>
<th>Cost Perspective</th>
<th>Outcomes Perspective</th>
<th>Effectiveness Units</th>
<th>Discount Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>79.3</td>
<td>$4,826</td>
<td>Publicly funded health care payer</td>
<td>Direct health affects + Caretakers</td>
<td>QALYs</td>
<td>3%</td>
</tr>
<tr>
<td>UK</td>
<td>81.2</td>
<td>$4,264</td>
<td>Publicly funded health care payer</td>
<td>Direct health affects + Caretakers</td>
<td>QALYs</td>
<td>4%</td>
</tr>
<tr>
<td>US</td>
<td>82.2</td>
<td>$10,209</td>
<td>Widest possible perspective (all payers)</td>
<td>Direct health affects + Caretakers</td>
<td>QALYs</td>
<td>2%</td>
</tr>
<tr>
<td>France</td>
<td>82.4</td>
<td>$4,902</td>
<td>Widest possible perspective (all payers)</td>
<td>Individual</td>
<td>Patient relevant outcomes</td>
<td>4%</td>
</tr>
<tr>
<td>Germany</td>
<td>81</td>
<td>$5,728</td>
<td>Publicly funded health care payer</td>
<td>Individual</td>
<td>Patient relevant outcomes</td>
<td>3%</td>
</tr>
<tr>
<td>Italy</td>
<td>82.7</td>
<td>$3,542</td>
<td>Societal</td>
<td>Societal</td>
<td>QALYs</td>
<td>3%</td>
</tr>
<tr>
<td>Japan</td>
<td>83.7</td>
<td>$4,717</td>
<td>Publicly funded health care payer</td>
<td>Individual</td>
<td>QALYs</td>
<td>2%</td>
</tr>
<tr>
<td>China</td>
<td>76.1</td>
<td>$762</td>
<td>Societal</td>
<td>Individual</td>
<td>QALYs</td>
<td>4%</td>
</tr>
<tr>
<td>Brazil</td>
<td>75</td>
<td>$1,402</td>
<td>Publicly funded health care payer</td>
<td>Individual</td>
<td>QALYs</td>
<td>5%</td>
</tr>
<tr>
<td>Mexico</td>
<td>76.7</td>
<td>$1,034</td>
<td>Publicly funded health care payer</td>
<td>Health system</td>
<td>QALYs</td>
<td>5%</td>
</tr>
<tr>
<td>Thailand</td>
<td>74.9</td>
<td>$216</td>
<td>Society</td>
<td>Individual</td>
<td>QALYs</td>
<td>3%</td>
</tr>
<tr>
<td>South Africa</td>
<td>62.9</td>
<td>$1,090</td>
<td>Third-party payer</td>
<td>Societal</td>
<td>QALYs</td>
<td>5%</td>
</tr>
<tr>
<td>India</td>
<td>68.3</td>
<td>$238</td>
<td>Societal</td>
<td>Societal</td>
<td>QALYs</td>
<td>5%</td>
</tr>
</tbody>
</table>

Figure 4: Approach variables collected for CEA attribute analysis. Choice of comparator and time horizon categories were removed from the dataset as there was minimal variation across selected countries; all referenced the same choice for comparator and same time horizon.
4.3 First Round Regressions

Least squares regression were run for all variables of interest on two principal health outcomes: health expenditures per capita and life expectancy from the country level of observation. The resulting coefficient estimates from multivariate models are shown below.

**Least Squares Regression on Country Life Expectancy**

| Term                          | Estimate  | Std Error | t Ratio | Prob>|t| |
|-------------------------------|-----------|-----------|---------|-----|---|
| Intercept                     | 57.295038 | 2.127987  | 26.92   | 0.0236* |
| WTP                           | -0.000176 | 1.652e-5  | -10.66  | 0.0595 |
| Discounting                   | 54.072004 | 29.64558  | 1.82    | 0.3193 |
| GDPPC                         | 0.5611988 | 0.038698  | 14.50   | 0.0438* |
| Population Size               | -1.073e-9 | 4.9e-10   | -2.19   | 0.2727 |
| All Payers Costs[No]          | 0.9404105 | 0.454469  | 2.07    | 0.2866 |
| Societal Costs[No]            | -0.789594 | 0.336041  | -2.35   | 0.2562 |
| Third Party Costs[No]         | 3.6466703 | 0.487097  | 7.49    | 0.0845 |
| Direct-caretakers Outcomes[No]| 4.0426817 | 0.357874  | 11.30   | 0.0562 |
| Societal Outcomes[No]         | -2.170378 | 0.314694  | -6.90   | 0.0917 |
| Health System Outcomes[No]    | -1.314179 | 0.358184  | -3.67   | 0.1694 |
| QALYs[No]                     | -2.808854 | 0.394725  | -7.12   | 0.0889 |

