Value of Expanding First-Line Treatment Choices: New Metrics for Economics Evaluation

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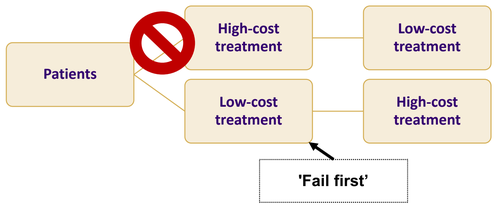
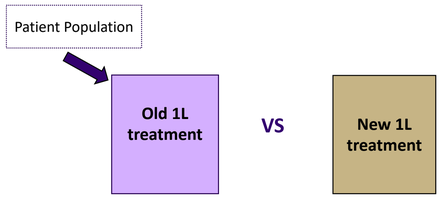
Background

- Clinical guidelines often recommend sequential lines of treatments
  - First-line (1L) treatment → 2L treatment →…
- Clinical trial of a novel therapy is conducted
  - In the late line initially
  - In the front line after years of experiences
- Healthcare payers frequently implement insurance policy to restrict the access to high-cost, novel 1L therapy
  - e.g., step therapy (‘fail-first policy”)

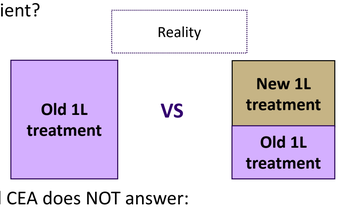


- To inform this policy, traditional cost-effectiveness analysis (CEA) can be conducted
  - Compute incremental cost-effectiveness ratio (ICER) of new vs. old 1L treatment based on clinical trial results
  - New 1L treatment is not cost-effective → Restricting its use

Traditional CEA Framework



- The assumption underlying traditional CEA:
  - Entire population taking new treatment vs. old treatment
  - New treatment would completely substitute old treatment once covered
- Traditional CEA answers:
  - Is **new 1L treatment** cost-effective vs. **old 1L treatment** for an average patient?



- Traditional CEA does NOT answer:
  - Is **expansion policy** cost-effective vs. **restriction policy**?

Proposed CEA Framework

- Comparison: **expanded choice set vs. restricted choice set** (i.e., expansion policy vs. restriction policy)
  - Expanded choice set: allowing the choices of new and old 1L treatments
  - Restricted choice set: only allowing the choice of old 1L treatment
- We consider **two scenarios**
  - Two treatment choices
  - More than two treatment choices
- We relax **two assumptions**
  - No treatment selection driven by treatment effect heterogeneity
  - No policy implementation cost

Two Treatment Choices

- ICER of **expanded choice set vs. restricted choice set**

$$\text{ICER} = \frac{\overbrace{P^A \cdot C^A + P^B \cdot C^B}^{\text{Average costs of expanded choice set}} - \overbrace{C^B}^{\text{Average costs of restricted choice set}}}{\underbrace{P^A \cdot Q^A + P^B \cdot Q^B}_{\text{Average QALYs of expanded choice set}} - \underbrace{Q^B}_{\text{Average QALYs of restricted choice set}}} = \frac{P^A \cdot \Delta C^{A,B}}{P^A \cdot \Delta Q^{A,B}}$$

  - New treatment: A; Old treatment: B
  - C^j: average cost of treatment j; Q^j: average QALYs of treatment j
  - P^j: probability of choosing treatment j
- Relax Assumption 1: **Selective treatment adoption**
  - CEA should consider heterogeneous treatment effect [1,2,3]
  - Evidence of heterogeneity → treatment selection

$$\text{ICER} = \frac{\sum_1^I G_i \cdot P_i^A \cdot \Delta C_i^{A,B}}{\sum_1^I G_i \cdot P_i^A \cdot \Delta Q_i^{A,B}}$$

  - G_i: size of subgroup i
  - Treatment choice variable P^j differs across subgroups
- Relax Assumption 2: **Policy implementation costs**
  - CEA should account for non-trivial policy implementation cost
  - Step therapy: considerable administrative burden (prior authorization)[4,5]

$$\text{ICER} = \frac{\sum_1^I G_i \cdot P_i^A \cdot \Delta C_i^{A,B} - \Delta C^\pi}{\sum_1^I G_i \cdot P_i^A \cdot \Delta Q_i^{A,B}}$$

  - ΔC^π: incremental policy implementation costs

More than Two Treatment Choices

- Patients often have choices in addition to A and B
  - No treatment is a typical example (e.g., patients who are unable to undergo 1L chemotherapy would take no treatment)

$$\text{ICER} = \frac{\sum_{i=1}^I \sum_{j=1}^J \sum_{k=J+1}^K G_i \cdot P_i^{k,j} \cdot \Delta C_i^{k,j} - \Delta C^\pi}{\sum_{i=1}^I \sum_{j=1}^J \sum_{k=J+1}^K G_i \cdot P_i^{k,j} \cdot \Delta Q_i^{k,j}}$$

  - $P_i^{k,j}$: probability of choosing a new treatment k over an old treatment j in subgroup i

Expected Value of Expanding Choices

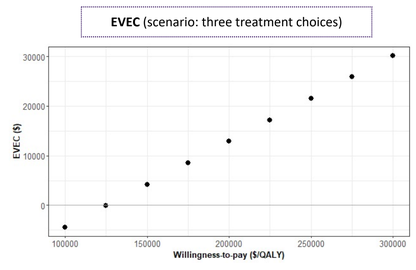
- We formulate a metric of Expected Value of Expanding Choices (EVEC)
  - Expressed in terms of net monetary benefit (NMB)
  - To quantify the value of expanding vs. restricting treatment choices

$$\text{EVEC} = \sum_{i=1}^I \sum_{j=1}^J \sum_{k=J+1}^K G_i \cdot P_i^{k,j} \cdot \Delta \text{NMB}_i^{k,j} - \Delta C^\pi$$

Case Study

- We illustrate the framework using the case of abiraterone acetate plus prednisone (AAP) as 1L treatment for metastatic hormone-sensitive prostate cancer from societal perspective
- Choice sets in comparison:
  - Expanded choice set: Allowing androgen deprivation therapy (ADT)+AAP
  - Restricted choice set: Not allowing ADT+AAP
- Two Scenarios:
  - Two treatment choices: ADT+AAP and ADT alone
  - Three treatment choices: ADT+AAP, ADT alone, and ADT+docetaxel
- Relax Two assumptions
  - Treatment heterogeneity and selection between ≥70 and <70 years old men
  - Time costs associated with prior authorization under a hypothetical restriction policy
- Results

	ICER ($/QALY gained)
Two Treatment Choices	
Traditional CEA: ADT+AAP vs. ADT alone	102,793
Proposed CEA: Expanded Choice Set vs. Restricted Choice Set Relax Assumption 1	87,262
Proposed CEA: Expanded Choice Set vs. Restricted Choice Set Relax Assumption 2	86,663
Three Treatment Choices	
Traditional CEA: ADT+AAP vs. ADT alone	102,793
Traditional CEA: ADT+AAP vs. ADT+docetaxel	210,223
Proposed CEA: Expanded Choice Set vs. Restricted Choice Set Relax Assumption 1	126,758
Proposed CEA: Expanded Choice Set vs. Restricted Choice Set Relax Assumption 2	125,754



Conclusions

- We propose a new framework to evaluate the cost-effectiveness of expanding versus restricting 1L treatment choices and quantify the realized value of expansion policy
- Our framework explicitly accounts for treatment selection due to heterogenous treatment effect and administrative burden of restriction policy
- The empirical case shows that the proposed CEA framework would generate substantially different results compared to traditional CEA

References

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