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Pragmatic application of economic and cost-effectiveness analysis: Examples from genomic medicine implementation projects

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Geisinger Health System

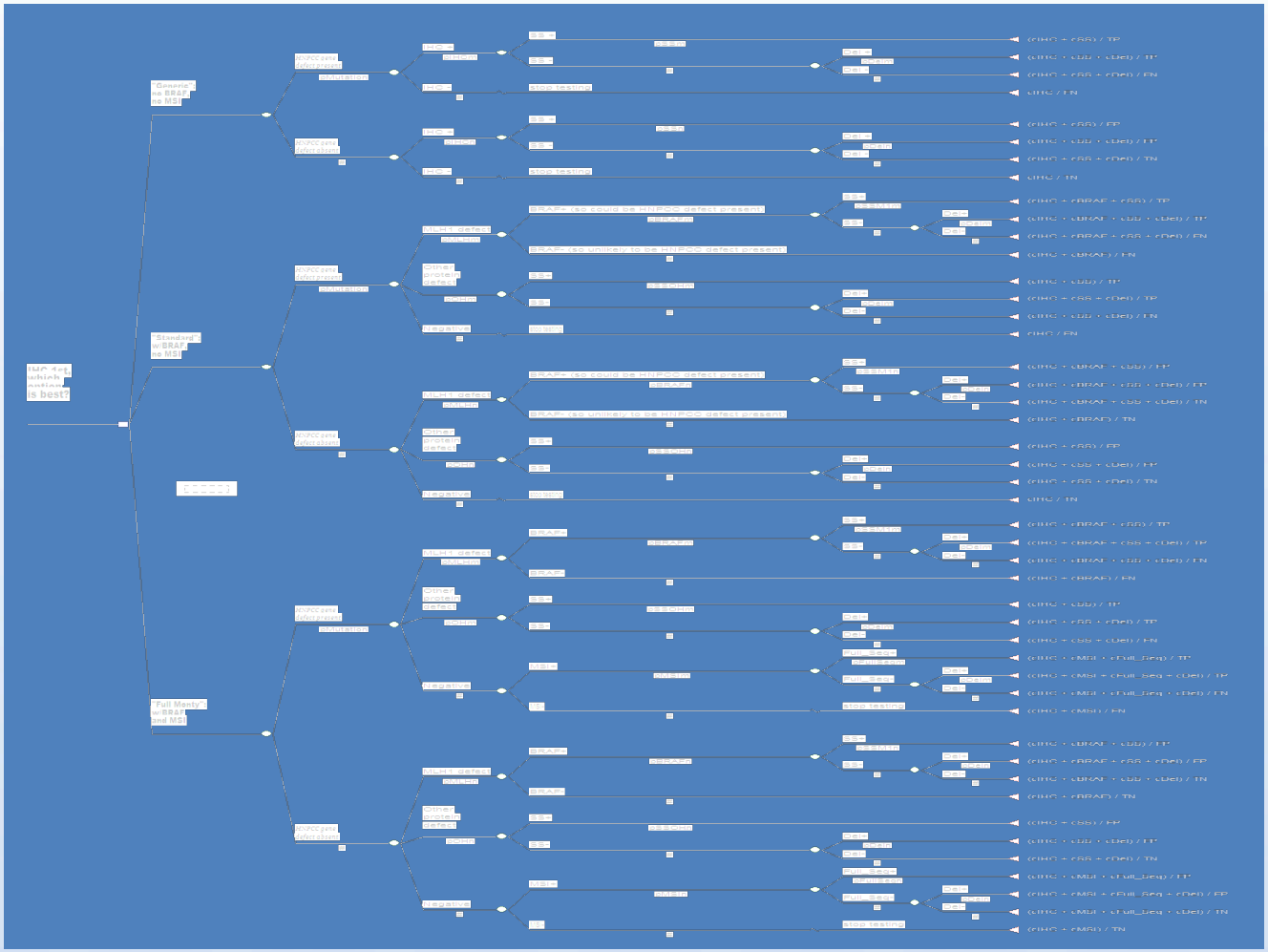
Importance of Perspective

- Most economic analyses are performed from the societal perspective
- This perspective does not translate well to decision making at the health system level
- Adapt the tools for use in different settings

