15.482 Healthcare Finance
Spring 2017

Andrew W. Lo, MIT

Unit 9, Part 4: Bayesian Decision Analysis for Randomized Clinical Trials

Unit Outline

- Risk and Return in the Biopharma Industries, 1930-2015
- Estimating Clinical Success Rates
- Predicting Phase Transitions and Approvals
- Patient-Centered Clinical Trials

Patient-Centered Randomized Clinical Trials in Oncology via Bayesian Decision Analysis

Vahid Montazerhodjat, Shomesh E. Chaudhuri,
Daniel J. Sargent, Andrew W. Lo

Statistical Inference Involves Trade-offs

	Approve	**Reject**
Effective Therapy	✓	Type II error
Ineffective Therapy	Type I error	✓

- Standard approach sets Type I error = 5%; why?
- What if patients prefer higher Type I error in exchange for smaller Type II error?

Statistical Inference Involves Trade-offs

	Approve	Reject
Effective Therapy	✓	Type II error
Ineffective Therapy	Type I error	✓

- Standar
- What if
  exchang

Research

JAMA Oncology | Original Investigation

Use of Bayesian Decision Analysis to Minimize Harm in Patient-Centered Randomized Clinical Trials in Oncology

Vahid Montazerhodjat, PhD; Shomesh E. Chaudhuri, MS; Daniel J. Sargent, PhD; Andrew W. Lo, PhD

Statistical Inference Involves Trade-offs

Guidance for Industry & FDA Staff (2012)

"FDA recognizes that patient tolerance for risk and a patient-centric assessment of risk may reveal reasonable patients who are willing to tolerate a very high level of risk to achieve a probable benefit, especially if that benefit results in an improvement in quality of life."

21st Century Cures, Sec. 3002. "Patient-Focused Drug Development Guidance."

"How the FDA plans to use relevant patient experience data and related information when evaluating the risks and benefits of a drug.

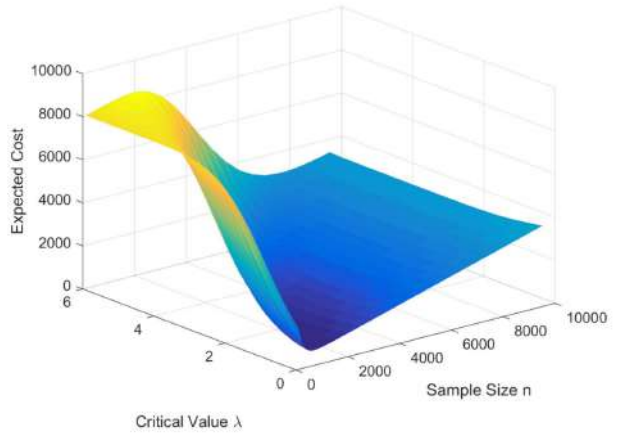
Bayesian Decision Analysis

$$\underset{p,n}{\text{Min}}\ \text{E}[\text{Cost}] \;=\; \underset{p,n}{\text{Min}}\Big(\text{E}[\text{Cost}|\text{H}_0]p_0 \;+\; \text{E}[\text{Cost}|\text{H}_1](1-p_0)\Big)$$

