Real World Cost-Effectiveness of Cancer Drugs:
Comparative effectiveness research using retrospective Canadian registry data before and after drug approval

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- Dr. Carol Sawka
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Outline

Overview & Objectives

Rituximab Study
  • Cohort Selection
  • Survival
  • Costs
  • Cost-effectiveness

Conclusion
The need of evidence-based data in CER

Healthcare payers, providers, pharmaceutical manufacturers rely on the use of evidence-based data to evaluate the effectiveness and "value for money" of innovative therapies relative to current standard-of-care practices.
Evidence to evaluate clinical outcomes

- Randomized controlled trials is the golden standard:
  - Challenging to conduct
    - Costly, require a lot resources, restricted to short time frames
  - Might not reflect the real-world
    - Selected group of patients, specific procedures, ethical issues
  - Might not reflect how the drug is used in practice
  - Toxicities/side effects may not be determined
Why real-world cost-effectiveness analysis?

- Accurate information about how a drug is actually used or how much it actually costs is only available after a drug is funded.

- Allows us to evaluate real benefits or harms and value for money of new agents, especially expensive ones.
Our study

- First study in Ontario that evaluates population-based post-market effectiveness and cost-effectiveness of very expensive cancer drugs

- First study in Canada incorporating recently developed statistical methods for analyzing incomplete costs and cost-effectiveness of cancer treatments
Overall Objectives

- To determine whether it is feasible to conduct post-market evaluation of cancer drugs using Ontario’s administrative databases.

- To compare survival benefits and costs from the real-world to what is being reported in RCTs and economic models.
Real-world outcomes

Population-based retrospective analysis of cancer drugs

Patterns of Care:
Who used these drugs and how?

Clinical Outcomes:
Did the drugs improve survival?
Were they safe?

Direct Costs:
How much did Ontario spend?

Cost-effectiveness:
What was the real added value for each extra dollar spent?
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Conclusion
Diffuse-large-B-cell lymphoma

- 3000 new cases of non-Hodgkin lymphoma in Ontario in 2010
- 1300 deaths attributed to the disease
- Diffuse-large-B-cell lymphoma is the most common form, represents approx. 25% of new cases

- Standard treatment: CHOP*
- New treatment: Rituximab + CHOP (RCHOP)

* cyclophosphamide, doxorubicin, vincristine and prednisone
In Ontario

- Rituximab approved for funding via the New Drug Funding Program in Ontario:
  - Jan 10th, 2001 – 60-80 years old
  - April 2nd, 2001 – ≥80 years old
  - July 1st, 2004 – <60 years old

- Based on efficacy results from out-of-province trials and theoretical economic models
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Historical cohort selection

Pre-era CHOP

Jan, 1997

<60

≥80

60-80

Jan, 2001

April, 2001

July, 2004

Dec 31, 2007

Mar 31, 2009

Post-era RCHOP
### Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Pre-era CHOP</th>
<th>Post-era RCHOP</th>
<th>Std. diff</th>
<th>P value</th>
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<tr>
<td></td>
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#### Before matching

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*ACG – adjusted clinical group scores

- **Hard-matched on age group**
- **Propensity score-matched on:**
  - Sex
  - Adjusted clinical group (ACG) score
  - Income quintile
  - Treatment intensity
  - Primary histology diagnosis code
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Kaplan-Meier Survival Curves

Survival Curves after matching

- Pre-era CHOP
- Post-era RCHOP

3-year: 10%↑
5-year: 8%↑

p<0.001
Outline

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Conclusion
Cost analysis

- Perspective: Payer – Ministry of Health

- Adjusted for incomplete cost data (due to not enough follow-up time) by using Bang and Tsiatis’ estimator (2000)

- Fixed time-frames: 3-year and 5-year

- Discounted by 3%
5-year costs

- **CHOP**
  - Unadjusted: $71,639
  - Adjusted: $71,640

- **RCHOP**
  - Unadjusted: $79,668
  - Adjusted: $88,536

The graph shows the total healthcare cost for 5 years, comparing CHOP and RCHOP treatments. The adjusted costs are slightly higher than the unadjusted costs.
Cost drivers

All ages cost (censor adjusted and discounted)
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Conclusion
### Incremental Cost-effectiveness Ratios

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<tr>
<th>Year</th>
<th>Incremental cost (CAD$)</th>
<th>Incremental survival (Years)</th>
<th>ICER ($/LYG)</th>
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<td>15,032</td>
<td>0.16</td>
<td>96,764</td>
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<td>5 year</td>
<td>16,785</td>
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3% discounted
Cost-effectiveness acceptability curve

Bootstrap ICERs vs WTP

Percentage

Willingness-to-pay ($/LYG)

0 50000 100000 150000 200000 250000

0 20 40 60 80 100

23% 92% 99.7% 91%
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Conclusion
How do we compare?

2-year Absolute Survival Benefit

- **Our study**: 8
- **Europe GELA Trial**: 13
- **BC observational study**: 26
How do we compare?

- **Our study**: 16,785
- **US model**: 12,740
- **BC microsimulation (High)**: 9,700
- **BC microsimulation (Low)**: 7,900

5-yr Incremental Cost

Cost ($)

0 5000 10000 15000 20000
Key methodological findings

- Using appropriate methods to adjust for confounding variables is important
- Adjusting for incomplete cost data is essential
- Selection of timeframe has a big effect on cost-effectiveness results
Overall Conclusions

- It is feasible to perform real-world cost-effectiveness analysis with Ontario’s administrative data.

- Cost-effectiveness results in a real-world analysis differ from those from clinical trials and economic models.

- Healthcare payers, providers and pharmaceutical manufacturers should be cautious about conclusions from results of trials/models.
Thank you

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http://www.cc-arcc.ca