4 Examples

- The health system perspective
  - Universal Lynch syndrome screening
- Hypothetical analysis to facilitate future decision making
  - *IL28B* testing to inform use of protease inhibitor in Hepatitis C viral genotypes 2 and 3
- Patient perspective
  - Pharmacogenomic testing to inform warfarin dosing
- Lowering Barriers to Economic Modeling
  - Generic Model Development and Testing

Universal Lynch syndrome screening



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Comparison of Models

100 CRC cases protocol	total cost to test	incremental increase in cost	# LS cases found	increase in cases found versus protocol above	average cost per case detected	cost to find additional case of LS
IHC with *BRAF* and Methylation	$35,203	--	3.28	--	$10,730	--
IHC with Methylation (no *BRAF*)	$37,369	$2,166	3.29	0.0076	$11,363	285,807
IHC with *BRAF* (no Methylation)	$38,338	$969	3.34	0.0512	$11,481	$19,056
IHC straight to Sequencing	$44,652	$6,313	3.35	0.0039	$13,355	$1,604,113

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IL28B and Protease inhibitors in HCV

- Routinely used in HCV viral genotype 1
  - Economic analyses support cost-effectiveness
- HCV viral genotypes 2 and 3 more responsive to therapy
  - Standard therapy is dual therapy not including PI
- Patient *IL28B* genotype predicts response to treatment in all HCV viral genotypes
  - Very limited evidence in HCV genotypes 2 and 3
- Questions:
  - Could *IL28B* genotyping be used to select candidates for use of triple therapy?
  - How much improvement in sustained viral response is needed to cross a threshold of cost effectiveness?

Results

Ref.	SOC duration, weeks	HCV cohort	Telaprevir recipients	Therapy cost, USD	Cost-effectiveness threshold, SVR rate		Threshold increase from SOC	
					cohort A	cohort B	cohort A	cohort B
[7]	24	Treatment Arm 1	All SNPs	46,294.49	≥94.85	≥97.67	7.91	11.11
[7]	24	Treatment Arm 2	All SNPs	44,334.71	≥80.92	≥83.70	9.06	12.80
[7]	24	Treatment Arm 3	TG/GG (rs8099917) or TT (rs12979860)	27,613.03	≥83.85	≥84.74	2.63	3.72
[14]	12	Treatment Arm 4a	TT (rs12979860)	14,050.81	≥61.71	≥62.02	1.66	2.17
[14]	24	Treatment Arm 5a	TT (rs12979860)	24,529.28	≥79.60	≥80.16	1.40	2.11
[14]	12	Treatment Arm 4b	CT or TT (rs12979860)	24,881.22	≥64.64	≥66.11	6.49	8.91
[14]	24	Treatment Arm 5b	CT or TT (rs12979860)	37,056.93	≥82.82	≥84.74	5.50	7.95

Administering triple therapy to patients with resistant *IL28B* genotype requires an improvement in SVR of slightly greater than 2% to cross cost-effectiveness threshold. Treating all patients requires an improvement of over 11%.

PGX informed Warfarin Dosing
Patient Perspective

- Used prospective trial data from Intermountain Healthcare
- Use a policy model approach to assess cost-effectiveness
- Testing vs. no testing arms essentially equivalent
- Prospective trial data showed that tested patients required 2-3 fewer INRs
- Patient-centered perspective would strongly favor testing based on reduced disruption of patient/family life

