The Benefit-Cost Analysis Adjustment Through the Generalized Risk-Adjustment Cost-Effectiveness (GRACE) Framework: An Application on Acute Ischemic Stroke Patients

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Introduction

In 2018, the Johns Hopkins Hospital adapted advanced AI tools (RapidAI) to improve processes of acute ischemic stroke diagnostics and logistics, aiming to improve the proportion of "good outcomes." However, with the traditional cost-effectiveness analysis (CEA) and a willingness-to-pay (WTP) per quality-adjusted life year (QALY) combo from previous literature (Gyrd-Hansen, 2005), we saw limited improvements with concerns underestimating interventional contributions without adjusting heterogeneous features and disability.

Hence, our research project aims to reevaluate the value of AI interventions with the Generalized Risk-Adjusted Cost-Effectiveness (GRACE) framework proposed by Lakdawalla and Phelps (2019, 2020, 2021, 2022, 2023), and place additional emphasis on the disability adjustments through a widely-adapted standard for stroke severity measurement—Modified Rankin Scale (mRS).

Data and Method

Dataset:

Deidentified acute ischemic stroke (*excl.* hemorrhage) admissions at AED
Control Group (2014-2017): 206 Cases , Treatment Group (2019): 45 Cases

Methods and Models:

(1) First-order Markov Model with a 10-year horizon for stroke survivors
(2) Transitional matrix by GRG Nonlinear for health state changes
(3) Repeated Latent Response Matching (NN = 3) through Ordered Probit
(4) Set up GRACE-based multipliers for different age and mRS states
(5) Adapt traditional WTP-QALY combo to consider interventional benefits
(6) Apply a 5% discount rate to calculate the net present value
(7) Link values from Step (3) to caregiver's burden with Federal Median Wage
(8) Compare CEA and GRACE differences and projected loss from Step (7)

Rationale

Based on the enriched literature on dynamic health state through mRS and constant survival analyses setting 5 and 10 years as time horizons, our project targets finding the post-intervention state transitions with minimum distance to given survival rates in conditions to an upper limit of population outcomes without re-hospitalization through the Generalized Reduced Gradient (GRG) Nonlinear engine, and repeated matching patterns with the strictly increasing age and state-based incubated status.

Additionally, the mRS-based health state changes are cardinally represented in previous experimental designs (Hong & Saver, 2009), which we can adapt from the WTP-QALY combo after setting a baseline standard where CEA and GRACE show nearly identical results. Finally, the validation projecting absenteeism of caregivers based on excessive mental stress (based on the survivor's mRS) to different baseline standards shows potential justification given the hypothesis that "GRACE initializes externalities of the disability status."

(1)

$$y_i^\star = \mathbf{X_i'}\beta + \gamma \cdot T_i + \epsilon_i;\ \epsilon_i \sim N(0,1),\ \forall i = 1, \cdots, 251 \tag{1}$$

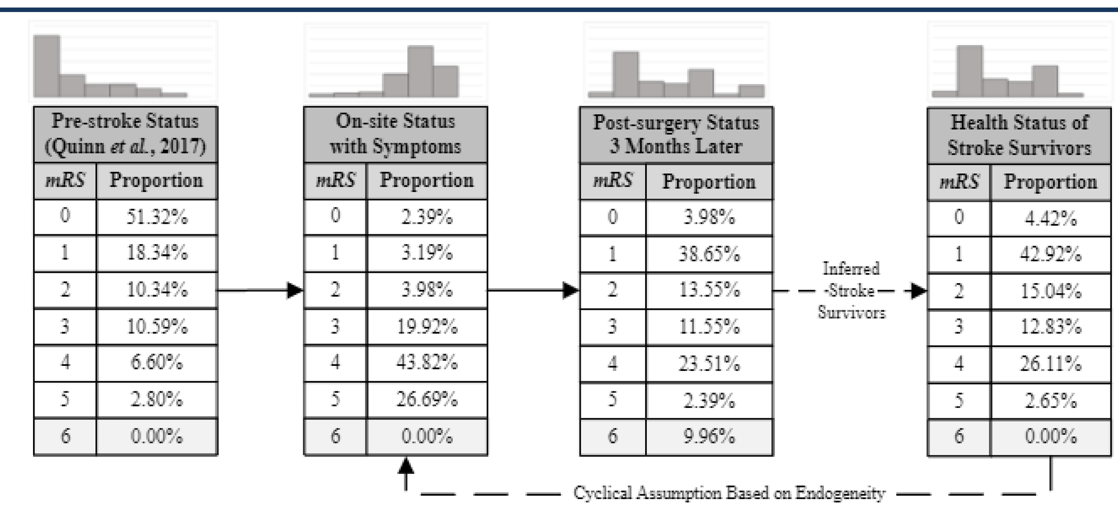
$$\begin{cases} y_i = 0 \text{ (Not Disabled)} & \text{if } y_i^\star \leq \alpha_1 \\ \dots & \\ y_i = 5 \text{ (Severely Disabled/Bedridden)} & \text{if } \alpha_5 < y_i^\star \leq \alpha_6 \\ y_i = 6 \text{ (Deceased)} & \text{if } \alpha_6 < y_i^\star \end{cases} \tag{2}$$

