F1: EXTENDING COST-EFFECTIVENESS ANALYSIS WITH PARTIAL OPTIMIZATION MODELLING AND FISCAL MODELLING IN VACCINE VALUE ASSESSMENTS

ISPOR Forum of the

Economic Value Assessment of Vaccines Designed to Prevent Infectious Disease Task Force

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ECONOMIC MODELS IN VACCINE VALUE ASSESSMENTS

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ECONOMIC EVALUATION OF VACCINES DESIGNED TO PREVENT INFECTIOUS DISEASE TASK FORCE

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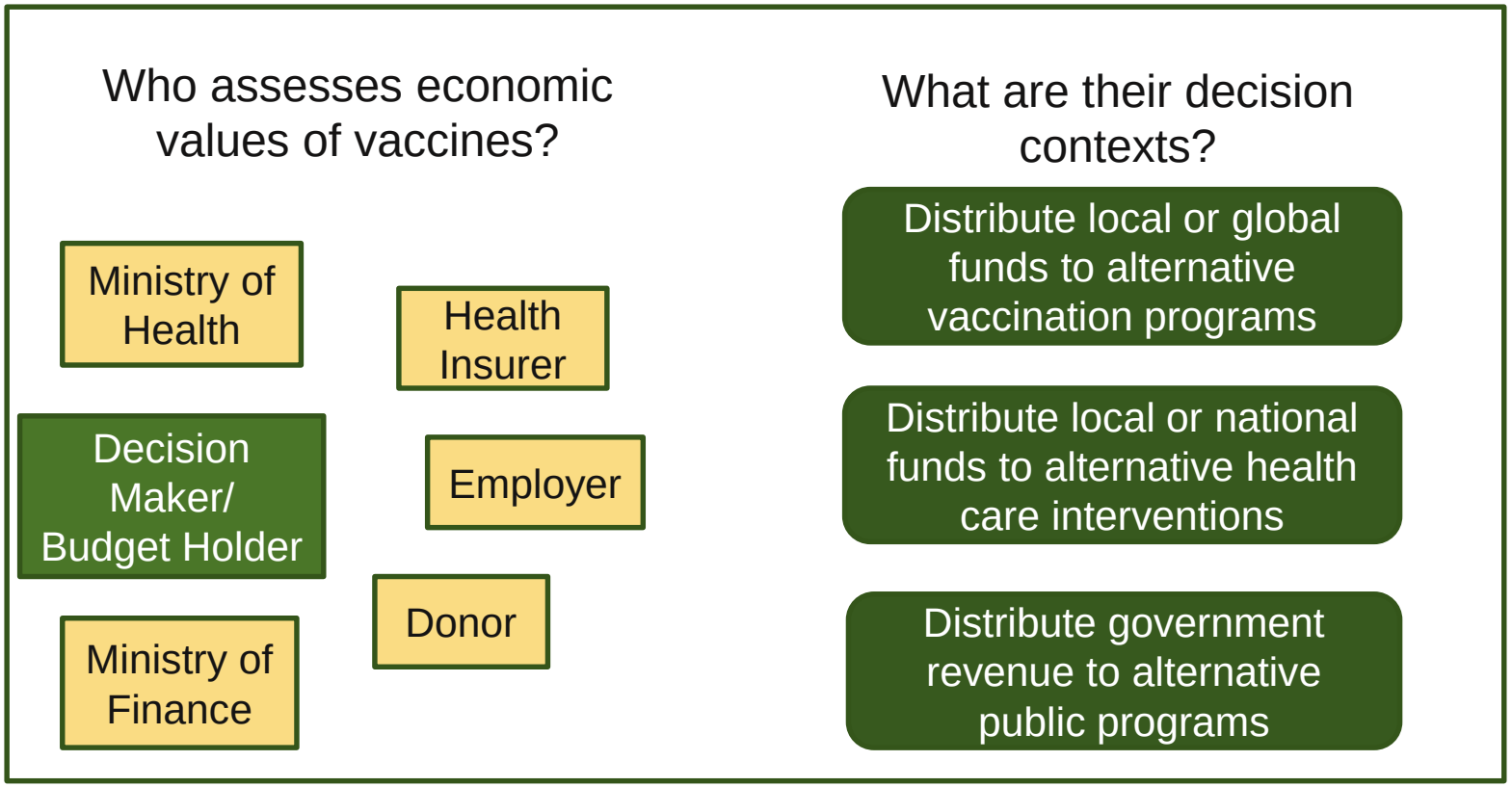
Vaccine decision process