Generic Modeling

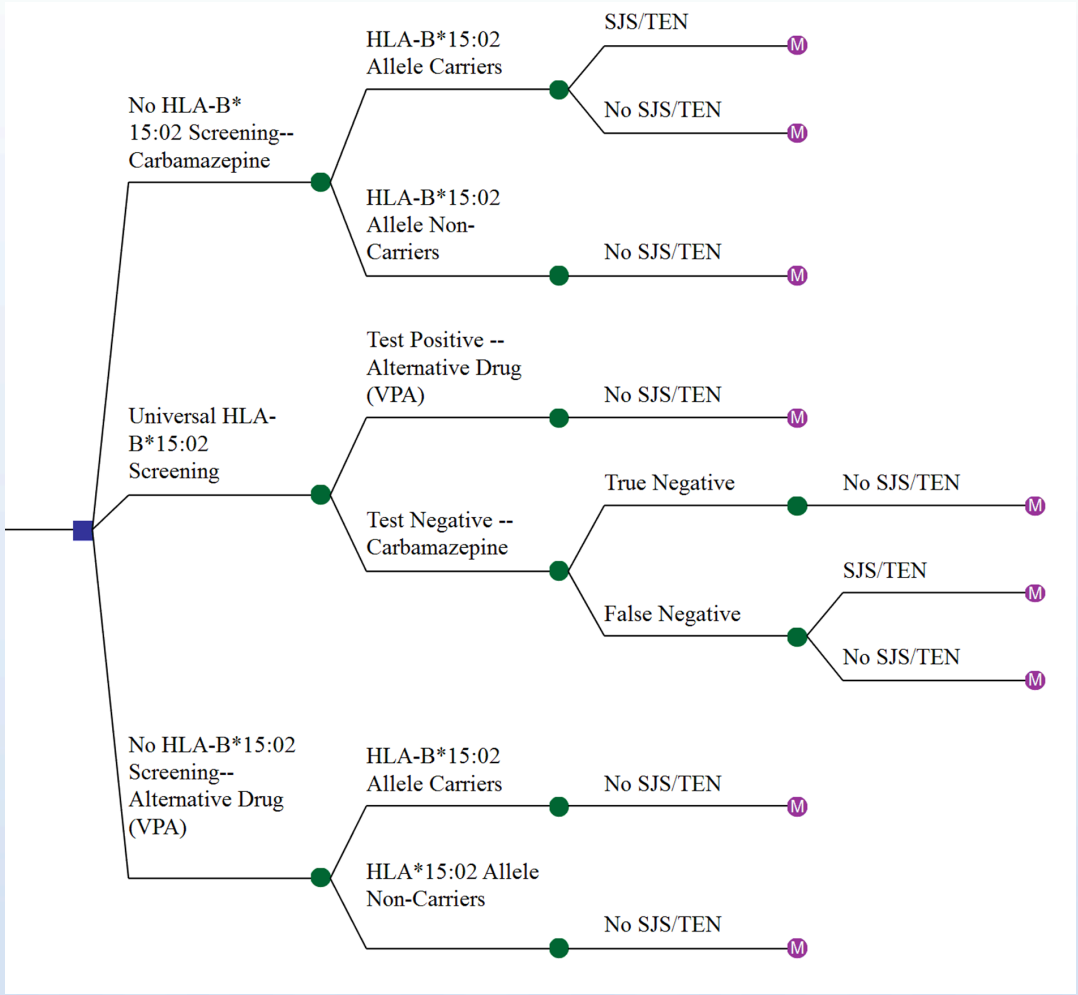
- Development of economic models requires significant expertise and resources
- Most models are created for a specific perspective, with customized inputs limiting reuse
- Could a generic model be created to allow stakeholders to enter relevant key parameters and generate results relevant to decision-making?
  - How does the model perform against gold-standard modeling?

Generic Modeling

- Use case: HLA-B*15:02 testing prior to use of carbamazepine to reduce the risk of SCAR
- Rationale:
  - Medically significant issue
  - Testing implemented in some settings
  - Differences in allele frequencies in different populations, cost and practice patterns leading to variations in cost-effectiveness
  - Existing gold-standard model (Thailand)
- GENOMIC MEDICINE IMPLEMENTATION: THE PERSONALIZED MEDICINE PROGRAM U Florida U01 HG007269 Subaward FDSP00010620 (Economic modeling project for pharmacogenomics prevention of Stevens-Johnson syndrome).