$$\begin{cases} P(y_i = 0|\mathbf{X}) = P(y_i^\star \leq \alpha_1) & = \Phi(\alpha_1 - \mathbf{X_i}'\beta) \\ \dots & \\ P(y_i = 5|\mathbf{X}) = P(\alpha_5 < y_i^\star \leq \alpha_6) & = \Phi(\alpha_6 - \mathbf{X_i}'\beta) - \Phi(\alpha_5 - \mathbf{X_i}'\beta) \\ P(y_i = 6|\mathbf{X}) = P(\alpha_6 < y_i^\star) & = 1 - \Phi(\alpha_6 - \mathbf{X_i}'\beta) \end{cases} \tag{3}$$

We have y representing the mRS we observed 3 months after the surgery, $\mathbf{X}$ as a matrix of characteristics (age, gender, common comorbidities, and mRS at arrival), and T as the binary response of AI intervention. Based on non-randomized selection, I adapted latent response matching with linear probability (Rubin & Thomas, 1992) to ease heterogeneity.

By directly running the ordered probit model, AI intervention shows an average 0.64 to 0.72-unit improvement of mRS after controlling individual-based binary responses, which represents the positive tendency in a reduced-form solution.

(2)



$$\mathbf{b_t} = 0.055\mathbf{F}(\mathbf{M_h}\mathbf{b_{t-1}}) + 0.945\mathbf{M_g}\mathbf{b_{t-1}} \tag{4}$$

$\mathbf{b_t}$: Vector of different health states of an individual stroke patient
$\mathbf{M_g}$: Transitional matrix of health states across periods—See Step (3)
$\mathbf{M_h}$: Transitional matrix of exacerbation before re-hospitalization based on our sampled distribution with non-superior results
$\mathbf{F}(\cdot)$: The intervention-matching combo for each of the given states, applied for re-hospitalized cases

I take **5.5%** as the probability for any stroke survivor to be re-hospitalized annually based on the collective facts of 5-year and 10-year results, which fits in a dynamic structure of stroke patients' health state changes.

Summary Statistics

	Treatment Group	Control Group	Difference Level
Unique Patient Count (N)	45	206	
Modified Rankin Scale (mRS) Right Before Intervention			
$mRS = 0$	0 (0.0%)	6 (2.9%)	-
$mRS = 1$	0 (0.0%)	8 (3.9%)	-
$mRS = 2$	2 (4.4%)	8 (3.9%)	-
$mRS = 3$	4 (8.9%)	46 (22.4%)	**
$mRS = 4$	21 (46.7%)	89 (43.4%)	-
$mRS = 5$	18 (40.0%)	49 (23.9%)	**
Modified Rankin Scale (mRS) 3 Months After Intervention			
$mRS = 0$	1 (2.2%)	9 (4.4%)	-
$mRS = 1$	3 (6.7%)	15 (7.3%)	-
$mRS = 2$	8 (17.8%)	31 (15.1%)	-
$mRS = 3$	13 (28.9%)	54 (26.3%)	-
$mRS = 4$	8 (17.8%)	43 (21.0%)	-
$mRS = 5$	5 (11.1%)	25 (12.2%)	-
$mRS = 6$ (Expired)	7 (15.6%)	29 (14.1%)	-
Age at Intervention			
Mean	68	65	-
1[st] Quartile	57	58	
Median	71	67	
3[rd] Quartile	80	74	
Gender			
Male	15	84	-
	33.3%	40.8%	
Female	30	122	-
	66.7%	59.2%	