- Overall approval for marketing authorization by regulatory bodies based on efficacy, safety and quality of the studies conducted (e.g. FDA (CBER), EMA)
- Recommendation about the use and financing of the vaccines for infectious diseases is country specific
  - Submit dossier to NITAGs (e.g. ACIP in the US; JCVI in UK)
    - population needs assessment (disease burden, therapeutic options)
    - effectiveness
    - specific at risk groups
    - acceptability
    - urgency
  - Based on NITAG-advice and proposed vaccine price government agencies determine to recommend the vaccine to be included in their prevention program (e.g. CDC, MOH) and identify ways of funding (reimbursement, tender, mixed, co-payment) (e.g. private or public health insurance, MOH, MOF, GAVI)

Key Decision Contexts in the Vaccine Process



Economic Evaluation of Vaccines

Overall Objective:
Maximize socially agreed benefits within constraints

Specific tools & methods of evaluation

1. Maximizing health using cost-effectiveness analysis and threshold values representing opportunity costs

2. Maximize health with budget and other constraints using optimization modelling

3. Estimate the government ROI using fiscal modelling

Recommendations for Economic Evaluations of Vaccines

- Decision problem
- Perspective
- Model structure
- Time horizon
- Comparators
- Data requirements and sources
- Outcome measures
- Discounting
- Analysis and interpreting results
- Analysis of uncertainty
- Validation
- Transparency
- Software
- Reporting

Decision Problem

Recommendations	CEA	OM	FM
Decision problem including identification of decision makers and decisions to be made should be clearly stated and guide the rest of the analysis	✓	✓	✓
Present decision problem as an estimate of net health benefits or incremental cost per unit health gain with a vaccination program compared with a threshold value	✓		
Present decision problem as optimization exercise with constraints with different interventions available including vaccination to meet a target health outcome		✓	
Present decision problem as estimate of return on investment measured as the net present value of tax income of population cohort eligible for vaccination			✓

Perspective

Recommendations	CEA	OM	FM
Perspective taken should reflect needs of decision maker and should be clearly stated	✓	✓	✓
At least two perspectives should be included: Payer perspective Broader perspective in direct effects and positive and negative externalities both inside and outside the health program; listing of qualitative and quantitative outcomes	✓		
Perspective of budget holder with budget and other relevant constraints presented		✓	
Perspective of government for distribution of tax revenues among public programs; include impact of money spent on health on other public programs			✓

Model Structure

Recommendations	CEA	OM	FM
To estimate the impact of vaccination programs and other comparators on population or cohort health outcomes a dynamic transmission process is preferred	✓	✓	✓
A static epidemic model can be used where indirect effects are minimal/unknown or computationally difficult	✓	✓	✓
A population-based or cohort-based CE model estimating either cumulative or lifetime costs and health outcomes	✓		
Defined objective function for a population under study with the desired health outcome influenced by decision variables and with specific constraints including budget		✓	
Cohort model that estimates changes in governmental money transfer by age and gender			✓

Time Horizon

Recommendations	CEA	OM	FM
If a population CEA modeling approach is used, time horizon long enough for cumulative population net health benefits or ICER to be stable	✓		
If a cohort modeling approach is used the time horizon should be long enough to capture any long-term effects; if there are mortality effects, a lifetime time horizon is needed	✓		✓
Time horizon limited to 1 to 5 years which is generally important for budget impact		✓	

Comparators

Recommendation	CEA	OM	FM
Comparisons should include a scenario without the vaccination program	✓	✓	✓
Comparisons should include other prevention interventions for the same disease if available	✓	✓	✓
Comparisons should include with and without using an optimization process		✓	
Comparisons of population subgroups should be considered	✓	✓	✓
Comparisons of vaccination programs for different diseases should be included if part of the decision problem	✓	✓	✓

Data Requirements and Sources

Recommendations	CEA	OM	FM
A comprehensive and transparent approach should be used to select the inputs from best available evidence	✓	✓	✓
Vaccine coverage rates, efficacy, waning estimates and infectious disease externalities should be based on evidence and/or scientific plausibility	✓	✓	✓
Resource use, costs and health outcomes should be based on published studies and/or prevention or treatment strategies	✓	✓	✓
Constraints should be determined by budget holders based on local conditions		✓	
Government cost transfers by age based on health outcomes should be assessed using country-specific ministry data sources			✓

Outcome Measures

Recommendations	CEA	OM	FM
Changes in number of cases, hospitalizations, mortality, medical visits	✓	✓	✓
Changes in QALYs or DALYs or life years (LY)	✓	✓	
Changes in health care costs	✓	✓	✓
Changes in government revenue and transfer costs			✓
Incremental cost per QALY or DALY or LY and relevant threshold value	✓		
League table for ICERS and budget constraint	✓		
Changes in a broader set of outcomes – productivity, educational attainment, household financial risk, antibiotic resistance, disease eradication	✓		✓
Ranking of interventions to optimize health outcomes		✓	
Fiscal prioritization based on net present value, return on investment, internal rate of return to the government			✓