*Figure 5: All explanatory variables of interest tested for effect on life expectancy. GDPPC represents the per capita gross domestic product of the country. All dummy variables modeled in the analysis took either yes or no values as input, with baseline metrics (‘Variable[No]’) listed above representing the lack of variable presence in the economic analysis.*

A least squares fit of variable country CEA approaches on country mortality rates, described by the life expectancy proxy, showed the above results. The table highlights the GDP per capita of the nation as the only statistically significant variable contributing to the health outcomes of the country at the 5% level of rigor; all other CEA approach variables are not statistically significant with a p-value > 0.05. However, multiple remaining variables hold close proximity to a 0.05 threshold with many p-values ranging between 0.05 and 0.15, with WTP, third party costs, direct & caretaker outcomes, societal outcomes, and QALYs as marginally significant with statistical
significance at the 10% level. This poses near significant variables that should be investigated more closely in stepwise second round ANOVA regressions.

According to the data table, GDPPC serves as the best predictor of life expectancy, given that it was used as a controlling factor for the country’s development status. The predictor thus illustrates that while approach characteristics vary across all countries selected in the analysis, ultimate health outcomes are not dictated by CEA approach factors but rather in the broader context of country development. No clear correlation exists between country CEA approach and life expectancy, signaling that variability among factors in economic analysis calculations do not significantly correlate with a country’s health outcomes.

**Least Squares Regression on Country Health Expenditure**

<table>
<thead>
<tr>
<th>Parameter Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term</td>
</tr>
<tr>
<td>Intercept</td>
</tr>
<tr>
<td>WTP</td>
</tr>
<tr>
<td>Discounting</td>
</tr>
<tr>
<td>GDPPC</td>
</tr>
<tr>
<td>All Payers Costs[No]</td>
</tr>
<tr>
<td>Societal Costs[No]</td>
</tr>
<tr>
<td>Third Party Costs[No]</td>
</tr>
<tr>
<td>Direct-caretakers Outcomes[No]</td>
</tr>
<tr>
<td>Societal Outcomes[No]</td>
</tr>
<tr>
<td>Health System Outcomes[No]</td>
</tr>
<tr>
<td>GAYLs[No]</td>
</tr>
</tbody>
</table>

*Figure 6: All explanatory variables of interest tested for effect on health expenditure*

The least squares fit of CEA approach variables on country health expenditure show minimal correlation with no variables holding statistically significant effect on per capita health expenditures. The explanatory variables used in the analysis include all economic factor approaches in cost-effectiveness while removing country population as the health expenditure outcome accounts for per capita effect. Given no p-value < 0.05, the model results suggest that CEA approach factors do not significantly correlate with health expenditure. Both least square
regression fits serve to validate that heterogeneity indeed exists within country CEA approaches with minimal correlation to health outcomes.

### 4.4 Second Round Regressions

The second analysis conducted on the dataset relied on a multivariate stepwise ANOVA study with a minimum BIC approach set on a forward direction. This stepwise regression model functions as a method for identification of the optimal parameters in each regression, maximizing the likelihood function given in equation 4.

#### Stepwise Regression on Country Life Expectancy

![Table](image)

*Figure 7: A minimum BIC stepwise regression of multivariate character on life expectancy*

The maximization of probability density for parameter fit given by the stepwise analysis show that all CEA approach variables fall within the optimal model. P-values of explanatory variables show distinct differences in strength from least squares regression but all fall within a general range of 0.05 to 0.30. Such resulting values demonstrate that we are unable to form a correlation of CEA approach variables on country life expectancy with 95% confidence. Rather, a lower
confidence level assumed in the model is taken in stepwise regression with greater density distribution fit.

**Stepwise Regression on Country Health Expenditure**

<table>
<thead>
<tr>
<th>SSE</th>
<th>DFE</th>
<th>RMSE</th>
<th>RSquare</th>
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<th>Cp</th>
<th>p</th>
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**Current Estimates**

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<tr>
<th>Parameter</th>
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<th>SS</th>
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<th>&quot;Prob&gt;F&quot;</th>
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*Figure 8: A minimum BIC stepwise regression of multivariate character on health expenditure*

An evaluation of CEA approach on country health expenditures per capita using a stepwise fit model shows statistically significant fit of four particular characters noted above in Figure 8, with p-values < 0.10. According to the forward minimum BIC stepwise regression, testing combinations of parameters resulted in the best correlation fit including the continuous variables WTP, cost and outcomes discount rate, GDPPC and the dummy variable of societal cost inclusion. The stepwise model thus illustrates the correlative effect of specific explanatory variables on country health expenditures, with GDPPC being the only statistically significant input under 95% confidence interval assumptions.
4.5 Discussion