	Treatment Group	Control Group	Difference Level
Unique Patient Count (N)	45	206	
Race			
White	26	96	-
	57.8%	46.6%	
Black	13	77	-
	28.9%	37.4%	
Comorbidities (CC)			
Hypertension	44	145	***
	97.8%	70.4%	
Cardiac Stents	5	14	-
	11.1%	6.8%	
Diabetes Mellitus	14	63	-
	31.1%	30.6%	
Chronic Kidney Disease	2	21	-
	4.4%	10.2%	
Prior Stroke	33	109	***
	73.3%	52.9%	
tPA Administrated	16	115	**
	4.4%	10.2%	
Ever Incubated	33	109	***
	73.3%	52.9%	

Cost Estimations

Table 1. One-time Installation Cost by Medical Imaging Information Technology

Detail	Quantity	Unit Cost	Total
Modality Config Costs	11	\$ 445.00	\$ 4,895.00
MIIT Prof. Service Hours	40	\$ 106.00	\$ 4,240.00
			\$ 9,135.00

Table 2. Monthly Cost Estimation by Medical Imaging Information Technology

Detail	Quantity	Monthly Cost	Monthly Total	Annual Total
Server	1	\$ 45.00	\$ 45.00	\$ 540.00
vCPU	8	\$ 5.00	\$ 40.00	\$ 480.00
RAM (GB)	16	\$ 2.00	\$ 32.00	\$ 384.00
Local Storage (GB)	540	\$ 0.16	\$ 86.40	\$ 1,036.80
			\$ 203.4	\$ 2,440.80

(3)

$$\mathbf{M_g} = [1 - P(Death|Age_t, Gender_t)] \times \begin{bmatrix} g_{1,1} & g_{1,2} & g_{1,3} & 0 & 0 & 0 & 0 \\ g_{2,1} & g_{2,2} & g_{2,3} & g_{2,4} & 0 & 0 & 0 \\ g_{3,1} & g_{3,2} & g_{3,3} & g_{3,4} & g_{3,5} & 0 & 0 \\ 0 & g_{4,2} & g_{4,3} & g_{4,4} & g_{4,5} & g_{4,6} & 0 \\ 0 & 0 & g_{5,3} & g_{5,4} & g_{5,5} & g_{5,6} & 0 \\ 0 & 0 & 0 & g_{6,4} & g_{6,5} & g_{6,6} & 0 \\ 0 & 0 & 0 & 0 & g_{7,5} & g_{7,6} & 1 \end{bmatrix} + P(Death|Age_t, Gender_t) \times \begin{bmatrix} 0 & \cdots & 0 \\ 0 & \cdots & 0 \\ 0 & \cdots & 0 \\ 0 & \cdots & 0 \\ 0 & \cdots & 0 \\ 0 & \cdots & 0 \\ 1 & \cdots & 1 \end{bmatrix} \tag{5}$$

$$\underset{\{\mathbf{M_g}\}}{argmin}[\mathbf{b_1} - \mathbf{M_g}\mathbf{b_0}][\mathbf{b_1} - \mathbf{M_g}\mathbf{b_0}]^{\mathbf{T}} \ s.t.\ (\mathbb{L} - \mathbb{I})\mathbf{M_g} \leq (\mathbb{L} - \mathbb{I})\mathbf{M_f} \tag{6}$$

Based on the matching results and calculation of excess death based on the actuarial life table used in the Social Security Administration's 2023 Trustees report, with the assumption that surviving patients are only improving or exacerbating by 0-2 units in mRS, we can set up the Generalized Reduced Gradient algorithm to satisfy a non-inferior assumption (comparing to rehospitalized cases) to fulfill the 5-year and 10-year mortality rates (Hankey *et al.*, 2000; Lakshminarayan *et al.*, 2014).