Conceptual Framework and Decision Tree

- Overview
- Model Diagrams
- Input Tables
- Results
- ICER
- CE Plane
- CEAC



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Inputs

Required Input Variables	Input Value
Prevalence	
Prevalence of HLA-B*1502 allele (carrier status) in study population, please note that this is not allele frequency, it is twice of allele frequency	0.208
Cost	
Selected Currency	-
Base year	-
Cost of HLA-B*1502 screening test (includes all costs related to screening test)	1000000
Cost of SJS/TEN treatment (1 year): Annual direct medical cost of CBZ-induced SJS/TEN	5026302
Cost of follow up with SJS/TEN sequelae: Annual direct medical cost of sequelae (base-case value assume ~ dry eye syndrome)	3540000
Cost of disease treatment	
Annual direct medical cost of epilepsy treatment with CBZ	1064909
Annual direct medical cost of epilepsy treatment with VPA	2457384
Ceiling ratio and threshold value	
Maximum acceptable ceiling value for use in the maximum acceptable ceiling ratio (in selected currency/QALY gained)	1,500,000,000
Cost-effectiveness threshold value (in selected currency/QALY gained)	150,000,000

Optional Input Variables	Input value
Probabilities	
Probability of CBZ-induced SJS/TEN in HLA-B*1502 +ve patient	0.015
Utility	
Utility score of patient with epilepsy	0.85
Utility score of patient with SJS/TEN sequelae	0.68
Treatment Duration	
Treatment duration of epilepsy	30
Discount rate	
Discount rate for costs	0.03
Discount rate for outcomes	0.03

Generic Model Inputs

Model variables and assumptions were identified that would considered unlikely to be readily available or generalizable and were thoroughly reviewed by the model development team with decisions made to eliminate or retain them in the generic model. Variables and assumptions retained requiring an input value were assigned to one of three categories.

1) *Input value only* based on the need for a user-specified value (e.g., all medical cost variables, population allele prevalence for pharmacogenomics test);

2) *Default value only* supported by very strong available evidence (e.g., test sensitivity and specificity); the unlikely availability of information due to very limited evidence (e.g., health state utility of a very rare disease), or otherwise required by the model to meet certain logic requirements (e.g., health state utility value is constrained by its relationship to other state values).

3) *Default value with an input option* to allow the generic model user to select either approach to address the need for information for an input value which is not readily available by providing a default based on available evidence.

Results

	Thailand Model			Generic Model with Thailand Inputs		
Result	Baseline Current practice	Option 1 HLA-B*1502 screening	Option 2 No HLA-B*1502 screening	Baseline Current practice	Option 1 HLA-B*1502 screening	Option 2 No HLA-B*1502 screening
Cost	17,915	26,006	61,104	16424.56	24752.01	61211.84
QALYs	25.18	25.21	25.22	13.81	13.83	13.83
Incremental cost	-	8,091	43,190	-	8327.45	44787.27
Incremental QALYs	-	0.032	0.038	-	0.017	0.017
ICER	-	250,896	1,140,944	-	493,483	2,651,431
	Malaysia Model			**Generic Model with Malaysia Inputs**		
Result	Baseline Current practice	Option 1 HLA-B*1502 screening	Option 2 No HLA-B*1502 screening	Baseline Current practice	Option 1 HLA-B*1502 screening	Option 2 No HLA-B*1502 screening
Cost	31,643	34,555	48,645	19881.46	20132.49	20191.91
QALYs gained	22.44	22.41	21.18	13.82	13.83	13.83
Incremental cost	-	2,912	17,002	-	251.03	310.45
Incremental QALYs	-	-0.0255	-0.2622	-	0.006	0.006
ICER	-	Dominated	Dominated	-	42,471	52,473
	Singapore Model			**Generic Model with Singapore Inputs**		
Result	Baseline Current practice	Option 1 HLA-B*1502 screening	Option 2 No HLA-B*1502 screening	Baseline Current practice	Option 1 HLA-B*1502 screening	Option 2 No HLA-B*1502 screening
Cost	4,110	4,680	6,780	1203.21	1668.33	3016.08
QALYs	18.846	18.865	18.865	17.88	17.92	17.92
Incremental cost	-	570	2,100	-	465.11	1812.87
Incremental QALYs	-	0.019	-	-	0.048	0.048
ICER	-	29,750	-	-	9,717	37,834