The motivation behind the research question presented in this paper relies on the heterogeneous approach factors in a cost-effectiveness economic analysis of each country. Through literature reviews and pulling metrics from datasets, we were able to run multivariate regressional analyses testing correlative strength of CEA approach characteristics. By modeling correlations of country economic approach variables with health related outcomes of interest, the strength of each variable’s effect on country health outcomes is measured. It was hypothesized that CEA approach variability would demonstrate correlation to health outcomes in line with different economic perspectives in an HTA corresponding to different health outcomes. To control for tests of interest with CEA approach and health outcome variables in addition to country-specific economic character, univariate fit lines constructed for WTP on outcome variables demonstrated valid inclusion of a country’s threshold value in the CEA approach regression analysis.

Results from the first round multivariate regression tests show minimal variable correlation with outcomes of interest. Using a p-value threshold of 0.05, country GDP per capita is the only statistically significant value to correlate with life expectancy. The basis behind the correlation can be explained through country development status where a higher GDPPC signifies a more overall developed country, including its healthcare system thus correlating with quality of healthcare given by the life expectancy proxy. A similar model applied to health expenditure shows minimal correlation, with no variables in the analysis showing statistically significant p-values. These results from first round suggest that while CEA approach variables are heterogenous across countries, they hold no significant effect on influencing country health outcomes.
A second round multivariate regression using a stepwise fitting method maximized the likelihood function, $L(\beta)$, and formed correlative fits based on optimization models. The stepwise fit against country life expectancy registered all CEA approach variables in the model, fitting all economic perspective variation to explain quality of healthcare. This direct contrast to the first round regression in which only GDPPC was significantly correlated with life expectancy demonstrate the need for further statistical examinations and methods to pinpoint effect. Similarly, a contrast was observed to first round regressions in a fit on health expenditure in which key variables held statistical significance whereas no correlation was observed in the least squares model.

Nonetheless, as the stepwise regression holds a lower confidence interval of significance and includes variables with $p$-values of lower strength than the least squares multivariate fit, the results of first round regression hold greater precision and acts as a more robust analysis. Thus we infer from our data reports that while stepwise regression contributes a separate perspective in a cost-effectiveness approach model, the least squares models holds greater probability of explanation in which GDPPC correlates with country life expectancy and no approach variation correlate with country health expenditure.
4.6 Limitations

The study faces limitations in scope due to data-collection constraints. As WTP threshold metrics are non-disclosed points kept within government records, it is difficult to pinpoint precision behind the values used in the analysis. A general scope of public literature is not as accurate as primary research from source officials, requiring broader research methods and further direct investigation with government data reports. Additionally, similar issues arose in data collection of cost-effectiveness approach variables as report information is not clearly delineated across country government reports. The variables used in the analysis consisted of all heterogenous approach variations despite some similarities across country economic approaches. Other variables to control for country-specific characteristics in affecting outcomes of interest may be required as the usage of GDPPC and population size are only nominally correlative with health expenditure and life expectancy.
5 Summary and Recommendations

5.1 Summary

Through an investigation of country specific cost-effective approaches, the study aimed to derive correlations between variability across country CEA approach attributes and health outcomes of interest. A least squares regression supported with a stepwise multivariate method showed that while heterogeneity exists among a government’s HTA economic analysis, CEA approach differences do not significantly correlate directly with country health expenditure nor quality of care delivered. Additionally, the study was able to successfully characterize country WTP thresholds and correlate the threshold values, both implicit and explicit, with outcomes of interest. It was determined that both these threshold values exist for each country and such values held relationships with country health outcomes. Overall, despite proper characterization of country WTP and CEA approach attributes across a country’s HTA or Health Economics & Outcomes Research (HEOR) body, there are no statistically significant effects of a variable in CEA approach on country related health outcomes.
5.2 Recommendations for Further Studies

In further investigation of HTA economic approach, two primary recommendations are offered:

First, it is recommended that economic approach characteristics are broken down further across countries to capture greater perspective variation. While the current study captured various categorical and continuous variables across government systems, breakdown of economic analysis approaches can be categorized into greater segments. Through assessing greater variability across country methods, one is able to add additional explanatory effect into a regression analysis and capture greater detail in country differences to CEA approach.

Second, emphasis must be placed on this study as a correlative analysis and not causal. It is suggested that in order to study causal links of a CEA approach on health outcomes of interest, one must track cross-sectional time points by tracking data over multiple years to account for how a country’s change in CEA approach affects its respective health system. More data points across a greater number of countries may be utilized in a future analysis to expand the explanatory strength of the regression tests. Through incorporating further statistical models on both a greater n and a causal analysis, researchers may be able to derive optimal CEA approach links to health outcomes.
References


11. OECD (2018), Health spending (indicator).