(4)

$$TVMI_{CEA}^{[10]} = \sum_{t=1}^{10} 0.95^i \cdot W(\mathbf{y_t^i}) \tag{7}$$

$$TVMI_{GRACE,t} = \frac{K\phi\mathbf{y_0}}{W(\mathbf{y_0}(1 - d_{t-1}^*))}\{\mu_{\mathbf{X}} E[W(\mathbf{y_t})]\} \tag{8}$$

$W(\cdot)$: Transformational function from a given mRS to quality-of-life (QoL)
$1 - d_t^*$: QoL loss based on disability—alternated by mRS in this case (Hong & Saver, 2009)
$\mathbf{y_0}$: The initial state of the stroke survivor—mRS on site in this case
K: Adjustment feature derived from the personalized income (Lakdawalla & Phelps, 2023)
ϕ: Occurrence rate of state changes, which echoes the transitional matrices above
$\mu_{\mathbf{X}}$: Adjustment toward risk attitude based on personal traits—age only in this case

According to the literature (Gyrd-Hansen, 2005; Cameron *et al.*, 2018), we can transform the CEA version of the Total Value of Medical Intervention ($TVMI_{CEA}$) with a mean of \$77,509 per perfect QoL with the 2018 CPI, discounted by 5% per year as a conservative measurement (Attema *et al.*, 2018). Therefore, we have a total cost of \$896,975.23 over the 10-year horizon, given the implementation costs as listed below, and an average net gain of \$15,842.02 per patient through CEA. Note that the immediate gain (Ordered Probit) is around \$10,690.90 through mRS distribution on site, showing that nearly one-third of gains from the structural estimation is omitted through reduced-form solutions.

Finally, I alternated part of Lakdawalla and Phelps's paper (2023) to transform CEA into GRACE. First, I add a layer of referring baseline to reward improvements from disability and penalize the opposite while setting "unchanged status" as a neutral reference. Next, I adopt odds ratio of willingness to accept/pay for QoL improvements in Hong and Saver's paper (2009) with 36 interstate measurements (*e.g.*, mRS 5 $\rightarrow$ 4 values 6.21 times to *status quo*). Finally, by adjusting age and disability level for risk preference (which affected $< 5\%$) and localized income, the average gains with different baselines are: unadjusted $\Rightarrow$ \$20,685.24/patient, $mRS = 1$ baseline $\Rightarrow$ \$19,700.23/patient, and $mRS = 2$ baseline $\Rightarrow$ \$16,281.18/patient.

Assuming the additional value from CEA to GRACE is based on externalities, I set up a validation process through caregiver's burden. I adapt calculations of absenteeism and presenteeism from a stroke-based research project (Ganapathy *et al.*, 2015), which shows a national average of \$835 per month before local adjustments based on Bureau of Labor Statistics data aside from the 62% at-home status of stroke survivors (Yu *et al.*, 2017). By aggregating all features, the total value of interventions based on CEA as \$18,391.08 per patient, with an upper bound of $mRS = 1$ baseline and lower bound $\in$ [1,2].

Conclusion

Our project demonstrates how GRACE could be applied to work on acute ischemic stroke through a repeated structure given the group distribution.

Our primary findings are:

(1) Reduced-form estimations could miss nearly $\frac{1}{3}$ of subsequent values
(2) GRACE could value up to 30.5% more than CEA in a conservative setting
(3) As GRACE internalizes externalities, the baseline is close to $mRS = 1$

Future topics to be discussed:

How do we integrate income, family, and labor to measure risk preferences accurately? How can we econometrically pick the optimum $\mathbf{M_g}$ instead of the likelihood of non-singleton solutions? Since Johns Hopkins Medicine takes sicker patients, how do we find a fairground to represent a larger population?