Lessons Learned

- A generic pharmacogenomic cost-effectiveness model enabling use of local input values is feasible and can offer an efficient and timely value-based decisionmaking tool.
- Implementing this approach demonstrates that cost-effectiveness analyses can be rapidly performed without extensive training in decision modeling to provide useful evidence for decisionmaking and facilitate understanding about what conditions can meet cost-effectiveness thresholds.

Conclusion

- Defining perspective is critically important
- Economic analysis tools can be used pragmatically to rationalize decision-making
- Tough to publish!!

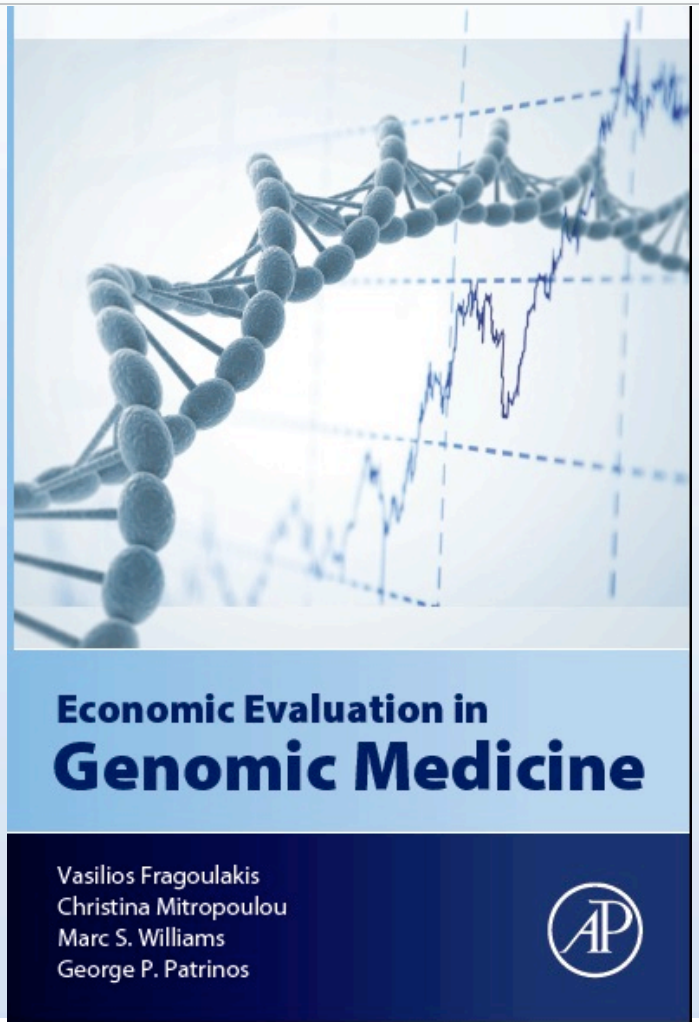
References

Gudgeon JM, Williams JL, Burt RW, Samowitz WS, Snow GL, Williams MS. Lynch Syndrome Screening Implementation: Business Analysis by a Healthcare System. Am J Manag Care 17:e288-300, 2011.

Bock JA, Fairley KJ, Smith RE, Maeng DD, Pitcavage JM, Inverso NA, Williams MS. Cost-Effectiveness of IL28B Genotype-Guided Protease Inhibitor Triple Therapy versus Standard of Care Treatment in Patients with Hepatitis C Genotypes 2 or 3 Infection. Public Health Genomics 2014;17(5-6):306-19.

Meckley LM, Gudgeon JM, Anderson JL, Williams MS, Veenstra DL. A Policy model to evaluate the benefits, risks and costs of Warfarin pharmacogenomic testing. Pharmacoeconomics 28(1):61-74, 2010.

Shameless Plug



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