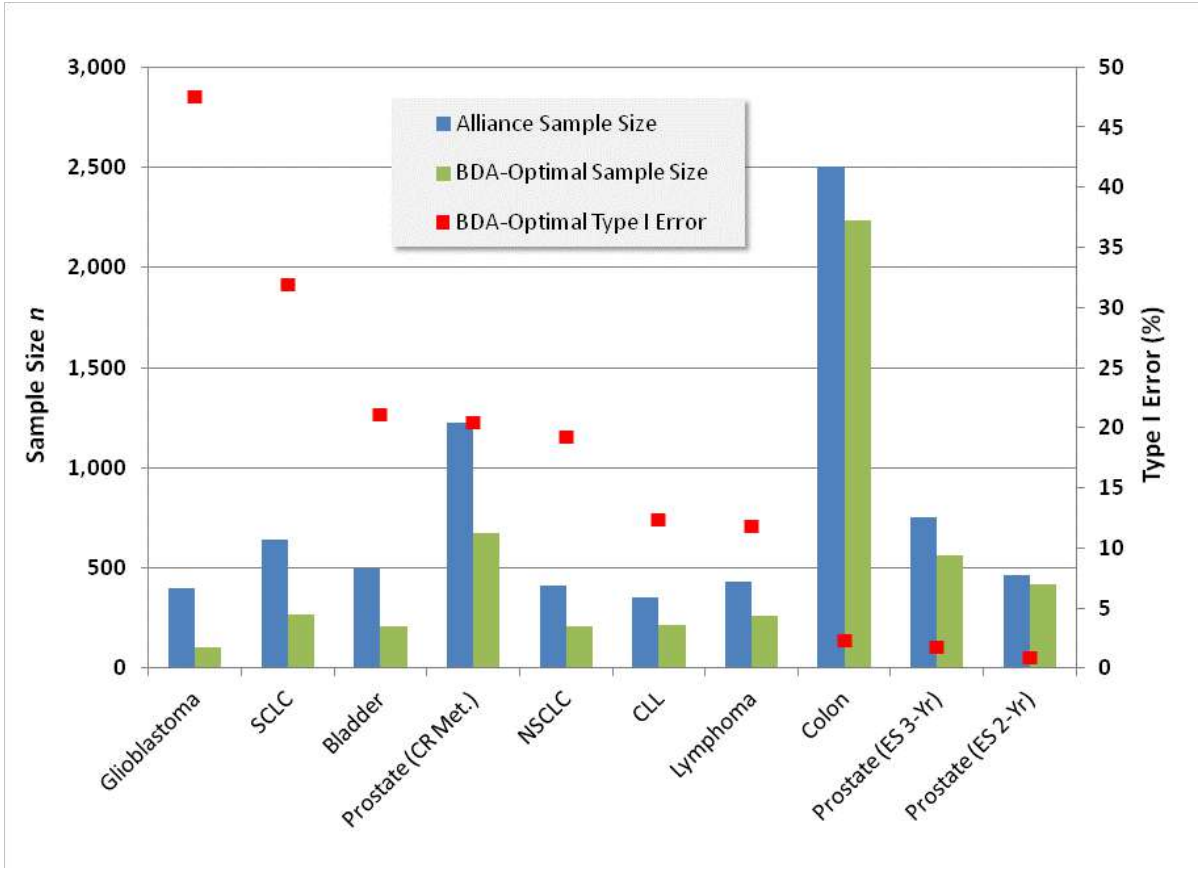
$$\text{E}[\text{Cost}] \;=\; c_1 p_o\Big[N\Phi(-\lambda_n) \;+\; N\xi\Phi\Big(\lambda_n - \delta_o\sqrt{\mathcal{I}_n}\Big) \;+\; n(1+\gamma N\xi)\Big]$$

$$\xi \equiv \frac{c_2}{c_1}\frac{1-p_0}{p_0}$$

- BDA-optimal decision **minimizes** expected cost



Bayesian Decision Analysis



Bayesian Decision Analysis

No.	Cancer site	Primary endpoint	Control group outcome	Stage prevalence	Sample size	One-sided α (%)	Power (%)	BDA sample size	BDA one-sided α (%)	BDA power (%)
1	**Glioblastoma**	**OS**	**Median 21 months**	**25,299**	**400**	**5.0**	**90**	**104**	**47.5**	**90**
4	Prostate (CR Met.)	OS	Median 35 months	111,824	1,224	2.5	90	676	20.4	90
5	NSCLC	OS	Median 5 years	64,769	410	2.5	85	210	19.2	90
7	Lymphoma	EFS	Median 42 months	164,888	430	2.5	90	264	11.8	90
8	Colon	DFS	3-year DFS rate of 72%	319,118	2,500	2.5	91	2,232	2.3	90
9	**Prostate (ES 3-Yr)**	**PFS**	**3-year PFS rate of 57.7%**	**2,236,474**	**750**	**2.5**	**89**	**560**	**1.8**	**90**

Qualifications

- Not fully Bayesian (“feature” or “bug”??)
- How to choose parameters?
- Whose preferences should be reflected?
- Potential backlash from toxicities and side effects?
- Ethical considerations

But these issues already exist for current methods; BDA provides a more systematic framework for addressing them

Conclusion

- Technology is transforming many fields and industries
- Cheap storage, big data, and machine learning have created new approaches to decision making
- Machine-learning techniques show promising levels of predictive power, able to discriminate between high- and low-potential therapeutic candidates
- Possibility of more powerful prediction models with better quality data and more scientific judgment
- Implications for translational medicine, biopharma investments, and regulatory science