Discounting

Recommendations	CEA	OM	FM
Discount rates should be consistent with those used for other health programs unless different rates can be justified for the decision context	✓	✓	✓
Discount rates for benefits should be lower than for costs only if CE threshold is expected to increase over time	✓		
Model should allow user to change discount rates	✓	✓	✓
Sensitivity analyses are needed for alternative discount rates (including no discounting and differential discounting)	✓	✓	✓
Additional research on discounting is needed	✓	✓	✓

Analysis and Interpreting Results

Recommendations	CEA	OM	FM
Compute incremental cost per QALY/DALY ratios for new vaccination program using decision-analytic models and assess against a threshold value; threshold value should reflect opportunity cost or willingness-to-pay for intervention	✓		
Linear programming with continuous variables using the simplex method where feasible; otherwise use non-linear methods and integer variables; results provide ranking of interventions		✓	
Financial calculations to estimate net present value, and internal rate of return on investment in the vaccine program for a government; results can be compared with other health and non-health public programs			✓

Analysis of Uncertainty

Recommendations	CEA	OM	FM
Scenario analyses with epidemic models using different combinations of assumptions and input values to assess variability of disease outcomes	✓	✓	✓
Extensive one-way sensitivity analyses and multi-way scenario analyses using credible ranges for all input parameters	✓		✓
For CEAs using a population approach show the impact of assumed time period on the cumulative cost-effectiveness ratio	✓		
Sensitivity analyses for population subgroups are desirable	✓		✓
Carefully evaluate the sensitivity analyses for critical variables produced by standard OM software packages; in addition examine program results for plausibility		✓	

Validation

Recommendations	CEA	OM	FM
Face validity for model structure, assumptions, input parameter values by experts in jurisdictions of interest	✓	✓	✓
Internal validity of calculations by quality-checking by a programmer not involved in performing the analysis	✓	✓	✓
Input parameters for the epidemic model calibrated to ensure that model disease outcomes match those in the dataset used to generate input values	✓	✓	✓
Selected outcomes of the model should be compared to those observed before implementation of the vaccination program in a data set other than that used to develop input values	✓		✓
Dual model development used to assess outcomes		✓	

Transparency

Recommendations	CEA	OM	FM
Present a clear overview and flow diagram in the main text for all models; provide all model equations, assumptions and input parameters, including ranges and distributions, in a technical appendix	✓	✓	✓
Simplify the model structure and assumptions as much as possible to increase transparency	✓	✓	✓

Software

Recommendations	CEA	OM	FM
Software that is readily accessible such as MS Excel® should be used to create a linked epidemic and economic model to estimate the impact of the vaccination program on cost-effectiveness estimates unless the run time is too long; if the run time is too long use Matlab, R or C/C++; all programs should be extensively documented	✓	✓	✓
Software for solving optimization programs should be selected based on complexity of problem to be analyzed, budget limitations, frequency of use, and technical support for the software		✓	
Model code should be made available to decision makers	✓	✓	✓

Reporting

Recommendations	CEA	OM	FM
Follow CHEERS reporting guidelines with goal that sufficient information is provided about the model structure, assumptions and input parameter values so that a researcher could replicate the results	✓	✓	✓

Summary

- The three types of economic evaluation presented provide useful information for different decision contexts
- CEA should be estimated for all decision contexts but discount rates and threshold values are likely to be different in different jurisdictions
- Extended CEA including a broader set of outcomes such as impact on productivity, educational attainment, family financial risk, may also provide useful information about value; in this case a listing of outcomes is preferred rather than a ratio
- Optimization modeling should also be used when the goal is to maximize health of a population subject to budget and other feasibility constraints
- Fiscal modeling should also be used when determining the value of using government funds to pay for the vaccination program.
- Recommendations are provided for each type of economic evaluation to ensure that each is performed to a common standard using well accepted methods for model structure, assumptions and input parameter value estimation
- Other methods (e.g. cost-benefit analysis or multi-criteria decision analysis) should be considered

Discussion Topics

- How should model results be applied in the real world?
- Do population cost-effectiveness models make sense for treatments as well as vaccination programs?
- Should we discount the results using the same rates for costs and benefits for all three methods? What about variable discounting?
- What is the preferred method for determining a threshold value for cost-effectiveness?
- When might static epidemic models or empirical data be more appropriate than dynamic epidemic models for estimating cases of disease avoided for all three methods?
- If we want to include a broader set of outcomes for any of the methods which of these can be reliably estimated?
- Should a broader set of outcomes be estimated for other types of healthcare interventions as well?

Further Comments

THANK YOU!

- Sign up as Review Group Member
- Join ISPOR Special Interest Groups
- Need ISPOR membership number
- Business card to Theresa or email
- ttesoro@ispor.org